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Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 03-06 May 2021

Chair: Sabine Straus – Vice-Chair: Martin Huber

03 May 2021, 10:30 – 19:30, via teleconference

04 May 2021, 08:30 – 19:30, via teleconference

05 May 2021, 08:30 – 19:30, via teleconference

06 May 2021, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

20 May 2021, 09:00 – 12:00, 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.

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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 ongoing 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 03-06 May 2021. See May 2021 PRAC minutes (to be published post June 2021 PRAC meeting).

1.2. Agenda of the meeting on 03-06 May 2021

Action: For adoption

1.3. Minutes of the previous meeting on 06-09 April 2021

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures¹

None

3.5. Others

None

4. Signals assessment and prioritisation²

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Ipilimumab – YERVOY (CAP)

Applicant(s): Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Signal of transverse myelitis

Action: For adoption of PRAC recommendation

EPITT 19677 – New signal

Lead Member State(s): NL

4.1.2. Ponatinib – ICLUSIG (CAP)

Applicant(s): Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Annika Folin

Scope: Signal of panniculitis

Action: For adoption of PRAC recommendation

EPITT 19681 – New signal

Lead Member State(s): SE

4.2. New signals detected from other sources

None

¹ Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC

² Each signal refers to a substance or therapeutic class. The route of marketing authorisation is indicated in brackets (CAP for Centrally Authorised Products; NAP for Nationally Authorised Products including products authorised via Mutual Recognition Procedures and Decentralised Procedure). Product names are listed for reference Centrally Authorised Products (CAP) only. PRAC recommendations will specify the products concerned in case of any regulatory action required

4.3. Signals follow-up and prioritisation

4.3.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/SDA/011

Applicant(s): Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of sarcoidosis

Action: For adoption of PRAC recommendation

EPITT 19638 – Follow-up to January 2021

4.3.2. Clindamycin (NAP)

Applicant(s): various

PRAC Rapporteur: Sonja Hrabcik

Scope: Signal of acute renal failure

Action: For adoption of PRAC recommendation

EPITT 19647 – Follow-up to January 2021

4.3.3. Coronavirus (COVID-19) mRNA³ vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/SDA/023

Applicant(s): BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of localised swelling in persons with history of dermal filler injections

Action: For adoption of PRAC recommendation

EPITT 19674 – Follow-up to March 2021

4.3.4. Coronavirus (COVID-19) mRNA⁴ vaccine (nucleoside-modified) - COVID-19 VACCINE MODERNA (CAP) - EMEA/H/C/005791/SDA/026

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

PRAC Rapporteur: Hans Christian Siersted

Scope: Signal of immune thrombocytopenia

Action: For adoption of PRAC recommendation

EPITT 19679 – Follow-up to March 2021

³ Messenger ribonucleic acid

⁴ Messenger ribonucleic acid

4.3.5. Coronavirus (COVID-19) vaccine (Ad26.COV2-S [recombinant]) - COVID-19 vaccine JANSSEN (CAP) - EMEA/H/C/005737/SDA/018.1

Applicant(s): Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of embolic and thrombotic events

Action: For adoption of PRAC recommendation

EPITT 19689 – Follow-up to April 2021

4.3.6. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/SDA/034

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Signal of immune thrombocytopenia

Action: For adoption of PRAC recommendation

EPITT 19678 - Follow-up to March 2021

4.3.7. Eliglustat - CERDELGA (CAP) - EMEA/H/C/003724/SDA/016

Applicant(s): Genzyme Europe BV

PRAC Rapporteur: Eva Segovia

Scope: Signal of erectile dysfunction

Action: For adoption of PRAC recommendation

EPITT 19644 – Follow-up to January 2021

4.3.8. Immune checkpoint inhibitors: atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/SDA/021; avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/SDA/007; cemiplimab - LIBTAYO (CAP) - EMEA/H/C/004844/SDA/007; durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/SDA/007; ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/SDA/041; pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/SDA/029; nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/SDA/042

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

PRAC Rapporteur: Menno van der Elst

Scope: Signal of immune-mediated cystitis

Action: For adoption of PRAC recommendation

EPITT 19610 – Follow-up to November 2020

4.3.9. Labetalol (NAP)

Applicant(s): various

PRAC Rapporteur: Karen Pernille Harg

Scope: Signal of nipple pain and suppressed lactation

Action: For adoption of PRAC recommendation

EPITT 19639 – Follow-up to January 2021

4.3.10. Methotrexate - JYLAMVO (CAP) - EMEA/H/C/003756/SDA/003, NORDIMET (CAP) - EMEA/H/C/003983/SDA/004; NAP

Applicant(s): Nordic Group B.V. (Nordimet), Therakind (Europe) Limited (Jylamvo); various

PRAC Rapporteur: Martin Huber

Scope: Signal of progressive multifocal leukoencephalopathy (PML)

EPITT 18473 – Follow-up to December 2020

4.3.11. Romosozumab - EVENITY (CAP) - EMEA/H/C/004465/SDA/006

Applicant(s): UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Signal of cardiac arrhythmia

Action: For adoption of PRAC recommendation

EPITT 19629 – Follow-up to January 2021

4.3.12. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/SDA/011

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Signal of Henoch-Schonlein purpura

Action: For adoption of PRAC recommendation

EPITT 19640 – Follow-up to January 2021

4.3.13. Sulfamethoxazole, trimethoprim (co-trimoxazole) (NAP)

Applicant(s): various

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Signal of acute respiratory distress syndrome

Action: For adoption of PRAC recommendation

EPITT 19625 – Follow-up to January 2021

4.3.14. Sulfametoazole, trimethoprim (co-trimoxazole) (NAP)

Applicant(s): various

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Signal of haemophagocytic lymphohistiocytosis (HLH)

Action: For adoption of PRAC recommendation

EPITT 19655 – Follow-up to January 2021

4.3.15. Tramadol (NAP); tramadol, dexketoprofen (NAP); tramadol, paracetamol (NAP)

Applicant(s): various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Signal of serotonin syndrome

Action: For adoption of PRAC recommendation

EPITT 19635 – Follow-up to January 2021

4.3.16. Warfarin (NAP)

Applicant(s): various

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of anticoagulant-related nephropathy

Action: For adoption of PRAC recommendation

EPITT 19652 – Follow-up to January 2021

4.4. Variation procedure(s) resulting from signal evaluation

4.4.1. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/II/0014

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.3, 4.4 and 4.8 of the SmPC, following an update to the company core data sheet (CCDS) in relation to thromboembolism with thrombocytopenia in order to contraindicate the vaccine to patients who have experienced major venous and/or arterial thrombosis in combination with thrombocytopenia following vaccination with any COVID-19 vaccine, update the warnings on thrombocytopenia and coagulation disorders and include the frequency thrombosis with thrombocytopenia of 'less than 1/100,000'. The package leaflet is updated accordingly. The variation is linked to the signal procedure (EPITT 19683) finalised in April 2021

Action: For adoption of PRAC Assessment Report

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. [Avalglucosidase alfa - EMEA/H/C/005501, Orphan](#)

Applicant: Genzyme Europe BV

Scope: Long-term enzyme replacement therapy for the treatment of patients with Pompe disease

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

5.1.2. [Bamlanivimab - EMEA/H/C/005836](#)

Scope: Treatment of coronavirus (COVID-19)

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

5.1.3. [Bevacizumab - EMEA/H/C/005433](#)

Scope: Treatment in adults of neovascular macular degeneration associated with aging and diabetes

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

5.1.4. [Coronavirus \(COVID-19\) mRNA⁵ vaccine - EMEA/H/C/005845](#)

Scope: Active immunisation for prevention of coronavirus disease-2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in adults ≥ 18 years old

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

5.1.5. [Etesevimab - EMEA/H/C/005837](#)

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

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

5.1.6. [Icatibant - EMEA/H/C/005083](#)

Scope: Treatment of hereditary angioedema

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

5.1.7. [Ranibizumab - EMEA/H/C/005545](#)

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

⁵ Messenger ribonucleic acid

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

5.1.8. Sitagliptin - EMEA/H/C/005598

Scope: Treatment of type 2 diabetes mellitus (T2DM)

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

5.1.9. Sugammadex - EMEA/H/C/005403

Scope: Treatment of neuromuscular blockade induced by rocuronium or vecuronium

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

5.1.10. Tafasitamab –/H/C/005436, Orphan

Applicant: Incyte Biosciences Distribution B.V.

Scope: Treatment in combination with lenalidomide of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), including DLBCL arising from I low grade lymphoma, who are not eligible for, or refuse, autologous stem cell transplant (ASCT)

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. Alectinib - ALECENSA (CAP) - EMEA/H/C/004164/II/0033

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Submission of an updated RMP (version 3.1) in order to remove the safety concern of 'long term safety' as missing information based on a report of the cumulative safety data from pivotal study BO28984 (ALEX): a randomized, multicentre, phase 3, open-label study of alectinib versus crizotinib in treatment-naive anaplastic lymphoma kinase-positive advanced non-small cell lung cancer (NSCLC). In addition, the MAH took the opportunity to update the RMP to remove from the pharmacovigilance plan study BO40643: a survey measuring the effectiveness of the risk minimisation activities to prescribers: correct implementation of Alecensa (alectinib) label guidance by prescribers of the following important identified risks: interstitial lung disease (ILD)/pneumonitis, hepatotoxicity, photosensitivity, bradycardia, severe myalgia and creatine phosphokinase (CPK) elevations, following the conclusions of variation II/0030 concluded in February 2021

Action: For adoption of PRAC Assessment Report

5.2.2. Bazedoxifene - CONBRIZA (CAP) - EMEA/H/C/000913/II/0054

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 4.4) to include several updated study milestones and to bring it in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

5.2.3. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/II/0092

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 40) in order to add study 213928 (as a category 3 study in the RMP): a prospective cohort study based on the existing infrastructure of Teratology Information Services (TIS) within the US and Canada to evaluate pregnancy and infant outcomes for pregnancies in women with systemic lupus erythematosus (SLE) exposed to belimumab, as an alternative pregnancy exposure study for the missing information on limited data in pregnant and lactating patients. The RMP includes also the completion date and effectiveness for the distribution of the direct healthcare professional communication (DHPC) in relation to the important identified risk of psychiatric events including depression and suicidality

Action: For adoption of PRAC Assessment Report

5.2.4. Bevacizumab - AYBINTIO (CAP) - EMEA/H/C/005106/WS2040/0004/G; ONBEVZI (CAP) - EMEA/H/C/005640/WS2040/0001/G

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Grouped variations consisting of: 1) submission of updated RMP (version 4.0 for Aybintio, version 2.0 for Onbevzi) to remove the missing information of 'long term effects of bevacizumab when used in the paediatric population' in order to align the safety concerns to those of the medicinal product of reference; 2) update of sections 4.4, 5.1 and 6.6 of the SmPC following assessment of the same changes for the medicinal product of reference (variation IB/0118 finalised in January 2021). In addition, the MAH took the opportunity to introduce minor changes in the SmPC and to align the product information for Onbevzi (bevacizumab) with the latest quality review of documents (QRD) template (version 10.2)

Action: For adoption of PRAC Assessment Report

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

Applicant: Merck Europe B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Submission of an updated RMP (version 1.5) in order to bring it in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template). In addition, the MAH took the opportunity to include long-term safety data from the completed PREMIERE registry: a prospective observational long-term safety registry of multiple sclerosis patients who have participated in cladribine clinical studies; and to remove it from the pharmacovigilance plan. Furthermore, the status of the post-approval safety study MS 700568-0002: a long term,

prospective, observational cohort study evaluating the safety profile in patients with highly active relapsing multiple sclerosis (RMS) newly started on oral cladribine (CLARION); and study MS 700568-0004: pregnancy outcomes in women exposed to oral cladribine: a multi-country cohort database study (CLEAR). Finally, the RMP is updated in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010634/201907) adopted in January 2020

Action: For adoption of PRAC Assessment Report

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

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

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

Action: For adoption of PRAC Assessment Report

5.2.7. [Epoetin alfa - ABSEAMED \(CAP\) - EMEA/H/C/000727/WS2013/0092; BINOCRIT \(CAP\) - EMEA/H/C/000725/WS2013/0091; EPOETIN ALFA HEXAL \(CAP\) - EMEA/H/C/000726/WS2013/0091](#)

Applicant: Sandoz GmbH

PRAC Rapporteur: Tiphaine Vaillant

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

Action: For adoption of PRAC Assessment Report

5.2.8. [Lopinavir, ritonavir - LOPINAVIR/RITONAVIR MYLAN \(CAP\) - EMEA/H/C/004025/II/0016](#)

Applicant: Mylan S.A.S

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of an updated RMP (version 4.0) in order to bring the RMP in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template) and revision 2 of

GVP module V on 'Risk management systems' and to align the safety concerns with those of the reference medicinal product

Action: For adoption of PRAC Assessment Report

5.2.9. [Obeticholic acid - OCALIVA \(CAP\) - EMEA/H/C/004093/II/0026, Orphan](#)

Applicant: Intercept Pharma International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of an updated RMP (version 1.2) in order to bring it in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template) and to add clinical studies (listed as specific obligations in Annex II-E on 'Specific obligation to complete post-authorisation measures for the conditional marketing authorisation') to the pharmacovigilance plan, namely study 747-302: a phase 4, double-blind, randomized, placebo-controlled, multicentre study evaluating the effect of obeticholic acid on clinical outcomes in patients with primary biliary cholangitis; and study 747-401: a phase 4, double-blind, randomized, placebo-controlled study evaluating the pharmacokinetics and safety of obeticholic acid in patients with primary biliary cholangitis and moderate to severe hepatic impairment; as agreed in the conclusions of the conditional renewal procedure (R/0023) finalised in November 2020. Other changes also include an update to the exposure data from clinical studies, addition of data on post-marketing experience and addition of some specific relevant SmPC wording in the risk minimisation measures

Action: For adoption of PRAC Assessment Report

5.2.10. [Rotavirus vaccine \(live, oral\) - ROTATEQ \(CAP\) - EMEA/H/C/000669/II/0085](#)

Applicant: MSD Vaccins

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 7.2) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems'. As a consequence, the list of safety concerns is updated and a reclassification of important risks is proposed. In addition, the updated RMP includes the removal of hypersensitivity and severe combined immunodeficiency (SCID) from the list of safety concerns as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002666/201911) adopted in June 2020

Action: For adoption of PRAC Assessment Report

5.2.11. [Sildenafil - REVATIO \(CAP\) - EMEA/H/C/000638/II/0091](#)

Applicant: Upjohn EESV

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 7.0) in line with revision 2 of GVP module V on 'Risk management systems'. Consequently, the educational programme for the risk of hypotension is proposed to be terminated

Action: For adoption of PRAC Assessment Report

5.2.12. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0038

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of an updated RMP (version 17.1) in order to incorporate study A3921348: a US-based drug utilisation study (DUS) using either electronic health records (HER) or administrative claims database into study A3921347: a prospective non-interventional active surveillance study in the US to quantify the incidence of key safety events of interest in moderate-to-severe UC patients treated with tofacitinib and other systemic therapies in the clinical practice (real world) setting (both listed as category 3 studies in the RMP)

Action: For adoption of PRAC Assessment Report

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

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Submission of an updated RMP (version 15.0) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' and aligned with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00003113/201802) adopted in October 2018. In addition, Annex II-D on 'conditions or restrictions with regard to the safe and effective use of the medicinal product' of the product information is updated to remove the statement on submission of an RMP update every 3 years

Action: For adoption of PRAC Assessment Report

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

5.3.1. Ambrisentan - VOLIBRIS (CAP) - EMEA/H/C/000839/X/0061/G

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Eva Segovia

Scope: Grouped applications consisting of: 1) extension application to introduce a new strength (2.5 mg film-coated tablet); 2) extension of indication to include paediatric use (8 to less than 18 years). The RMP (version 9.0) is updated accordingly.

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

5.3.2. Atazanavir, cobicistat - EVOTAZ (CAP) - EMEA/H/C/003904/II/0038

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Adrien Inoubli

Scope: Extension of indication to include the use of Evotaz (atazanavir/cobicistat) in combination with other antiretroviral agents in the treatment of human immunodeficiency virus 1 (HIV-1) infection in adolescent patients aged ≥ 12 to < 18 years, weighing ≥ 35 kg without known mutations associated with resistance to atazanavir. 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 make minor editorial corrections

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

5.3.3. [Blinatumomab - BLINCYTO \(CAP\) - EMEA/H/C/003731/II/0038, Orphan](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include the use of blinatumomab as monotherapy for the treatment of paediatric patients aged 1 year or older with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-precursor acute lymphoblastic leukaemia (ALL) as consolidation therapy. 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 13.0) are updated in accordance

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

5.3.4. [Burosumab - CRYSVITA \(CAP\) - EMEA/H/C/004275/II/0021, Orphan](#)

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.2 of the SmPC in order to modify administration instructions to include the option of self/carer-administration based on results from two interventional clinical safety and efficacy studies, namely: 1) study KRN23-003: a phase 3 open-label trial to assess the efficacy and safety of burosumab (KRN23) in paediatric patients with X-linked hypophosphataemic rickets/osteomalacia (final study report); 2) study KRN23-004: a phase 3 long-term extension study of burosumab in adult patients with X-linked hypophosphataemic rickets/osteomalacia and a post-marketing study of burosumab switched from the phase 3 long-term extension study (interim report). The package leaflet is updated accordingly and includes a new section with instructions for use. In addition, the MAH took the opportunity to implement editorial changes throughout the product information. The RMP (version 3.0) is also updated in accordance

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

5.3.5. [Dapagliflozin - EDISTRIDE \(CAP\) - EMEA/H/C/004161/WS1941/0043; FORXIGA \(CAP\) - EMEA/H/C/002322/WS1941/0062](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to include treatment of chronic kidney disease. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC for Forxiga and Edistride (dapagliflozin) are updated based on the results from the renal outcomes study D169AC00001 (DAPA-CKD) (listed as a category 3 study in the RMP): a multicentre, event-driven, randomized, double-blind, parallel group, placebo-controlled study evaluating the effect of dapagliflozin versus placebo given once daily in addition to standard of care to evaluate the potential risk of lower limb amputation to prevent the progression of chronic kidney disease (CKD) or cardiovascular (CV)/renal death. Annex II-B on 'Conditions or restrictions regarding supply and use' and the package leaflet are updated accordingly. The RMP (version 22.1) is also updated in accordance

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

5.3.6. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0043, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include treatment of adult patients with systemic light chain (AL) amyloidosis. 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 8.2) are updated in accordance

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

5.3.7. Daunorubicin, cytarabine - VYXEOS LIPOSOMAL (CAP) - EMEA/H/C/004282/II/0018/G, Orphan

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Grouped variations consisting of: 1) extension of indication to add treatment of relapsed/refractory Acute myeloid leukaemia (AML) in paediatric patients. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated based on the new safety and efficacy data from the paediatric clinical study AAML1421: a phase 1/2 study of liposomal daunorubicin/cytarabine alone followed by fludarabine, cytarabine, and granulocyte colony-stimulating factor (G-CSF) (FLAG) for children with relapsed AML. The package leaflet and the RMP (version 1.1) are updated accordingly. In addition, the product information is updated in line with the latest quality review of documents (QRD) template (version 10.2); 2) submission of the final data from paediatric clinical study CPX-MA-1201: a phase 1/pilot study of liposomal daunorubicin/cytarabine for children, adolescents and young adults with recurrent or refractory hematologic malignancies, in support of the extension of indication

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

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

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Laurence de Fays

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

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

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

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

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

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

5.3.10. Erenumab - AIMOVIG (CAP) - EMEA/H/C/004447/II/0013/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped variations consisting of: 1) update of section 4.8 of the SmPC to add alopecia, oral sores and rash in line with revised clinical safety data; 2) update of sections 4.8 and 5.1 of the SmPC based on the study report from 5-year open-label study 20120178: a phase 2, multicentre, randomized, double-blind, placebo-controlled, parallel-group study of subjects with episodic migraine; 3) update of section 5.1 of the SmPC to include of the anatomical therapeutic chemical (ATC) classification system code for erenumab. The package leaflet and the RMP (version 3.0) are updated accordingly

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

5.3.11. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/II/0001

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to include the treatment of active ulcerative colitis in adult patients. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. In addition, the package leaflet and the RMP (version 1.1) are updated accordingly. In addition, the MAH took the opportunity to include minor updates to Annex II

and to implement minor editorial changes throughout the product information

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

5.3.12. [Human papillomavirus vaccine \[types 16, 18\] \(recombinant, adjuvanted, adsorbed\) - CERVARIX \(CAP\) - EMEA/H/C/000721/II/0110](#)

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Extension of indication to include the prevention of head and neck cancers causally related to certain oncogenic human papillomavirus types. As a consequence, sections 4.1 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 23.0) are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.13. [Lorlatinib - LORVIQUA \(CAP\) - EMEA/H/C/004646/II/0015](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to include the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously not treated with an ALK inhibitor based on results from study 1006 (CROWN) (listed as a specific obligation (SOB) in the Annex II): a phase 3 randomised open-label study of lorlatinib monotherapy versus crizotinib monotherapy in the first-line treatment of patients with advanced ALK-positive NSCLC. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 3.0) are updated accordingly. In addition, the applicant proposes to downgrade the specific obligation to conduct a single arm study in patients who progressed after alectinib or ceritinib to a recommendation and convert the conditional marketing authorisation to a full marketing authorisation (MA)

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

5.3.14. [Meningococcal group B vaccine \(recombinant, adsorbed\) - TRUMENBA \(CAP\) - EMEA/H/C/004051/II/0032](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.8 and 5.1 of the SmPC based on the interim data from the primary vaccination phase (stage 1) of study B1971057: a phase 3, randomised, active-controlled, observer-blinded study to assess the immunogenicity, safety and tolerability of Trumenba (meningococcal group B vaccine) when administered as a 2-dose regimen and a first-in-human study to describe the immunogenicity, safety and tolerability of a bivalent rLP2086 containing pentavalent vaccine (MenABCWY) in healthy subjects ≥ 10 to < 26 years of age. The RMP (version 5.0) is updated accordingly. The MAH took the opportunity to implement some editorial changes in section 4.4 of the SmPC and in the package leaflet to

introduce information on sodium content in line with the Annex to the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'

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

5.3.15. Nilotinib - TASIGNA (CAP) - EMEA/H/C/000798/II/0109

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of SmPC sections 4.4, 4.8 and 5.1 based on the 5-year follow up data from study CAMN107A2203: a multicentre, open label, non-controlled phase 2 study to evaluate efficacy and safety of oral nilotinib in paediatric patients with newly diagnosed Philadelphia chromosome positive (Ph+) chronic myelogenous leukaemia (CML) in chronic phase (CP) or with Ph+ CML in CP or accelerated phase (AP) resistant or intolerant to either imatinib or dasatinib. Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated to reflect the fulfilment of the obligation to conduct the post authorisation efficacy study (PAES). The package leaflet and the RMP (version 24.0) are updated accordingly

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

5.3.16. Padeliporfin - TOOKAD (CAP) - EMEA/H/C/004182/II/0013

Applicant: Steba Biotech S.A

PRAC Rapporteur: Maia Uusküla

Scope: Extension of indication to modify the wording of the existing indication to treatment of adult patients with previously untreated, unilateral, low-risk, adenocarcinoma of the prostate with a life expectancy ≥ 10 years and clinical stage T1c or T2a, International Society of Urological Pathology (ISUP) grade group ≤ 2 , based on high-resolution biopsy strategies, prostate-specific antigen (PSA) ≤ 10 ng/mL, low core positivity. As a consequence, section 4.1 of the SmPC is updated. The RMP (version 6.0) is updated accordingly

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

5.3.17. Pyronaridine, artesunate - PYRAMAX (Art 58⁶) - EMEA/H/W/002319/II/0023/G

Applicant: Shin Poong Pharmaceutical Co., Ltd.

PRAC Rapporteur: Adrien Inoubli

Scope: Grouped variations consisting of the submission of the final clinical study reports (CSR) of two completed studies: 1) study SP-C-021-15 (listed as a category 3 study in the RMP): a phase 3b/4 cohort event monitoring study conducted in Central Africa to evaluate the safety in patients after the local registration of Pyramax (pyronaridine/artesunate) (CANTAM study); 2) study SP-C-026-18: a randomized open-label exploratory study to

⁶ 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)

determine the efficacy of different treatment regimens of Pyramax (pyronaridine/artesunate) in asymptomatic carriers of Plasmodium falciparum mono-infections. This non-imposed study was conducted in Gambia and Zambia and compared asymptomatic subjects with parasitaemia dosed according to the approved label of 3-day dosing with 2-day and 1-day dosing. As a consequence, sections 4.2, 4.4, 4.6, 4.8 and 5.1 are updated. The package leaflet is updated in accordance. The RMP (version 17) is also updated accordingly and 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

5.3.18. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/II/0016

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include treatment of adults with pneumonia not requiring supplemental oxygen (moderate COVID-19), based on: 1) part A of study GS-US-540-5774: a phase 3, randomized, open-label, multicentre study comparing 2 remdesivir (RDV) regimens (5 days and 10 days) versus standard of care in 584 participants with moderate COVID 19; 2) study CO-US-540-5776 (adaptive COVID-19 treatment trial (ACTT)): a National Institute of Allergy and Infectious Diseases (NIAID)-sponsored phase 3, multicentre, adaptive, randomized, double blind, placebo controlled trial on the safety and efficacy study of investigational therapeutics for the treatment of COVID-19. As a consequence, sections 4.1 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 1.2) are updated in accordance

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

5.3.19. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/X/0067

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Extension application to introduce a new strength of 75 mg solution for injection. The RMP (version 8.0) is updated accordingly

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

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

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

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

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

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

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Grouped application consisting of: 1) extension application to introduce a new strength (200 mg /50 mg /50 mg film-coated tablets). The new presentation is indicated for the treatment of chronic hepatitis C virus (HCV) infection in patients aged 12 years and older or weighing at least 30 kg. In addition, the MAH took the opportunity to implement minor editorial updates in module 3.2.P; 2) extension of indication to include paediatric use in patients aged 12 years and older or weighing at least 30 kg to the existing presentation. As a consequence, sections 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 3.2) are updated in accordance

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

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

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

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

5.3.23. Trastuzumab - ZERCEPAC (CAP) - EMEA/H/C/005209/II/0008

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Addition of a new fill weight for Zercepac (trastuzumab) powder for concentrate for solution for infusion, 420 mg/vial (EU/1/20/1456/003). The strength (concentration after reconstitution) is identical to the previously authorised finished product 150mg/vial presentation. The RMP (version 1.2) is updated accordingly

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

5.3.24. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/X/0006/G

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Grouped variations consisting of: 1) extension application to introduce a new strength (30 mg prolonged-release tablet); 2) extension of indication to add treatment of moderate to severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 4.0) are updated in

accordance. In addition, the MAH took the opportunity to include a minor update in Annex II

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

5.3.25. Velmanase alfa - LAMZEDE (CAP) - EMEA/H/C/003922/II/0018, Orphan

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC based on the final results of study rhLAMAN-08 (listed as an Annex II study in the RMP): a 24-month multicentre, open-label phase 2 trial investigating the safety and efficacy of repeated velmanase alfa (recombinant human alfa-mannosidase) treatment in paediatric patients below 6 years of age with alfa-mannosidosis. The package leaflet and the RMP (version 8.1) are updated accordingly. The RMPv8.1 has also been submitted. In addition, the product information is updated in line with the latest quality review of documents (QRD) template (version 10.2)

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

5.3.26. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/II/0031

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Update sections 4.2 and 4.4 of the SmPC on tumour lysis syndrome (TLS) prophylaxis and management following an update to the company core data sheet (CCDS) as result of a medical safety assessment conducted on TLS post-marketing reports

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. Abemaciclib - VERZENIOS (CAP) - PSUSA/00010724/202009

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Aztreonam⁷ - CAYSTON (CAP) - PSUSA/00000283/202009

Applicant: Gilead Sciences Ireland UC

⁷ Inhalation use only

PRAC Rapporteur: Liana Gross-Martirosyan
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.3. [Bexarotene - TARGRETIN \(CAP\) - PSUSA/00000404/202009](#)

Applicant: Eisai GmbH
PRAC Rapporteur: Tiphaine Vaillant
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.4. [Brolucizumab - BEOVU \(CAP\) - PSUSA/00010829/202010](#)

Applicant: Novartis Europharm Limited
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.5. [Cariprazine - REAGILA \(CAP\) - PSUSA/00010623/202010](#)

Applicant: Gedeon Richter Plc.
PRAC Rapporteur: Ana Sofia Diniz Martins
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.6. [Cemiplimab - LIBTAYO \(CAP\) - PSUSA/00010780/202009](#)

Applicant: Regeneron Ireland Designated Activity Company (DAC)
PRAC Rapporteur: Menno van der Elst
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.7. [Chenodeoxycholic acid^{8 9} - CHENODEOXYCHOLIC ACID LEADIANT \(CAP\) - PSUSA/00010590/202010](#)

Applicant: Leadiant GmbH
PRAC Rapporteur: Adam Przybylkowski
Scope: Evaluation of a PSUSA procedure

⁸ For the treatment of inborn error in primary bile acid synthesis due to sterol 27 hydroxylase deficiency (presenting as cerebrotendinous xanthomatosis (CTX)) in infants, children and adolescents aged 1 month to 18 years and adults

⁹ Centrally authorised product(s) only

Action: For adoption of recommendation to CHMP

6.1.8. Dacomitinib - VIZIMPRO (CAP) - PSUSA/00010757/202009

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Dapagliflozin - EDISTRIDE (CAP); FORXIGA (CAP) - PSUSA/00010029/202010

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Dibotermin alfa - INDUCTOS (CAP) - PSUSA/00001034/202009

Applicant: Medtronic BioPharma B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Dupilumab - DUPIXENT (CAP) - PSUSA/00010645/202009

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Ebola vaccine(rDNA¹⁰, replication-incompetent) - MVABEA (CAP); ZABDENO (CAP) - PSUSA/00010857/202009

Applicant(s): Janssen-Cilag International N.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁰ Recombinant deoxyribonucleic acid

6.1.13. Etravirine - INTELENCE (CAP) - PSUSA/00001335/202009

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Galcanezumab - EMGALITY (CAP) - PSUSA/00010733/202009

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - PSUSA/00010678/202010

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Insulin aspart - FIASP (CAP); INSULIN ASPART SANOFI (CAP); NOVOMIX (CAP); NOVORAPID (CAP) - PSUSA/00001749/202009

Applicant(s): Novo Nordisk A/S (Fiasp, NovoMix, NovoRapid), Sanofi-aventis groupe (Insulin aspart Sanofi)

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Insulin human¹¹ - INSUMAN (CAP) - PSUSA/00010107/202009

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹¹ Intraperitoneal use only

6.1.18. [Lusutrombopag - MULPLEO \(CAP\) - PSUSA/00010755/202009](#)

Applicant: Shionogi B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. [Mogamulizumab - POTELIGEO \(CAP\) - PSUSA/00010741/202009](#)

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. [Netupitant, palonosetron - AKYNZEO \(CAP\) - PSUSA/00010393/202010](#)

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. [Niraparib - ZEJULA \(CAP\) - PSUSA/00010655/202009](#)

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. [Panitumumab - VECTIBIX \(CAP\) - PSUSA/00002283/202009](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. [Pitolisant - WAKIX \(CAP\) - PSUSA/00010490/202009](#)

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Ranibizumab - LUCENTIS (CAP) - PSUSA/00002609/202010

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Sirolimus - RAPAMUNE (CAP) - PSUSA/00002710/202009

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Sofosbuvir, ledipasvir - HARVONI (CAP) - PSUSA/00010306/202010

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Teriflunomide - AUBAGIO (CAP) - PSUSA/00010135/202009

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Vortioxetine - BRINTELLIX (CAP) - PSUSA/00010052/202009

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Laurence de Fays

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. Iloprost¹² - VENTAVIS (CAP); NAP - PSUSA/00001724/202009

Applicants: Bayer AG (Ventavis), various

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Leflunomide - ARAVA (CAP); LEFLUNOMIDE MEDAC (CAP); LEFLUNOMIDE ZENTIVA (CAP); NAP - PSUSA/00001837/202009

Applicants: Medac Gesellschaft für klinische Spezialpräparate mbH (Leflunomide medac), Sanofi-Aventis Deutschland GmbH (Arava), Zentiva, k.s. (Leflunomide Zentiva), various

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Sodium oxybate¹³ - XYREM (CAP); NAP - PSUSA/00010612/202010

Applicants: UCB Pharma S.A. (Xyrem), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Thalidomide - THALIDOMIDE CELGENE (CAP); NAP - PSUSA/00002919/202010

Applicants: Celgene Europe BV (Thalidomide Celgene), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Vigabatrin - KIGABEQ (CAP); NAP - PSUSA/00003112/202009

Applicants: Orphelia Pharma SAS (Kigabeq), various

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

¹² Nebuliser solution(s) only

¹³ Oral use only

Action: For adoption of recommendation to CHMP

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

6.3.1. [Ambrosia artemisiifolia^{14 15 16 17} \(NAP\) - PSUSA/00010693/202010](#)

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. [Bivalirudin \(NAP\) - PSUSA/00000421/202009](#)

Applicant(s): various

PRAC Lead: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. [Lactitol \(NAP\) - PSUSA/00001819/202009](#)

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. [Lisinopril \(NAP\); lisinopril, hydrochlorothiazide \(NAP\) - PSUSA/00010532/202009](#)

Applicant(s): various

PRAC Lead: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. [Opium \(NAP\) - PSUSA/00010670/202009](#)

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

¹⁴ Allergen for therapy

¹⁵ (302)

¹⁶ Sublingual use only

¹⁷ Medicinal product(s) authorised via decentralised procedure

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Podophyllotoxin (NAP) - PSUSA/00002454/202009

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Silver sulfadiazine (NAP) - PSUSA/00002702/202009

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Terizidone (NAP) - PSUSA/00002904/202009

Applicant(s): various

PRAC Lead: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Tobramycin¹⁸ (NAP) - PSUSA/00009318/202009

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Dexmedetomidine - DEXDOR (CAP) - EMEA/H/C/002268/LEG 016.2

Applicant: Orion Corporation

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to LEG 016.1 [analysis of available mortality data from controlled clinical trials in the dexmedetomidine development programme as requested in the

¹⁸ Systemic use only

conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00000998/201903) adopted in November 2019] as per the request for supplementary information (RSI) adopted in October 2020

Action: For adoption of advice to CHMP

6.4.2. [Infliximab - REMICADE \(CAP\) - EMEA/H/C/000240/LEG 159.1](#)

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to LEG 0159 [review on administration of live vaccines, including a literature review on postnatal clearance of tumour necrosis factor alfa (TNF α) inhibitors in the newborn, particularly of infliximab and of cases of disseminated BCG vaccinations associated with administration of BCG after birth as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010759/201908) adopted in April 2020] as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

6.4.3. [Infliximab - REMICADE \(CAP\) - EMEA/H/C/000240/LEG 161.1](#)

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to LEG 0161 [cumulative review of cases of abnormal lipid values in clinical studies and literature data on lipid derangements following tumour necrosis factor alfa (TNF α) inhibitor treatment in general and infliximab treatment in particular as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010759/201908) adopted in April 2020] as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

6.4.4. [Ivacaftor - KALYDECO \(CAP\) - EMEA/H/C/002494/LEG 031.1](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to LEG 031 [cumulative review of cases of acute pancreatitis as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00009204/202001) adopted in September 2020] as per the request for supplementary information (RSI) adopted in January 2021

Action: For adoption of advice to CHMP

6.5. **Variation procedure(s) resulting from PSUSA evaluation**

None

6.6. Expedited summary safety reviews¹⁹

6.6.1. Coronavirus (COVID-19) mRNA²⁰ vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 002.3

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

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

Action: For adoption of PRAC Assessment Report

6.6.2. Coronavirus (COVID-19) mRNA²¹ vaccine (nucleoside-modified) - COVID-19 VACCINE MODERNA (CAP) - EMEA/H/C/005791/MEA 011.2

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Third expedited monthly summary safety report for COVID-19 Vaccine Moderna (COVID-19 mRNA vaccine (nucleoside-modified)) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

6.6.3. Coronavirus (COVID-19) vaccine (Ad26.COVS-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) - EMEA/H/C/005737/MEA 014

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

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

Action: For adoption of PRAC Assessment Report

6.6.4. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 027.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

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

Action: For adoption of PRAC Assessment Report

¹⁹ 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

²⁰ Messenger ribonucleic acid

²¹ Messenger ribonucleic acid

6.6.5. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/MEA 017.7

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Ninth expedited summary safety report for Veklury (remdesivir) 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)²²

7.1.1. Cidofovir (NAP) - EMEA/H/N/PSA/S/0058.1

Applicant: Tillomed Laboratories Ltd. (Cidofovir Emcure Pharma)

PRAC Rapporteur: Rugile Pilviniene

Scope: MAH's response to PSA/S/0058 [substantial amendment to a protocol previously agreed in November 2018 (PSP/S/0052.3) for cidofovir exposure registry study: a non-interventional, prospective, exposure (safety outcome) registry study of cidofovir to further elucidate the characteristics of the different patient populations for cidofovir use, to evaluate patterns and compare rates of adverse events occurring in the on-label group with events occurring in the off-label group; and to assess patient outcome following treatment in specified indication] as per the request for supplementary information (RSI) adopted in October 2020

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

7.1.2. Fenfluramine – FINTEPLA (CAP) - EMEA/H/C/PSP/S/0093

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: Protocol for an observational registry to provide data on long-term safety of fenfluramine in routine practice, with a focus on characterising and quantifying the important potential risks of valvular heart disease (VHD) and pulmonary arterial hypertension (PAH) (primary objective), and growth retardation (secondary objective). In addition, data on the frequency of echocardiographic monitoring contribute to assess the effectiveness of risk minimisation measures

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

7.1.3. Parathyroid hormone – NATPAR (CAP) - EMEA/H/C/PSA/S/0053.2

Applicant: Shire Pharmaceuticals Ireland Limited

²² In accordance with Article 107n of Directive 2001/83/EC

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to PSA/S/0053.1 [substantial amendment to a protocol previously agreed in March 2018 (PSA/S/0026) for study PARADIGM (physicians advancing disease knowledge in hypoparathyroidism): a registry for subjects with chronic hypoparathyroidism to explore physicians advancing disease knowledge in hypoparathyroidism] as per the request for supplementary information (RSI) adopted in November 2020

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

7.1.4. Valproate (NAP) - EMEA/H/N/PSP/J/0072.4

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

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Progress report for a joint retrospective observational study to investigate the association between paternal exposure to valproate and the risk of congenital anomalies and neurodevelopmental disorders including autism in offspring, 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)]

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

7.1.5. Valproate (NAP) - EMEA/H/N/PSP/J/0075.4

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

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Progress report and substantial amendment to a protocol previously agreed in February 2020 for a joint drug utilisation study (DUS) to assess the effectiveness of the new risk minimisation measures (RMMs) and to further characterise the prescribing patterns for valproate as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in February 2018 (EMEA/H/A-31/1454]

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)²³

7.2.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 006.4

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to MEA 006.3 [MAH's request to discontinue pregnancy registry study OBS13436: an international Lemtrada pregnancy exposure cohort in multiple sclerosis [final clinical study report (CSR) initially expected in December 2021] as per the request for supplementary information (RSI) adopted in October 2020

²³ In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004

Action: For adoption of advice to CHMP

7.2.2. Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/MEA 004.2

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Substantial amendment to a protocol previously agreed in December 2018 for a non-interventional prospective cohort paediatric study in the treatment of children with X-linked hypophosphataemia (XLH) to assess the long term safety of Crysvisa (burosumab) during routine clinical care using data collected in a European disease registry for XLH [final report expected in December 2028]

Action: For adoption of advice to CHMP

7.2.3. Coronavirus (COVID-19) mRNA²⁴ vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 011.1

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 011 [protocol for study C4591010: assessment of occurrence of safety events in real-world use of COVID-19 mRNA vaccine [final clinical study report (CSR) expected in March 2024] (from initial opinion/marketing authorisation)] as per the request for supplementary information (RSI) adopted in March 2021

Action: For adoption of advice to CHMP

7.2.4. Coronavirus (COVID-19) mRNA²⁵ vaccine (nucleoside-modified) - COVID-19 VACCINE MODERNA (CAP) - EMEA/H/C/005791/MEA 005.1

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: MAH's response to MEA 005 [protocol for a study (listed as a category 3 study in the RMP): Moderna mRNA-1273 observational pregnancy outcome study to evaluate outcomes of pregnancies in females exposed to mRNA-1273 vaccine during pregnancy [final clinical study report (CSR) expected in June 2024] (from initial opinion/marketing authorisation)] as per the request for supplementary information (RSI) adopted in March 2021

Action: For adoption of advice to CHMP

7.2.5. Coronavirus (COVID-19) vaccine (Ad26.COV2-S [recombinant]) - COVID-19 VACCINE JANSSEN (CAP) - EMEA/H/C/005737/MEA 007

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Protocol for study VAC31518COV4005 (listed as a category 3 study in the RMP):

²⁴ Messenger ribonucleic acid

²⁵ Messenger ribonucleic acid

COVID-19 vaccines International Pregnancy Exposure Registry (C-VIPER) to assess the occurrence of obstetric, neonatal, and infant outcomes among women administered with COVID-19 vaccine (Ad26.COVID-19-S, recombinant) during pregnancy [final study report expected in June 2027]

Action: For adoption of advice to CHMP

7.2.6. [Coronavirus \(COVID-19\) vaccine \(ChAdOx1-S \[recombinant\]\) - VAXZEVRIA \(CAP\) - EMEA/H/C/005675/MEA 007](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Protocol for study D8111R00006: a post-authorisation/post-marketing observational study using existing secondary health data sources to evaluate the association between exposure to COVID-19 vaccine (ChAdOx1-S [recombinant]) (AZD1222 / Vaxzevria) and safety concerns (from initial opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.2.7. [Fenfluramine - FINTEPLA \(CAP\) - EMEA/H/C/003933/MEA 005](#)

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: Protocol for study ZX008-2102: a drug utilisation study (DUS) in Europe to describe fenfluramine use in routine clinical practice [final report expected in August 2025] (from initial opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.2.8. [Fostamatinib - TAVLESSE \(CAP\) - EMEA/H/C/005012/MEA 002.2](#)

Applicant: Instituto Grifols, S.A.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 002.1 [protocol for study BIG-CL-PRT-000015: a post-authorisation long term safety surveillance study of fostamatinib in adult patients with chronic immune thrombocytopenia (cITP) who are refractory to previous treatment [final clinical study report (CSR) expected in March 2025]] as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

7.2.9. [Givosiran - GIVLAARI \(CAP\) - EMEA/H/C/004775/MEA 006.2](#)

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 006.1 [protocol for study ALN-AS1-006: a global observational longitudinal prospective registry of patients with acute hepatic porphyria]

(AHP) [ELEVATE]] as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

7.2.10. Luspatercept - REBLOZYL (CAP) - EMEA/H/C/004444/MEA 003.1

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Laurence de Fays

Scope: MAH's response to MEA 003 [protocol for study ACE-536-MDS-005 to evaluate the effectiveness of the additional risk minimisation measures in Europe in order to assess healthcare professionals (HCP) awareness of key messages included in the HCP checklist for luspatercept including recommendations for counselling of women of child bearing potential (WCBP) and instructions for providing WCBP with the patient card] as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

7.2.11. Siponimod - MAYZENT (CAP) - EMEA/H/C/004712/MEA 002.2

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA 002.1 [protocol for a study (listed as a category 3 study in the RMP) on pregnancy outcomes intensive monitoring (PRIM) in order to prospectively collect and evaluate safety data on pregnancy outcomes and congenital malformations related to siponimod exposure immediately before and during pregnancy [final clinical study report (CSR) expected in 2030]] as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

7.2.12. Siponimod - MAYZENT (CAP) - EMEA/H/C/004712/MEA 004.2

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA 004.1 [protocol for a survey study (listed as a category 3 study in the RMP) among healthcare professionals (HCPs) and patients/caregivers in selected European countries in order to evaluate whether HCPs and patients/caregivers receive the educational materials and to capture their knowledge and behaviour around specific siponimod safety measures] as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

7.2.13. Tacrolimus - ADVAGRAF (CAP) - EMEA/H/C/000712/MEA 030.1

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ronan Grimes

Scope: MAH's response to MEA 030 [protocol for study F506-PV-0001: a non-interventional PASS on outcomes associated with the use of tacrolimus around conception, or during pregnancy or lactation using data from the Transplant Pregnancy Registry International (TPRI) registry] as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

7.2.14. Tacrolimus - MODIGRAF (CAP) - EMEA/H/C/000954/MEA 022.1

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 022 [protocol for study F506-PV-0001: a non-interventional PASS on outcomes associated with the use of tacrolimus around conception, or during pregnancy or lactation using data from the Transplant Pregnancy Registry International (TPRI) registry] as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)²⁶

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

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

PRAC Rapporteur: Adrien Inoubli

Scope: Results for a joint retrospective, multinational, drug utilisation study (DUS) to assess the non-adherence of physicians in hydroxyethyl starch (HES) accredited hospitals to the approved European product information [regarding indication for use, contraindications and posology (dosage)] for HES 130-containing medicinal products in clinical routine after implementation of a set of risk minimisation measures as required in the outcome of the referral procedure under Article 107i of Directive 2001/83/EC for HES completed in 2018 (EMEA/H/A-107i/1457)

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

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

7.4.1. Epoetin zeta - RETACRIT (CAP) - EMEA/H/C/000872/II/0100

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

²⁶ In accordance with Article 107p-q of Directive 2001/83/EC

²⁷ In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

Scope: Submission of the final study report for study PASCO II (listed as a category 3 study in the RMP): a joint post-authorisation safety observational cohort study of Retacrit/Silapo (epoetin zeta) administered subcutaneously for the treatment of renal anaemia to estimate the incidence of pure red cell aplasia (PRCA), neutralising antibodies, lack of efficacy and thromboembolic events under treatment with Retacrit/Silapo (epoetin zeta). The RMP (version 16.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.2. [Epoetin zeta - SILAPO \(CAP\) - EMEA/H/C/000760/II/0062](#)

Applicant: Stada Arzneimittel AG

PRAC Rapporteur: Martin Huber

Scope: Submission of the final study report for study PASCO II (listed as a category 3 study in the RMP): a joint post-authorisation safety observational cohort study of Retacrit/Silapo (epoetin zeta) administered subcutaneously for the treatment of renal anaemia to estimate the incidence of pure red cell aplasia (PRCA), neutralising antibodies, lack of efficacy and thromboembolic events under treatment with Retacrit/Silapo (epoetin zeta). The RMP (version 12.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.3. [Etanercept - ENBREL \(CAP\) - EMEA/H/C/000262/WS1653/0230; LIFMIOR²⁸ - EMEA/H/C/004167/WS1653/0024](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Eva Segovia

Scope: Submission of the second 5-year report from the British Society for Rheumatology Biologics Register (BSRBR) also referred as study B1801309 (listed as a category 3 study in the RMP): a prospective observational cohort study which investigates the long-term outcomes of patients with rheumatoid arthritis treated with etanercept with particular reference to safety

Action: For adoption of PRAC Assessment Report

7.4.4. [Follitropin alfa - OVALEAP \(CAP\) - EMEA/H/C/002608/II/0034](#)

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final study report for study SOFIA (listed as a category 3 study in the RMP): a phase 4, multinational, comparative, prospective, non-interventional, observational cohort study evaluating the safety of Ovaleap (follitropin alfa) in infertile women undergoing superovulation for assisted reproductive technologies. The RMP (version 3.3) is updated accordingly

Action: For adoption of PRAC Assessment Report

²⁸ Marketing authorisation(s) ceased to be valid in the European Union (EU) on 16 February 2020

7.4.5. Loxapine - ADASUVE (CAP) - EMEA/H/C/002400/II/0032

Applicant: Ferrer Internacional s.a.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of the final clinical study report (CSR) for study AMDC-204-401: a post-authorisation observational study to evaluate the safety of Adasuve (loxapine for inhalation) in agitated persons in routine clinical care (EU PASS). The RMP (version 9.3) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

Applicant: Amgen Europe B.V., ATMP²⁹

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

Action: For adoption of PRAC Assessment Report

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

7.5.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.11

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Sixth 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

7.5.2. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/MEA 019.6

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 019.5 [second interim report for drug utilisation survey OBS14697: a drug utilisation study to assess the effectiveness of dosing recommendation of Praluent (alirocumab) as per the product information to avoid very low-density lipoprotein (LDL)-C levels [final results expected in Q3 2021]] as per the request for supplementary information (RSI) adopted in January 2021

²⁹ Advanced therapy medicinal product

Action: For adoption of advice to CHMP

7.5.3. [Avelumab - BAVENCIO \(CAP\) - EMEA/H/C/004338/MEA 002.3](#)

Applicant: Merck Europe B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Second yearly progress update report for study MS100070-0031 (listed as a category 3 study in the RMP): a non-interventional cohort study to assess characteristics and management of patients with Merkel cell carcinoma (MCC) in Germany [final study report expected in Q1/2024]

Action: For adoption of advice to CHMP

7.5.4. [Damoctocog alfa pegol - JIVI \(CAP\) - EMEA/H/C/004054/MEA 003.2](#)

Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

Scope: Eleventh annual European Haemophilia Safety Surveillance (EUHASS) report for study 14149 (listed as a category 3 study in the RMP): evaluation of cases with adverse events (AEs) of special interest in the EUHASS registry [final clinical study report (CSR) expected in December 2021]

Action: For adoption of advice to CHMP

7.5.5. [Filgrastim - FILGRASTIM HEXAL \(CAP\) - EMEA/H/C/000918/MEA 007.9](#)

Applicant: Hexal AG

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 007.8 [5-year interim results 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, in light of available data [final clinical study report (CSR) expected in December 2024]] as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

7.5.6. [Filgrastim - ZARZIO \(CAP\) - EMEA/H/C/000917/MEA 007.9](#)

Applicant: Sandoz GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 007.8 [5-year interim results 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, in light of available data [final clinical study report (CSR) expected in December 2024]] as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

7.5.7. Levofloxacin - QUINSAIR (CAP) - EMEA/H/C/002789/ANX 004.5

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Third annual interim report for a post-marketing, open-label, observational safety study of Quinsair (nebulised levofloxacin hemihydrate) in patients with cystic fibrosis and chronic *Pseudomonas aeruginosa* infection, using data collected through European cystic fibrosis registries [final clinical study report (CSR) expected in June 2022]

Action: For adoption of advice to CHMP

7.5.8. Lutetium (¹⁷⁷Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/MEA 001.6

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Quarterly progress report for study A-LUT-T-E02-402 (SALUS study) (listed as a category 3 study in the RMP): an international post-authorisation safety registry to assess the long-term safety of Lutathera (lutetium (¹⁷⁷Lu)) for unresectable or metastatic, somatostatin receptor positive gastroenteropancreatic neuroendocrine tumours (GEP-NETs) [final clinical study report (CSR) expected in December 2025]

Action: For adoption of advice to CHMP

7.5.9. Octocog alfa - KOGENATE BAYER (CAP) - EMEA/H/C/000275/MEA 086.9

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Eleventh annual European Haemophilia Safety Surveillance (EUHASS) report for study 14149 (listed as a category 3 study in the RMP): evaluation of cases with adverse events (AEs) of special interest in the EUHASS registry [final clinical study report (CSR) expected in December 2021]

Action: For adoption of advice to CHMP

7.5.10. Octocog alfa - KOVALTRY (CAP) - EMEA/H/C/003825/MEA 004.3

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Eleventh annual European Haemophilia Safety Surveillance (EUHASS) report for study 14149 (listed as a category 3 study in the RMP): evaluation of cases with adverse events (AEs) of special interest in the EUHASS registry [final clinical study report (CSR) expected in December 2021]

Action: For adoption of advice to CHMP

7.5.11. Semaglutide - OZEMPIC (CAP) - EMEA/H/C/004174/MEA 002.3

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: First study progress report for study NN9535-4447: an epidemiological database study to estimate the risk of pancreatic cancer in patients with type 2 diabetes mellitus (T2DM) taking semaglutide - a cohort study based on Nordic registry data [final clinical study report (CSR) expected in Q3 2025]

Action: For adoption of advice to CHMP

7.5.12. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 022.22

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Tenth annual report for study C0168Z03 (PSOLAR: PSOriasis Longitudinal Assessment and Registry): an international prospective cohort study/registry programme designed to collect data on psoriasis (PSO) patients that are eligible to receive systemic therapies, including generalised phototherapy and biologics

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Coronavirus (COVID-19) mRNA³⁰ vaccine (nucleoside-modified) - COVID-19 VACCINE MODERNA (CAP) - EMEA/H/C/005791/MEA 004.1

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: MAH's response to MEA 004 [feasibility assessment for a study (listed as a category 3 study in the RMP): a post-authorisation active surveillance safety study using secondary data to monitor real-world safety of the mRNA-1273 Vaccine in the EU - an enhanced pharmacovigilance study to provide additional evaluation of adverse events of special interest (AESI) and emerging validated safety signals in European populations; Electronic database assessment of use in pregnant women) [final clinical study report (CSR) expected in December 2023] (from initial opinion/marketing authorisation)] as per the request for supplementary information (RSI) adopted in March 2021

Action: For adoption of advice to CHMP

7.6.2. Guanfacine - INTUNIV (CAP) - EMEA/H/C/003759/ANX 004.4

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to ANX 004.3 [substantial amendment to a protocol previously

³⁰ Messenger ribonucleic acid

agreed by CHMP in September 2017 for study SHP503-401: a phase 4, interventional, multicentre, 2-part study composed of a 1-year randomised, double-blind, parallel-group, placebo-controlled, active-comparator, dose-optimisation evaluation followed by a 1-year open-label evaluation to assess the long-term safety of Intuniv (guanfacine) on selected domains of cognition in children and adolescents aged 6-17 years with attention deficit hyperactivity disorder (ADHD) for whom stimulants are not suitable, not tolerable, or shown to be ineffective] as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

7.6.3. **Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/MEA 003.9**

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's responses to MEA 003.8 [second feasibility assessment report for study NB-451: an observational retrospective study based on secondary data analysis using existing databases, in order to evaluate the potential population of patients or prescriptions in each database and confirm the ability to use each database for the drug utilisation study (DUS) of Mysimba (naltrexone hydrochloride/bupropion hydrochloride) in selected European countries to describe the demographic and baseline characteristics of users of Mysimba (naltrexone hydrochloride/bupropion hydrochloride)] as per the request for supplementary information (RSI) adopted in October 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. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/S/0035 (without RMP)

Applicant: Clinuvel Europe Limited

PRAC Rapporteur : Martin Huber

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. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/005208/R/0007 (without RMP)

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Imlifidase - IDEFIRIX (CAP) - EMEA/H/C/004849/R/0003 (without RMP)

Applicant: Hansa Biopharma AB

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Larotrectinib - VITRAKVI (CAP) - EMEA/H/C/004919/R/0014 (without RMP)

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.4. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/R/0015 (with RMP)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/R/0071 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/R/0039 (without RMP)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Emtricitabine, tenofovir disoproxil - EMTRICITABINE/TENOFOVIR DISOPROXIL ZENTIVA (CAP) - EMEA/H/C/004137/R/0019 (without RMP)

Applicant: Zentiva k.s.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Follitropin delta - REKOVELLE (CAP) - EMEA/H/C/003994/R/0028 (with RMP)

Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Irinotecan hydrochloride trihydrate - ONIVYDE PEGYLATED LIPOSOMAL (CAP) - EMEA/H/C/004125/R/0025 (without RMP)

Applicant: Les Laboratoires Servier

PRAC Rapporteur: David Olsen

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Zentiva k.s.

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Palbociclib - IBRANCE (CAP) - EMEA/H/C/003853/R/0034 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Anette Kirstine Stark

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Sildenafil - MYSILDECARD (CAP) - EMEA/H/C/004186/R/0009 (without RMP)

Applicant: Mylan S.A.S

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Tenofovir disoproxil - TENOFOVIR DISOPROXIL ZENTIVA (CAP) - EMEA/H/C/004120/R/0023 (without RMP)

Applicant: Zentiva k.s.

PRAC Rapporteur: Adrien Inoubli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

Disclosure of information on results of pharmacovigilance inspections could undermine the protection of the purpose of these inspections, investigations and audits. Therefore such

information is not reported in the agenda.

9.3. Others

None

10. Other safety issues for discussion requested by the CHMP or the EMA

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

- 12.1.1. PRAC efficiency and workload – optimisation in the context of the business continuity plan due to coronavirus 19 (COVID-19)
-

PRAC Lead: Sabine Straus, Martin Huber

Action: For adoption

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

- 12.3.1. Scientific Advisory Groups (SAG) – mandate renewals and request for nominations for all therapeutic SAGs
-

Action: For discussion

12.4. Cooperation within the EU regulatory network

- 12.4.1. Coronavirus (COVID-19) pandemic - update
-

Action: For discussion

- 12.4.1. Joint advisory board (JAB) for COVID-19 vaccines studies – feedback and update on COVID-19 observational vaccine safety studies
-

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system - quarterly workload measures and performance indicators - Q1 2021 and predictions

Action: For discussion

12.8.2. Marketing authorisation applications (MAA) – Three-year forecast (March 2021 – December 2023)

Action: For information

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC Lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC Lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.14.3. Coronavirus (COVID-19) pandemic - coreRMP19: variants guidance for RMP requirements, traceability and others – restart of drafting group

Action: For discussion

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. Others

12.20.1. Drug-induced hepatotoxicity - PRAC assessors' guide - update

PRAC Lead: Menno van der Elst, Martin Huber

Action: For adoption

12.20.2. Rapid data analytical process - Final report

PRAC Lead: Sabine Straus

Action: For discussion

12.20.3. Video conferencing tool - WebEx rollout plan for PRAC

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/