30 August 2021
EMA/PRAC/425079/2021
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 30 August - 02 September 2021

Chair: Sabine Straus – Vice-Chair: Martin Huber

30 August 2021, 10:30 – 19:30, via teleconference

31 August 2021, 08:30 – 19:30, via teleconference

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

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

Organisational, regulatory and methodological matters (ORGAM)

16 September 2021, 09:00 – 12:00, via teleconference

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 30 August-02 September 2021. See September 2021 PRAC minutes (to be published post October 2021 PRAC meeting).

1.2. Agenda of the meeting on 30 August-02 September 2021

Action: For adoption

1.3. Minutes of the previous meetings on 05-08 July 2021 and on 05 August 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 procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Alemtuzumab – LEMTRADA (CAP)

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of autoimmune encephalitis

Action: For adoption of PRAC recommendation

EPITT 19710 – New signal

Lead Member State(s): DK

4.1.2. Coronavirus (COVID-19) mRNA[3] vaccine (nucleoside-modified) - COMIRNATY (CAP)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of multisystem inflammatory syndrome in children

Action: For adoption of PRAC recommendation

EPITT 19732 – New signal

Lead Member State(s): NL

[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
[3] Messenger ribonucleic acid

4.1.3. Durvalumab – IMFINZI (CAP)

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Signal of arthralgia

Action: For adoption of PRAC recommendation

EPITT 19709 – New signal

Lead Member State(s): NO

4.1.4. Obinutuzumab – GAZYVARO (CAP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Signal of non-overt disseminated intravascular coagulation (DIC)

Action: For adoption of PRAC recommendation

EPITT 19711 – New signal

Lead Member State(s): SE

4.1.5. Pregabalin – LYRICA (CAP); NAP

Applicant(s): Upjohn EESV, various

PRAC Rapporteur: To be appointed

Scope: Signal of toxic epidermal necrolysis

Action: For adoption of PRAC recommendation

EPITT 19723 – New signal

Lead Member State(s): NL

4.1.6. Tocilizumab – ROACTEMRA (CAP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of sarcoidosis

Action: For adoption of PRAC recommendation

EPITT 18860 – New signal

Lead Member State(s): DE

4.2. New signals detected from other sources

4.2.1. Ibrutinib – IMBRUVICA (CAP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Signal of sudden death/cardiac death with ibrutinib and concomitant angiotensin-converting enzyme (ACE) inhibitors[4] from a clinical trial[5]

Action: For adoption of PRAC recommendation

EPITT 19726 – New signal

Lead Member State(s): HR

4.3. Signals follow-up and prioritisation

4.3.1. Coronavirus (COVID-19) mRNA[6] vaccine (nucleoside-modified) - COMIRNATY (CAP) – EMEA/H/C/005735/SDA/032

Applicant(s): BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of myocarditis and pericarditis

Action: For adoption of PRAC recommendation

EPITT 19712 – Follow-up to July 2021

4.3.2. Coronavirus (COVID-19) mRNA[7] vaccine (nucleoside-modified) - SPIKEVAX (CAP) – EMEA/H/C/005791/SDA/033

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

PRAC Rapporteur: Hans Christian Siersted

Scope: Signal of myocarditis and pericarditis

Action: For adoption of PRAC recommendation

EPITT 19713 – Follow-up to July 2021

4.3.3. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/SDA/047.1

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

[4] Benazepril, captopril, cilazapril, enalapril, enalaprilat, fosinopril, imidapril, lisinopril, perindopril, quinapril, ramipril, trandolapril, zofenopril and combinations
[5] Study 2013-001944-76 (FLAIR): a phase 3 study evaluating first-line treatment with ibrutinib+rituximab versus fludarabine, cyclophosphamide and rituximab in patients with chronic lymphocytic leukaemia who are up to 75 years of age
[6] Messenger ribonucleic acid
[7] Messenger ribonucleic acid

Scope: Signal of capillary leak syndrome

Action: For adoption of PRAC recommendation

EPITT 19672 – Follow-up to June 2021

4.3.4. Fluoroquinolones: ciprofloxacin (NAP); delafloxacin - QUOFENIX (CAP); levofloxacin – QUINSAIR (CAP), NAP; lomefloxacin (NAP); moxifloxacin (NAP); norfloxacin (NAP); ofloxacin (NAP); pefloxacin (NAP); prulifloxacin (NAP); rufloxacin (NAP)

Applicant(s): A. Menarini Industrie Farmaceutiche Riunite s.r.l. (Quofenix), Chiesi Farmaceutici S.p.A. (Quinsair), various

PRAC Rapporteur: Karen Pernille Harg

Scope: Signal of acquired thrombotic thrombocytopenia purpura

Action: For adoption of PRAC recommendation

EPITT 19669 – Follow-up to April 2021

4.3.5. Methotrexate - JYLAMVO (CAP) - EMEA/H/C/003756/SDA/003, NORDIMET (CAP) - EMEA/H/C/003983/SDA/004.1; 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 May 2021

4.3.6. Ponatinib – ICLUSIG (CAP) - EMEA/H/C/002695/SDA/018

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

PRAC Rapporteur: Annika Folin

Scope: Signal of panniculitis

Action: For adoption of PRAC recommendation

EPITT 19681 – Follow-up to May 2021

4.4. Variation procedure(s) resulting from signal evaluation

4.4.1. Coronavirus (COVID-19) mRNA[8] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0028

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of an updated RMP (version 2.1) to include myocarditis and pericarditis

[8] Messenger ribonucleic acid

in the list of the safety concerns as an important identified risk, as requested in the outcome of the signal procedure on myocarditis and pericarditis (EPITT 19713) adopted in July 2021 (SDA 033)

Action: For adoption of PRAC Assessment Report

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Amivantamab - EMEA/H/C/005454

Scope: Treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating epidermal growth factor receptor (EGFR) exon 20 insertion mutations, after failure of platinum-based chemotherapy

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

5.1.2. Arimoclomol - EMEA/H/C/005203, Orphan

Applicant: Orphazyme A/S

Scope: Treatment of Niemann-Pick disease type C (NPC)

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

5.1.3. Budesonide, micronised - EMEA/H/C/005653, Orphan

Applicant: Calliditas Therapeutics AB

Scope (accelerated assessment): Treatment of primary immunoglobulin A (IgA) nephropathy

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

5.1.4. Ciltacabtagene autoleucel - EMEA/H/C/005095, Orphan

Applicant: Janssen-Cilag International NV, ATMP[9]

Scope (accelerated assessment): Treatment of multiple myeloma

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

5.1.5. Eptinezumab - EMEA/H/C/005287

Scope: Prophylaxis of migraine in adults

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

[9] Advanced therapy medicinal product

5.1.6. Finerenone - EMEA/H/C/005200

Scope: Treatment to delay progression of kidney disease and to reduce the risk of cardiovascular mortality and morbidity in adults with chronic kidney disease (stage 3 and 4 with albuminuria) and type 2 diabetes (T2DM)

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

5.1.7. Hepatitis B surface antigen - EMEA/H/C/005466

Scope: Prevention of infection caused by all known subtypes of the hepatitis B virus in adults

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

5.1.8. Inebilizumab - EMEA/H/C/005818, Orphan

Applicant: Viela Bio

Scope: Treatment of adults with neuromyelitis optica spectrum disorders

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

5.1.9. Linzagolix choline - EMEA/H/C/005442

Scope: Management of heavy menstrual bleeding (HMB) associated with uterine fibroids

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

5.1.10. Pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/005477

Scope: Immunisation for the prevention of invasive disease and pneumonia caused by Streptococcus pneumoniae

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

5.1.11. Regdanvimab - EMEA/H/C/005854

Scope: Treatment of coronavirus disease-2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

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

5.1.12. Sotrovimab - EMEA/H/C/005676

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

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

5.1.13. Sotorasib - EMEA/H/C/005522

Scope: Treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC)

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

5.1.14. Tepotinib - EMEA/H/C/005524

Scope: Treatment of adult patients with advanced non-small cell lung cancer (NSCLC)

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

5.1.15. Vildagliptin, metformin hydrochloride - EMEA/H/C/005738

Scope: Treatment of type 2 diabetes mellitus (T2DM)

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. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/II/0075

Applicant: Bayer AG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of an updated RMP (version 30.1) to include a follow-up questionnaire on intraocular pressure (IOP) increase and timing of IOP increase report submission. In addition, the MAH proposed to simplify the educational material consisting of a prescriber guide and injection video based on collected data and following consultation with a panel of ophthalmologists, as per the conclusions of variation II/0068 concluded in March 2021

Action: For adoption of PRAC Assessment Report

5.2.2. 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 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

5.2.3. 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

5.2.4. Coronavirus (COVID-19) mRNA[10] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0022

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of an updated RMP (version 2.0) to include clinical safety data from study mRNA-1273 P203 (NCT04649151): a phase 2/3, randomised, observer-blind, placebo-controlled study evaluating the safety, reactogenicity and effectiveness of the mRNA-1273 vaccine in healthy adolescents aged ≥ 12 to < 18 years

Action: For adoption of PRAC Assessment Report

5.2.5. Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/II/0169

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of an updated RMP (version 16.1) to remove completed study GS-EU-276-4487 (as a category 3 study in the RMP): a prospective, longitudinal, observational registry of emtricitabine/tenofovir disoproxil fumarate for human immunodeficiency virus 1 (HIV-1) pre-exposure prophylaxis (PrEP) in the European Union

Action: For adoption of PRAC Assessment Report

5.2.6. Insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/WS2115/0191; LIPROLOG (CAP) - EMEA/H/C/000393/WS2115/0151

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Annika Folin

Scope: Submission of an updated RMP (version 11.1) to reflect the completion of a routine pharmacovigilance activity: a post-approval safety surveillance for monthly lot-specific adverse event review and analysis monitoring events on hypersensitivity, local injection site reactions, immunogenicity, lack of drug effect and increased drug effects and hypoglycaemia comparing events from the new manufacturing process with events reported using drug substance from both the historic and concurrent process. In addition, the MAH took this opportunity to modify milestones for a post-approval safety surveillance

[10] Messenger ribonucleic acid

programme for severe hypoglycaemia following the use of a new presentation (Tempo pen)

Action: For adoption of PRAC Assessment Report

5.2.7. Ritonavir - NORVIR (CAP) - EMEA/H/C/000127/II/0161

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of an updated RMP (version 7.1) 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 reviewed the information contained in the RMP and removed the important identified risk of toxicity of Norvir (ritonavir) oral solution in preterm neonates, removed missing information regarding use of ritonavir in elderly patients. Finally, the MAH proposed to provide an analysis of the antiretroviral pregnancy registry (APR) data with PSUR submission(s)

Action: For adoption of PRAC Assessment Report

5.2.8. Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/WS2064/0043; VIHUMA (CAP) - EMEA/H/C/004459/WS2064/0024

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 11) to remove the following completed studies: 1) study GENA-05: immunogenicity, efficacy and safety of treatment with simoctocog alfa in previously untreated patients with severe haemophilia A; 2) study GENA-15: extension study for patients who completed GENA-05 (NuProtect)- to investigate immunogenicity, efficacy and safety of treatment with simoctocog alfa. As a consequence, 'safety in previously untreated patients', 'children < 2 years' and 'immune tolerance induction' are removed as missing information in the list of safety concerns. Finally, the RMP is brought in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

5.2.9. Sitagliptin - JANUVIA (CAP) - EMEA/H/C/000722/WS2082/0075; RISTABEN (CAP) - EMEA/H/C/001234/WS2082/0068; TESAVEL (CAP) - EMEA/H/C/000910/WS2082/0075; XELEVIA (CAP) - EMEA/H/C/000762/WS2082/0080 sitagliptin, metformin hydrochloride - EFFICIB (CAP) - EMEA/H/C/000896/WS2082/0101; JANUMET (CAP) - EMEA/H/C/000861/WS2082/0101; RISTFOR (CAP) - EMEA/H/C/001235/WS2082/0089; VELMETIA (CAP) - EMEA/H/C/000862/WS2082/0104

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 10.1) to reflect clinical trial exposure to sitagliptin in patients of 10-17 years of age in the safety specifications and implement the already assessed clinical data from procedure WS1727 finalised in January 2020 for Januvia, Ristaben, Tesavel, Xelevia (sitagliptin) and from procedure WS1898 finalised in September

2020 for Efficib, Janumet, Ristfor, Velmetia (sitagliptin/metformin)

Action: For adoption of PRAC Assessment Report

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

5.3.1. Adalimumab - YUFLYMA (CAP) - EMEA/H/C/005188/X/0005

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application to introduce a new strength of 80 mg solution for injection. The RMP (version 1.1) is updated accordingly

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

5.3.2. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/II/0065

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 5.1 of the SmPC in order to include information on the effect of alirocumab on the neurocognitive function based on final results from study R727-CL-1532 (listed as a category 3 study in the RMP): an interventional study to evaluate the neurocognitive function during the treatment, as well as the effect of the medicinal product in comparison with placebo on lipoproteins and to assess the safety and tolerability. The RMP (version 6.0) is updated accordingly

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

5.3.3. Andexanet alfa - ONDEXXYA (CAP) - EMEA/H/C/004108/II/0022/G

Applicant: Alexion Europe SAS

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations consisting of: 1) update of sections 4.4, 4.8 and 5.1 of the SmPC based the final study report from study 14-505 (ANNEXA-4): a prospective, open-label study of andexanet alfa in patients receiving a factor Xa inhibitor who have acute major bleeding to confirm safety and efficacy in patients with acute major bleeds. The provision of this study report fulfils specific obligation 001. As a consequence, it is deleted from Annex II-E on 'Specific obligations to complete post-authorisation measures for the conditional marketing authorisation'. The package leaflet is updated accordingly. The MAH took the opportunity to implement editorial changes in the Annexes. The RMP (version 2.4) is updated accordingly; 2) change to the summary of pharmacovigilance system due to a change of qualified person responsible for pharmacovigilance (QPPV)

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

5.3.4. Autologous peripheral blood T cells CD[11]4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - TECARTUS (CAP) - EMEA/H/C/005102/II/0008/G, Orphan

Applicant: Kite Pharma EU B.V., ATMP[12]

PRAC Rapporteur: Menno van der Elst

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

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

5.3.5. Baloxavir marboxil - XOFLUZA (CAP) - EMEA/H/C/004974/X/0003/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Grouped applications consisting of: 1) extension application to add a new strength of 80 mg; 2) addition of a new pack size of 1 tablet for 40 mg strength. The RMP (version 1.2) is updated in accordance. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.2) to update the local representatives with 'United Kingdom (Northern Ireland)'

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

5.3.6. Bosutinib - BOSULIF (CAP) - EMEA/H/C/002373/II/0050/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of an update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to reflect results from: 1) study B1871039 (listed as a specific obligation (SOB) in Annex II) : a phase 4 safety and efficacy study of bosutinib in patients with Philadelphia chromosome positive chronic myeloid leukaemia (CML) previously treated with one or more tyrosine kinase inhibitors. As a consequence, the study is removed from Annex II-E on 'Specific obligations to complete post-authorisation measures for the conditional marketing authorisation' of the product information and the MAH requested a switch from the conditional marketing authorisation to a full marketing authorisation; 2) study B1871040 (listed a category 3 study in the RMP): an open-label bosutinib treatment extension study for subjects with CML who have previously participated in bosutinib studies B1871006 or B1871008. The package leaflet is updated accordingly. The RMP (version 6.0) is updated accordingly. In addition, the MAH took the opportunity to update the list of local

[11] Cluster of differentiation
[12] Advanced therapy medicinal product

representatives for Belgium, Luxemburg, Germany and Northern Ireland in the package leaflet. The MAH also requested the deletion of the medicinal product from the additional monitoring list

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

5.3.7. Brivaracetam - BRIVIACT (CAP) - EMEA/H/C/003898/II/0032/G

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Grouped variations consisting of: 1) extension of indication to include patients from 1 month to 4 years of age for treatment with Briviact (brivaracetam). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The RMP (version 8.0) is updated accordingly. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.2). The MAH took the opportunity to implement minor editorial updates; 2) extension of the shelf life after the first opening of Briviact (brivaracetam) oral solution (supported by real time data); 3) addition of a 1 mL oral syringe and its adaptor for the paediatric population. The package leaflet and labelling are updated in accordance

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

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

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC based on week 124 results from the FLAIR study: a phase 3, randomized, open-label study to evaluate the efficacy, safety and tolerability of the combined treatment cabotegravir and rilpivirine. The package leaflet and the RMP (version 2.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet, to introduce editorial changes and corrections throughout the product information and to bring the product information in line with the latest quality review of documents (QRD) template (version 10.2)

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

5.3.9. Cladribine - MAVENCLAD (CAP) - EMEA/H/C/004230/II/0020

Applicant: Merck Europe B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to change posology recommendations by adding an advice on preventive measures to avoid liver injury and to add a new warning on liver function and liver injury based on a review of post-approval data in the MAH's safety database, non-clinical, clinical trial data and scientific literature. The package leaflet and the RMP (version 1.6) are updated accordingly

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

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Extension of indication to include treatment of paediatric patients aged ≥ 6 to < 18 years with relapsed or refractory systemic anaplastic lymphoma kinase (ALK)-positive anaplastic large cell lymphoma (ALCL) and with unresectable, recurrent, or refractory ALK-positive inflammatory myofibroblastic tumour (IMT) based on the results from: 1) study ADVL0912: a phase 1/2 study of crizotinib, an oral small molecule inhibitor of ALK and C-Met, in children with relapsed/refractory solid tumours and anaplastic large cell lymphoma; 2) study A8081013: a phase 1b open-label study of the safety and clinical activity of crizotinib in tumours with genetic events involving the ALK gene locus. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 8.0) are updated in accordance. In addition, the MAH took the opportunity to update the anatomical therapeutic chemical (ATC) code for crizotinib. Moreover, the MAH took the opportunity to implement a minor change in the list of local representatives in the package leaflet

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

5.3.11. Dapagliflozin - FORXIGA (CAP) - EMEA/H/C/002322/II/0071

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Removal of the indication for 'the treatment of patients with type 1 diabetes mellitus (T1DM) as an adjunct to insulin in patients with body mass index (BMI) ≥ 27 kg/m^2 when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy' and related additional risk minimisation measures from Annex II for Forxiga (dapagliflozin) 5 mg film-coated tablets. As a consequence, affected sections of the SmPC of the 5 mg tablets are updated. The package leaflet is updated in accordance. A combined SmPC/package leaflet with the 10 mg tablets has been submitted. The RMP (version 26.s1) is updated accordingly

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

5.3.12. Darunavir, cobicistat, emtricitabine, tenofovir alafenamide - SYMTUZA (CAP) - EMEA/H/C/004391/II/0037

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report from final clinical study GS-US-292-0109 (listed as a category 3 study in the RMP): a phase 3, open-label study to evaluate switching from a tenofovir disoproxil fumarate (TDF)-containing combination regimen to a tenofovir alafenamide (TAF)-containing combination single tablet regimen (STR) in virologically-suppressed human immunodeficiency virus 1 (HIV-1) positive subjects final safety and efficacy. The RMP (version 7.1) is updated accordingly

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

5.3.13. 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 is 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

5.3.14. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0073

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include treatment of relapsing remitting multiple sclerosis (RRMS) in paediatrics patients from 10 years of age and over based on results from study 109MS306: an open-Label, randomized, multicentre, multiple-dose, active-controlled, parallel-group, efficacy and safety study of dimethyl fumarate in children from 10 to less than 18 years of age with RRMS with optional open-label extension. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 11.4) is updated in accordance. The MAH requested an extension of the market protection of one additional year in line with the guidance on elements required to support the significant clinical benefit in comparison with existing therapies of a new therapeutic indication in accordance with Article 14(11) of Regulation (EC) 726/2004

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

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

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

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

5.3.16. Elbasvir, grazoprevir - ZEPATIER (CAP) - EMEA/H/C/004126/II/0029

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication to include treatment of chronic hepatitis C (CHC) in paediatric patients 12 years of age and older who weigh at least 30 kg. 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 4.1) are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

5.3.17. Febuxostat - ADENURIC (CAP) - EMEA/H/C/000777/II/0062

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Update of sections 4.4 and 4.5 of the SmPC in order to amend an existing warning on the drug-drug interaction information with mercaptopurine/azathioprine based on final results from study FAI-01 (listed as a category 3 study in the RMP): a phase 1, drug-drug interaction study investigating the pharmacokinetic (PK) profile of 6-mercaptopurine following coadministration of two doses febuxostat and azathioprine in healthy subjects. The RMP (version 9.0) is updated accordingly

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

5.3.18. 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. Finally, 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

5.3.19. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/II/0006

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of sections 4.5 and 5.2 of the SmPC in order to update pharmacokinetic information on the effect of filgotinib on organic anion transporting polypeptide (OATP)/ cytochrome P450 3A4 (CYP3A), OATP/ breast cancer resistance protein (BCRP), and OATP substrates based on final results from study GS-US-417-5937: a phase 1, randomised, two-

way crossover, open-label, single and multiple dose, single centre study to evaluate the effect of filgotinib on a mixed OATP/CYP3A, OATP/BCRP and OATP substrates using phenotypic probes. The package leaflet and the RMP (version 2.1) are updated accordingly

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

5.3.20. Galsulfase - NAGLAZYME (CAP) - EMEA/H/C/000640/II/0086

Applicant: BioMarin International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report from the mucopolysaccharidosis (MPS VI clinical surveillance programme (CSP) (listed as a specific obligation (SOB002) in Annex II): an observational CSP to characterise the natural progression of MPS VI; to evaluate the long-term safety and efficacy data from Naglazyme (galsulfase) treatment; to collect information on the effect of Naglazyme (galsulfase) treatement on lactation, growth and development of infants of Naglazyme (galsulfase) treated mothers and to evaluate the effects of Naglazyme (galsulfase) treatment on children under 5 years of age. The RMP (version 6.4) is updated accordingly to remove gastrointestinal haemorrhage, hepatic impairment and thrombocytopenia from the list of important potential risks

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

5.3.21. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/II/0006, Orphan

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC to add 'blood homocysteine increase' as a new adverse drug reaction (ADR) and update of section 4.4 of the SmPC to add a related warning. The package leaflet and the RMP (version 1.1) are updated accordingly. In addition, the MAH took the opportunity to make editorial changes to the product information and to update the local representative details for Malta and Cyprus

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

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

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.8 and 5.1 of the SmPC to reflect 5 years data from the final study reports of pivotal psoriasis studies (listed as category 3 studies in the RMP), namely: 1) study PSO3001: a phase 3, multicentre, randomized, double-blind, placebo and active comparator-controlled study evaluating the efficacy and safety of guselkumab in the treatment of subjects with moderate to severe plaque-type psoriasis; 2) study PSO3002: a phase 3, multicentre, randomized, double-blind, placebo and active comparator-controlled study evaluating the efficacy and safety of guselkumab for the treatment of subjects with moderate to severe plaque-type psoriasis with randomized withdrawal and retreatment. In the long-term extension part of these studies subjects received open-label guselkumab every 8 weeks (q8w) starting at week 52 in PSO3001 and at week 76 in PSO3002, with the

last dose at week 252 and the last safety follow-up visit at week 264. The RMP (version 8.1) is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

5.3.23. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/II/0033, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Annika Folin

Scope: Submission of the final report for the final analysis of overall survival (OS) for study C16010 (listed as an obligation in Annex II): a phase 3, randomised, double-blind multicentre study comparing ixazomib in combination with lenalidomide and dexamethasone (LenDex) versus placebo plus LenDex in adult patients with relapsed and/or refractory multiple myeloma. Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' and the RMP (version 7.0) are updated accordingly

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

5.3.24. Lacosamide - LACOSAMIDE ACCORD (CAP) - EMEA/H/C/004443/X/0007

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application to introduce a new pharmaceutical form (solution for infusion), a new strength and a new route of administration (intravenous use). The RMP (version 1.0) is updated accordingly

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

5.3.25. Lacosamide - LACOSAMIDE UCB (CAP) - EMEA/H/C/005243/WS2049/0009/G; VIMPAT (CAP) - EMEA/H/C/000863/WS2049/0091/G

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped applications consisting of: 1) extension of indication to include patients from 1 month to 4 years of age for treatment of partial-onset seizures with or without secondary generalisation as monotherapy and adjunctive therapy. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The RMP (version 16.0) is updated accordingly; 2) change of a measuring or administration device; 3) extension of the shelf-life of the finished product. The package leaflet and labelling are updated in accordance

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

5.3.26. Lanadelumab - TAKHZYRO (CAP) - EMEA/H/C/004806/II/0022, Orphan

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.8 and 5.1 of the SmPC to reflect the result of study DX-2930-04 (HELP study extension): an open-label study to evaluate the long-term safety and efficacy of lanadelumab (DX-2930) for prevention against acute attacks of hereditary angioedema (HAE). The RMP (version 2.0) is updated accordingly and 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 a refrigeration statement for the multi-pack pre-filled syringe in the product information

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

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

Applicant: Eisai GmbH

PRAC Rapporteur: Annika Folin

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

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

5.3.28. 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 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 proposed to downgrade the SOB 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

5.3.29. Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/II/0036/G

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of: 1) extension of indication to include treatment of eosinophilic granulomatosis with polyangiitis (EGPA). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 7.0)

are updated in accordance. In addition, the MAH took the opportunity to update the local representative for Italy in the package leaflet; 2) addition of a new pack size of 9x100mg/mL multipack for pre-filled pens 100 mg/mL solution for injection and another pack size of 9x100mg/mL multipack for pre-filled syringes 100 mg/mL solution for injection. As a consequence, sections 6.5 and 8 of the SmPC and the package leaflet are updated accordingly. Annex III-A on 'labelling' is also updated to include information relating to the new pack sizes

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

5.3.30. Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/II/0037

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of hypereosinophilic syndrome (HES). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. In addition, section 6.6 of the SmPC for the powder for solution for injection presentations is updated. The package leaflet and the RMP (version 7.0) are updated in accordance. The MAH took the opportunity to update the local representative for Italy in the package leaflet

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

5.3.31. Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/X/0042

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension application to introduce a new strength of 40 mg for Nucala (mepolizumab) solution for injection in a pre-filled syringe for subcutaneous use to be used in children aged 6 to 11 years. The RMP (version 8.0) is updated accordingly

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

5.3.32. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0105

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC based on final results from study CA209205 (listed as a post-authorisation efficacy study (PAES) in Annex II): a phase 2, open-label, multi-cohort, single-arm study of nivolumab in patients with classical Hodgkin's lymphoma. The RMP (version 20.3) is updated accordingly

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

5.3.33. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0048

Applicant: AstraZeneca AB

PRAC Rapporteur: Ilaria Baldelli

Scope: Update of section 5.1 of the SmPC of olaparib tablet based on results from study D0816C00020 (OPINION) (listed as a post-authorisation efficacy study (PAES) in Annex II): a phase 3b single arm, multicentre study, investigating olaparib as a maintenance treatment in patients with platinum-sensitive relapsed ovarian, fallopian tube or primary peritoneal cancer following 2 or more lines of platinum based chemotherapy and who did not have a known deleterious or suspected deleterious germline breast cancer susceptibility gene (gBRCA) mutation. Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated accordingly. The RMP (version 22.1) is updated accordingly

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

5.3.34. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/II/0005

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning on progressive multifocal leukoencephalopathy (PML) and to add PML to the list of adverse drug reactions (ADRs) with a frequency 'rare' based on a PML case observed in study RPC01-3001 open-label extension (OLE): a phase 3, multicentre, randomized, double-blind, double-dummy, active controlled, parallel group study to evaluate the efficacy and safety of ozanimod (RPC1063) administered orally to relapsing multiple sclerosis patients. The package leaflet and the RMP (version 1.3) are updated accordingly

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

5.3.35. 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

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

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped applications consisting of: 1) extension application to introduce two new strengths of 700 mg and 1000 mg prolonged-release suspension for injection. The RMP (version 10.1) is updated accordingly; 2) change of the (invented) name of the medicinal

product from Paliperidone Janssen-Cilag International to Byannli; 3) deletion of the 25 mg, 50 mg, 75 mg, 100 mg and 150 mg/100 mg strengths from the Paliperidone Janssen-Cilag marketing authorisation (EU/1/20/1453/001-006)

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

5.3.37. Pertuzumab - PERJETA (CAP) - EMEA/H/C/002547/II/0059

Applicant: Roche Registration GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final clinical study report for study WO29217 (BERENICE): a multicentre, multinational, phase 2 study to evaluate Perjeta (pertuzumab) in combination with trastuzumab and standard neoadjuvant anthracycline-based chemotherapy in patients with epidermal growth factor receptor 2 (HER2)-positive, locally advanced, inflammatory, or early-stage breast cancer. The RMP (version 14.0) is updated accordingly

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

5.3.38. Pyronaridine, artesunate - PYRAMAX (Art 58[13]) - EMEA/H/W/002319/II/0023/G

Applicant: Shin Poong Pharmaceutical Co., Ltd.

PRAC Rapporteur: Tiphaine Vaillant

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 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

5.3.39. 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)

[13] 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)

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

5.3.40. Rilpivirine - REKAMBYS (CAP) - EMEA/H/C/005060/II/0004

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Liana Gross-Martirosyan

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

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

5.3.41. Saxagliptin - ONGLYZA (CAP) - EMEA/H/C/001039/WS2098/0053; saxagliptin, metformin hydrochloride - KOMBOGLYZE (CAP) - EMEA/H/C/002059/WS2098/0051

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study D1680C00016 (MEASURE HF) (listed as a category 3 study in the RMP): a 24-week, multicentre, randomised, double-blind, parallel group, placebo-controlled study to investigate the effects of saxagliptin and sitagliptin on cardiac dimensions and function in patients with type 2 diabetes mellitus (T2DM) and heart failure. The RMP (version 16) is updated accordingly

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

5.3.42. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/II/0076

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to introduce a new posology regimen for adult plaque psoriasis patients and psoriatic arthritis patients with concomitant moderate to severe plaque psoriasis based on the final results of study CAIN457A2324 (and exposure-response modelling): a randomised, double-blind, multicentre study assessing short (16 weeks) and long-term efficacy (up to 1 year), safety, and tolerability of sub-cutaneous secukinumab in subjects of body weight 90 kg or higher with moderate to severe chronic plaque-type psoriasis. The package leaflet and the RMP (version 9.0) are updated accordingly

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

5.3.43. Siponimod - MAYZENT (CAP) - EMEA/H/C/004712/X/0007

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension application to add a new strength of 1 mg film-coated tablet. The RMP (version 3.0) is updated in accordance

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

5.3.44. Sugammadex - BRIDION (CAP) - EMEA/H/C/000885/II/0042

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to change posology recommendations and update safety, efficacy and pharmacokinetic information in children and adolescents (2-17 years) following P46/025 and based on final results from study P089MK8616: a phase 4 double-blind, randomised, active comparator-controlled clinical trial to study the efficacy, safety and pharmacokinetics of sugammadex (MK-8616) for reversal of neuromuscular blockade in paediatric participants. In addition, the MAH took the opportunity to implement some minor editorial changes throughout the product information. The package leaflet is updated in accordance and the MAH took the opportunity to update the list of local representatives. The RMP (version 7.2) 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

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

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

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

5.3.46. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/X/0030/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Grouped application consisting of: 1) extension application to add a new strength (22 mg prolonged-release tablet); 2) update of sections 4.1, 4.2, 4.4 , 4.8, 5.1 and 5.2 of

the SmPC of Xeljanz (tofacitinib) 11 mg prolonged-release tablets in order to include the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent, as an alternative to the immediate release film-coated tablets. Section 4.2 of the SmPC of Xeljanz (tofacitinib) film-coated tablets is also updated to include switching with the prolonged-release tablet in the treatment of UC. The package leaflet and the RMP (version 15.1) are updated accordingly

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

5.3.47. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/II/0009

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of sections 4.4 and 5.1 of the SmPC in order to amend the existing warning on vaccination based on the final results from vaccination sub-study within study M13-538 (listed as a category 3 study in the RMP): an open-label extension to assess the impact of upadacitinib treatment with a stable background of methotrexate on immunological responses following administration of a pneumococcal vaccine in rheumatoid arthritis patients. The RMP (version 5.0) is updated accordingly

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Albutrepenonacog alfa - IDELVION (CAP) - PSUSA/00010497/202101

Applicant: CSL Behring GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Asparaginase[14] - SPECTRILA (CAP) - PSUSA/00010445/202101

Applicant: medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[14] Centrally authorised product(s) only

6.1.3. Atazanavir, cobicistat - EVOTAZ (CAP) - PSUSA/00010404/202101

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Autologous peripheral blood T cells CD[15]4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - TECARTUS (CAP) - PSUSA/00010903/202101

Applicant: Kite Pharma EU B.V., ATMP[16]

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.5. Avapritinib - AYVAKYT (CAP) - PSUSA/00010878/202101

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Beclometasone, formoterol, glycopyrronium bromide - RIARIFY (CAP); TRIMBOW (CAP); TRYDONIS (CAP) - PSUSA/00010617/202101

Applicant(s): Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Belantamab mafodotin - BLENREP (CAP) - PSUSA/00010869/202102

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[15] Cluster of differentiation
[16] Advanced therapy medicinal product

6.1.8. Bictegravir, emtricitabine, tenofovir alafenamide - BIKTARVY (CAP) - PSUSA/00010695/202102

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Birch bark extract[17] - EPISALVAN (CAP) - PSUSA/00010446/202101

Applicant: Amryt GmbH

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Botulinum toxin type A - NUCEIVA (CAP) - PSUSA/00010796/202101

Applicant: Evolus Pharma Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Brexpiprazole - RXULTI (CAP) - PSUSA/00010698/202101

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Michal Radik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Brivaracetam - BRIVIACT (CAP) - PSUSA/00010447/202101

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Budesonide[18] - JORVEZA (CAP) - PSUSA/00010664/202101

Applicant: Dr. Falk Pharma GmbH

[17] Centrally authorised product(s) only
[18] Centrally authorised product(s) only

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Bulevirtide - HEPCLUDEX (CAP) - PSUSA/00010873/202101

Applicant: MYR GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Ceftolozane, tazobactam - ZERBAXA (CAP) - PSUSA/00010411/202012

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Cenegermin - OXERVATE (CAP) - PSUSA/00010624/202101

Applicant: Dompe farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Concentrate of proteolytic enzymes enriched in bromelain - NEXOBRID (CAP) - PSUSA/00010028/202012

Applicant: MediWound Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Dapagliflozin, metformin - EBYMECT (CAP); XIGDUO (CAP) - PSUSA/00010294/202101

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Dapivirine - DAPIVIRINE VAGINAL RING 25 MG (Art 58[19]) - EMEA/H/W/002168/PSUV/0008

Applicant: International Partnership for Microbicides Belgium AISBL

PRAC Rapporteur: Jan Neuhauser; PRAC Co-rapporteur: Not applicable

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.20. Darolutamide - NUBEQA (CAP) - PSUSA/00010843/202101

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Defatted powder of Arachis hypogaea L., semen (peanuts) - PALFORZIA (CAP) - PSUSA/00010902/202101

Applicant: Aimmune Therapeutics Ireland Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Dolutegravir - TIVICAY (CAP); dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP); dolutegravir, lamivudine - DOVATO (CAP) - PSUSA/00010075/202101

Applicant(s): ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Elbasvir, grazoprevir - ZEPATIER (CAP) - PSUSA/00010519/202101

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[19] 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)

6.1.24. Epoetin zeta - RETACRIT (CAP), SILAPO (CAP) - PSUSA/00001241/202012

Applicant(s): Pfizer Europe MA EEIG (Retacrit), Stada AG (Silapo)

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Eptacog alfa - NOVOSEVEN (CAP) - PSUSA/00001245/202012

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Glucagon[20] - BAQSIMI (CAP) - PSUSA/00010826/202101

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Glycerol phenylbutyrate - RAVICTI (CAP) - PSUSA/00010454/202101

Applicant: Immedica Pharma AB

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Guselkumab - TREMFYA (CAP) - PSUSA/00010652/202101

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Imipenem, cilastatin, relebactam - RECARBRIO (CAP) - PSUSA/00010830/202101

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

[20] Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Indacaterol, glycopyrronium, mometasone - ENERZAIR BREEZHALER (CAP); ZIMBUS BREEZHALER (CAP) - PSUSA/00010861/202101

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Inotersen - TEGSEDI (CAP) - PSUSA/00010697/202101

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. L-lysine hydrochloride, L-arginine hydrochloride - LYSAKARE (CAP) - PSUSA/00010786/202101

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Liraglutide - SAXENDA (CAP); VICTOZA (CAP) - PSUSA/00001892/202012

Applicant(s): Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Lonoctocog alfa - AFSTYLA (CAP) - PSUSA/00010559/202101

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Macimorelin - MACIMORELIN CONSILIENT HEALTH (CAP) - PSUSA/00010746/202101

Applicant: Consilient Health Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Meningococcal group-B vaccine (rDNA[21], component, adsorbed) - BEXSERO (CAP) - PSUSA/00010043/202101

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Mercaptamine[22] - CYSTADROPS (CAP) - PSUSA/00010574/202101

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Metreleptin - MYALEPTA (CAP) - PSUSA/00010700/202101

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Neratinib - NERLYNX (CAP) - PSUSA/00010712/202101

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[21] Recombinant deoxyribonucleic acid
[22] Indicated for the treatment of corneal cystine crystal deposit only

6.1.40. Nilotinib - TASIGNA (CAP) - PSUSA/00002162/202101

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Osilodrostat - ISTURISA (CAP) - PSUSA/00010820/202101

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Patisiran - ONPATTRO (CAP) - PSUSA/00010715/202102

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Phenylephrine, ketorolac - OMIDRIA (CAP) - PSUSA/00010419/202101

Applicant: Omeros Ireland Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Quadrivalent influenza vaccine (recombinant, prepared in cell culture) - SUPEMTEK (CAP) - PSUSA/00010886/202101

Applicant: Sanofi Pasteur

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Roflumilast - DAXAS (CAP) - PSUSA/00002658/202101

Applicant: AstraZeneca AB

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Romosozumab - EVENITY (CAP) - PSUSA/00010824/202101

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Sarilumab - KEVZARA (CAP) - PSUSA/00010609/202101

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Simoctocog alfa - NUWIQ (CAP); VIHUMA (CAP) - PSUSA/00010276/202101

Applicant(s): Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Smallpox vaccine (live, modified vaccinia virus Ankara) - IMVANEX (CAP) - PSUSA/00010119/202101(with RMP)

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Tasimelteon - HETLIOZ (CAP) - PSUSA/00010394/202101

Applicant: Vanda Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Tezacaftor, ivacaftor - SYMKEVI (CAP) - PSUSA/00010730/202102

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Ticagrelor - BRILIQUE (CAP) - PSUSA/00002948/202012

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Ustekinumab - STELARA (CAP) - PSUSA/00003085/202012

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Vismodegib - ERIVEDGE (CAP) - PSUSA/00010140/202101

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.55. Vonicog alfa - VEYVONDI (CAP) - PSUSA/00010714/202012

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.56. Voretigene neparvovec - LUXTURNA (CAP) - PSUSA/00010742/202101

Applicant: Novartis Europharm Limited, ATMP[23]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

[23] Advanced therapy medicinal product

6.1.57. Zanamivir[24] - DECTOVA (CAP) - PSUSA/00010763/202101

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Ulla Wändel Liminga

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. Alendronic acid, colecalciferol - ADROVANCE (CAP), FOSAVANCE (CAP), VANTAVO (CAP), NAP; alendronic acid, calcium, colecalciferol - NAP - PSUSA/00000079/202101

Applicants: Organon N.V. (Adrovance, Fosavance, Vantavo), various

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Pregabalin - LYRICA (CAP); PREGABALIN PFIZER (CAP); NAP - PSUSA/00002511/202101

Applicants: Upjohn EESV (Lyrica, Pregabalin Pfizer), various

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Repaglinide - NOVONORM (CAP); PRANDIN (CAP); NAP - PSUSA/00002618/202012

Applicants: Novo Nordisk A/S (NovoNorm, Prandin), various

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[24] Centrally authorised product(s) only

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

6.3.1. 5-fluorouracil[25] (NAP) - PSUSA/00000007/202012

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Alendronate (NAP) - PSUSA/00000078/202101

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Alitretinoin[26] (NAP) - PSUSA/00010710/202101

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Alizapride (NAP) - PSUSA/00000091/202101

Applicant(s): various

PRAC Lead: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Allopurinol (NAP) - PSUSA/00000095/202012

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[25] Intravenous (IV) use only
[26] Oral use only

6.3.6. Altizide, spironolactone (NAP) - PSUSA/00002781/202101

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Amiodarone (NAP) - PSUSA/00000166/202012

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Amitriptyline, perphenazine (NAP) - PSUSA/00000170/202101

Applicant(s): various

PRAC Lead: Agni Kapou

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Amitriptyline (NAP); amitriptyline, amitriptylinoxide (NAP); amitriptylinoxide (NAP) - PSUSA/00010374/202101

Applicant(s): various

PRAC Lead: Agni Kapou

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Anthrax vaccine (NAP) - PSUSA/00010771/202012

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Antithrombin III (NAP) - PSUSA/00003159/202012

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Azelastine (NAP) - PSUSA/00000277/202012

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Betahistine (NAP) - PSUSA/00000389/202012

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Betamethasone (NAP) - PSUSA/00000391/202101

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Betamethasone dipropionate, calcipotriol (NAP) - PSUSA/00000393/202101

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Betamethasone dipropionate, clotrimazole (NAP) - PSUSA/00000394/202101

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Betamethasone dipropionate, salicylic acid (NAP) - PSUSA/00000395/202101

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Betamethasone sodium phosphate, neomycin sulfate (NAP) - PSUSA/00000397/202101

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Betamethasone valerate, clioquinol (NAP) - PSUSA/00000398/202101

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Betamethasone valerate, fusidic acid (NAP) - PSUSA/00000399/202101

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Betula verrucosa[27] [28] [29] (NAP) - PSUSA/00010815/202101

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Caffeine, drotaverine hydrochloride, metamizole sodium (NAP) - PSUSA/00001996/202101

Applicant(s): various

PRAC Lead: Marek Juracka

Scope: Evaluation of a PSUSA procedure

[27] Allergen for therapy
[28] De-centrally authorised product(s) only
[29] Sublingual tablet(s) only

Action: For adoption of recommendation to CMDh

6.3.23. Calcitriol (NAP) - PSUSA/00000495/202101

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Carbamazepine (NAP) - PSUSA/00000539/202012

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Carboprost (NAP) - PSUSA/00000560/202101

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Cefoperazone (NAP) - PSUSA/00000597/202101

Applicant(s): various

PRAC Lead: Rugilė Pilvinienė

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.27. Cefoperazone, sulbactam (NAP) - PSUSA/00000598/202101

Applicant(s): various

PRAC Lead: Rugilė Pilvinienė

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.28. Celecoxib (NAP) - PSUSA/00000616/202012

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.29. Cyproheptadine (NAP) - PSUSA/00000902/202012

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.30. Dapoxetine (NAP) - PSUSA/00000928/202012

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.31. Desmopressin (NAP) - PSUSA/00000964/202012

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.32. Diacerein (NAP) - PSUSA/00001026/202012

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.33. Doxazosin (NAP) - PSUSA/00001169/202012

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.34. Exemestane (NAP) - PSUSA/00001345/202012

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.35. Famciclovir (NAP) - PSUSA/00001349/202012

Applicant(s): various

PRAC Lead: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.36. Ferric carboxymaltose[30] (NAP) - PSUSA/00010865/202101

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.37. Hydrochlorothiazide, spironolactone (NAP) - PSUSA/00001662/202101

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.38. Iron dextran (NAP) - PSUSA/00010696/202101

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.39. Iron isomaltoside[31] (NAP) - PSUSA/00010866/202101

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[30] Parenteral preparation(s) only
[31] Parenteral preparation(s) only

6.3.40. Iron sucrose[32] (NAP) - PSUSA/00010864/202101

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.41. Levonorgestrel, ethinylestradiol; ethinylestradiol[33] (NAP) - PSUSA/00010442/202101

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.42. Lormetazepam (NAP) - PSUSA/00001910/202012

Applicant(s): various

PRAC Lead: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.43. Pseudoephedrine, triprolidine (NAP) - PSUSA/00003047/202012

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.44. Rupatadine (NAP) - PSUSA/00002673/202012

Applicant(s): various

PRAC Lead: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.45. Sodium iron gluconate[34] (NAP) - PSUSA/00010867/202101

Applicant(s): various

[32] Parenteral preparation(s) only
[33] Combination pack only
[34] Parenteral preparation(s) only

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.46. Tobramycin[35] [36] (NAP) - PSUSA/00009316/202012

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. Docetaxel - TAXOTERE (CAP) - EMEA/H/C/000073/LEG 039.1

Applicant: Sanofi Mature IP

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to LEG 039 [detailed review on the potential risk for decreased efficacy of docetaxel when used along with any selective cyclooxygenase-2 (Cox-2) inhibitors as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001152/201911) adopted in July 2020] as per the request for supplementary information (RSI) adopted in April 2021

Action: For adoption of advice to CHMP

6.4.2. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/LEG 174

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Eva Segovia

Scope: Cumulative review of cases of dyslipidaemia including clinical trial data, published medical literature, and post-marketing events reported in the MAH's global safety database, in line with the conclusions of the PSUR single assessment (PSUSA) procedure for infliximab (PSUSA/00010759/201908) adopted in April 2020 and as requested following the conclusions of LEG 0161 for infliximab dated December 2020

Action: For adoption of advice to CHMP

6.4.3. Sitagliptin - JANUVIA (CAP) - EMEA/H/C/000722/LEG 041

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Cumulative review and analysis on the risk of malignancies/neoplasms particularly

[35] Nebuliser solution only
[36] Non-centrally authorised product(s) only

pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021

Action: For adoption of advice to CHMP

6.4.4. Sitagliptin - RISTABEN (CAP) - EMEA/H/C/001234/LEG 019

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Cumulative review and analysis on the risk of malignancies/neoplasms particularly pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021

Action: For adoption of advice to CHMP

6.4.5. Sitagliptin - TESAVEL (CAP) - EMEA/H/C/000910/LEG 035

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Cumulative review and analysis on the risk of malignancies/neoplasms particularly pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021

Action: For adoption of advice to CHMP

6.4.6. Sitagliptin - XELEVIA (CAP) - EMEA/H/C/000762/LEG 040

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Cumulative review and analysis on the risk of malignancies/neoplasms particularly pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021

Action: For adoption of advice to CHMP

6.4.7. Sitagliptin, metformin hydrochloride - EFFICIB (CAP) - EMEA/H/C/000896/LEG 020

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Cumulative review and analysis on the risk of malignancies/neoplasms particularly pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021

Action: For adoption of advice to CHMP

6.4.8. Sitagliptin, metformin hydrochloride - JANUMET (CAP) - EMEA/H/C/000861/LEG 020

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Cumulative review and analysis on the risk of malignancies/neoplasms particularly pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021

Action: For adoption of advice to CHMP

6.4.9. Sitagliptin, metformin hydrochloride - RISTFOR (CAP) - EMEA/H/C/001235/LEG 016

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Cumulative review and analysis on the risk of malignancies/neoplasms particularly pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021

Action: For adoption of advice to CHMP

6.4.10. Sitagliptin, metformin hydrochloride - VELMETIA (CAP) - EMEA/H/C/000862/LEG 020

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Cumulative review and analysis on the risk of malignancies/neoplasms particularly pancreatic carcinoma from clinical trials, literature and post-marketing data as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010673/202008) adopted in March 2021

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) - EMEA/H/C/005737/II/0014

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.8 of the SmPC to include lymphadenopathy, paraesthesia, hypoesthesia, diarrhea, vomiting and tinnitus as adverse drug reactions (ADRs) as per the conclusions of post-authorisation measure MEA 014.2 (monthly summary safety report

(MSSR)) finalised in July 2021. In addition, the MAH took the opportunity to add editorial changes in sections 6.4 and 6.6 of the SmPC in line with the WHO[37] recommendation. Finally, Annex III-A on Labelling is updated to increase readability

Action: For adoption of PRAC Assessment Report

6.5.2. Coronavirus (COVID-19) mRNA[38] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0015/G

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Grouped variations to address PRAC requests raised as per the conclusions of the second and third monthly safety summary report (MSSR) procedures (MEA 011.1 and MEA 011.2) respectively: 1) update of sections 4.4 of the SmPC to provide additional safety information regarding hypersensitivity and anaphylaxis, as requested by the PRAC in the second MSSR. The package leaflet is updated accordingly; 2) update of section 4.8 of the SmPC to include 'delayed injection site reaction' as an adverse reaction with a frequency 'common', as requested by the PRAC in the third MSSR. The package leaflet is updated accordingly. In addition, the MAH submitted a justification for not adding diarrhoea to the product information as an adverse reaction as requested by the PRAC in the third MSSR and took the opportunity to introduce minor editorial changes in the product information

Action: For adoption of PRAC Assessment Report

6.5.3. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/II/0025

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ilaria Baldelli

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC concerning immunogenicity and loss of efficacy due to anti-emicizumab antibodies as requested in the conclusions of the latest periodic safety update report single assessment (PSUSA) procedure (PSUSA/00010668/202011) adopted in June 2021, together with a review of haemorrhagic cases as requested in the conclusions of the PSUSA procedure (PSUSA/00010668/202005) finalised in January 2021. The RMP (version 3.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews[39]

6.6.1. Coronavirus (COVID-19) mRNA[40] vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 002.7

Applicant: BioNTech Manufacturing GmbH

[37] World Health Organization
[38] Messenger ribonucleic acid
[39] 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
[40] Messenger ribonucleic acid

PRAC Rapporteur: Menno van der Elst

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

Action: For adoption of PRAC Assessment Report

6.6.2. Coronavirus (COVID-19) mRNA[41] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 011.6

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

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

Action: For adoption of PRAC Assessment Report

6.6.3. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) – EMEA/H/C/005737/MEA 014.4

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

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

Action: For adoption of PRAC Assessment Report

6.6.4. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 027.5

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

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

Action: For adoption of PRAC Assessment Report

[41] Messenger ribonucleic acid

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[42]

7.1.1. Cidofovir (NAP) - EMEA/H/N/PSA/S/0058.2

Applicant: Tillomed Laboratories Ltd. (Cidofovir Emcure Pharma)

PRAC Rapporteur: Rugile Pilviniene

Scope: MAH's response to PSA/S/0058.1 [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 May 2021

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

7.1.2. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/PSA/S/0075

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Substantial amendment to a protocol previously agreed in December 2017 (PSA/S/0016.2) for study CC-5013-MDS-012: a post-authorisation, non-interventional, retrospective, drug-utilisation study (DUS) to describe the pattern of use of lenalidomide in patients with myelodysplastic syndromes (MDS)

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

7.1.3. Levonorgestrel (NAP) - EMEA/H/N/PSA/S/0073

Applicant: Bayer Pharma AG (Jaydess, Luadei)

PRAC Rapporteur: Annika Folin

Scope: Substantial amendment to a protocol previously agreed in November 2019 (PSA/S/0044) for study EURAS-LCS12: a European active surveillance study of LCS-12 (levonorgestrel intrauterine contraceptive system releasing 12 µg levonorgestrel/24h in vitro), an intra-uterine device (IUD) for Jaydess and Luadei (levonorgestrel) to investigate whether LCS-12 is associated with an increased risk of unintended pregnancy compared to Mirena (levonorgestrel-releasing intrauterine system) and to copper IUDs

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

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

7.1.4. Methylphenidate hydrochloride (NAP) - EMEA/H/N/PSA/S/0074

Applicant: Medice Arzneimittel Pütter GmbH & Co. KG (Medikinet)

PRAC Rapporteur: Martin Huber

Scope: Substantial amendment to a protocol previously agreed in November 2020 (PSP/S/0064.5): a multicentre, observational, prospective PASS to evaluate the safety concerns of long-term cardiovascular and psychiatric risks within the adult attention deficit/hyperactivity disorder (ADHD) population taking Medikinet Retard (methylphenidate hydrochloride) according to normal standard clinical practice

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

7.1.5. Parathyroid hormone – NATPAR (CAP) - EMEA/H/C/PSA/S/0053.3

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to PSA/S/0053.2 [substantial amendment to a protocol previously agreed in March 2018 (PSA/S/0026) for study PARADIGHM (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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[43]

7.2.1. Alpelisib - PIQRAY (CAP) - EMEA/H/C/004804/MEA 003

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study CBYL719C2005: a survey among healthcare professionals treating patients with metastatic breast cancer in selected European countries to evaluate their knowledge on management of hyperglycemia when using Piqray (alpelisib) as included in the educational material

Action: For adoption of advice to CHMP

7.2.2. Cabotegravir - VOCABRIA (CAP) - EMEA/H/C/004976/MEA 004.1

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 004 [protocol for study 215162 (listed as a category 3 study in the RMP): a prospective observational cohort study to monitor for hepatotoxicity and regimen discontinuation due to liver related adverse events among patients initiating

[43] 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

cabotegravir-containing antiretroviral regimen [final clinical study report (CSR): expected in March 2027] as per the request for supplementary information (RSI) adopted in April 2021

Action: For adoption of advice to CHMP

7.2.3. Cabotegravir - VOCABRIA (CAP) - EMEA/H/C/004976/MEA 005.1

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 005 [protocol for study 215163: a study on pregnancy and neonatal outcomes following prenatal exposure to cabotegravir long acting (CAB LA) – data from the European Pregnancy and Paediatric human immunodeficiency virus (HIV) Cohort Collaboration (EPPICC)] as per the request for supplementary information (RSI) adopted in April 2021

Action: For adoption of advice to CHMP

7.2.4. Cabotegravir - VOCABRIA (CAP) - EMEA/H/C/004976/MEA 006.1

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 006 [protocol for study 215325: a study on pregnancy and neonatal outcomes following prenatal exposure to cabotegravir – data from the Antiretroviral Pregnancy Registry (APR)] as per the request for supplementary information (RSI) adopted in April 2021

Action: For adoption of advice to CHMP

7.2.5. Coronavirus (COVID-19) mRNA[44] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 004.3

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: MAH's response to MEA 004.2 [protocol for a study (listed as a category 3 study in the RMP): a post-authorisation active surveillance safety study using secondary data to monitor real-world safety of the COVID-19 mRNA-1273 vaccine in Europe [final clinical study report (CSR) expected in December 2023]] as per the request for supplementary information (RSI) adopted in July 2021

Action: For adoption of advice to CHMP

7.2.6. Coronavirus (COVID-19) mRNA[45] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 034.1

Applicant: Moderna Biotech Spain, S.L.

[44] Messenger ribonucleic acid
[45] Messenger ribonucleic acid

PRAC Rapporteur: Hans Christian Siersted

Scope: MAH's response to MEA 034 [protocol for a study monitoring the safety of Spikevax (COVID-19 vaccine) in pregnancy: an observational study using routinely collected health data in five European countries] as per the request for supplementary information (RSI) adopted in July 2021

Action: For adoption of advice to CHMP

7.2.7. Fenofibrate, pravastatin sodium - PRAVAFENIX (CAP) - EMEA/H/C/001243/MEA 007.8

Applicant: Laboratoires SMB s.a.

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to MEA 007.6 [amendment to a protocol previously agreed in 2014 for study POSE (Pravafenix Observational Study in Europe) (EUPAS13661): a European, observational, three-year cohort comparative study on the safety of the fixed dose combination pravastatin 40 mg/fenofibrate 160 mg (Pravafenix) versus statin alone in real clinical practice] as per the request for supplementary information (RSI) adopted in April 2021

Action: For adoption of advice to CHMP

7.2.8. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 011

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study GS-EU-417-9050: a non-interventional post-authorisation cross-sectional safety study evaluating the effectiveness of the additional risk minimisation measures for filgotinib use in patients with rheumatoid arthritis within the German registry Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT)

Action: For adoption of advice to CHMP

7.2.9. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 012

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study GS-EU-417-5885: a non-interventional post-authorisation cross-sectional safety study evaluating the effectiveness of the additional risk minimisation measures for filgotinib use in patients with rheumatoid arthritis within the Anti-Rheumatic Treatment in Denmark (DANBIO) register

Action: For adoption of advice to CHMP

7.2.10. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 013

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study GS-EU-417-5884: a non-interventional post-authorisation cross-sectional safety study evaluating the effectiveness of the additional risk minimisation measures for filgotinib use in patients within the Spanish Register of Adverse Events of Biological Therapies in Rheumatoid Diseases (BIOBADASER)]

Action: For adoption of advice to CHMP

7.2.11. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 014

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study GS-EU-417-9052: a non-interventional post-authorisation cross-sectional safety study evaluating the effectiveness of the additional risk minimisation measures for filgotinib use in patients with rheumatoid arthritis within British Society for Rheumatology Biologics Register Rheumatoid Arthritis (BSRBR-RA)

Action: For adoption of advice to CHMP

7.2.12. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 015

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study GS-EU-417-9051: a non-interventional post-authorisation cross-sectional safety study evaluating the effectiveness of the additional risk minimisation measures for filgotinib use in patients with rheumatoid arthritis within the Anti-Rheumatic Treatment in Sweden (ARTIS) register

Action: For adoption of advice to CHMP

7.2.13. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 001.6

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 001.5 [amendment to a protocol previously agreed in September 2020 for study TEG4001: a prospective, non-interventional, long-term, multinational cohort safety study of patients with hereditary transthyretin amyloidosis with polyneuropathy (hATTR-PN)] as per the request for supplementary information (RSI) adopted in April 2021

Action: For adoption of advice to CHMP

7.2.14. Isatuximab - SARCLISA (CAP) - EMEA/H/C/004977/MEA 002.1

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 002 [protocol for study SARSAC09715: a non-interventional

PASS survey to evaluate the effectiveness of isatuximab educational materials to minimise the risk of interference for blood typing (minor antigen) (positive indirect Coombs' test)] as per the request for supplementary information (RSI) adopted in March 2021

Action: For adoption of advice to CHMP

7.2.15. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/MEA 003.10

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Third feasibility assessment report and protocol for study NB-451: an observational retrospective drug utilisation study (DUS) of Mysimba (naltrexone hydrochloride/bupropion hydrochloride) in Europe and the United States to describe the demographic and baseline characteristics of users of Mysimba (naltrexone hydrochloride/bupropion hydrochloride), evaluate patterns of Mysimba (naltrexone hydrochloride/bupropion hydrochloride) initiation and use

Action: For adoption of advice to CHMP

7.2.16. Netarsudil - RHOKIINSA (CAP) - EMEA/H/C/004583/MEA 001.2

Applicant: Aerie Pharmaceuticals Ireland Limited

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 001.1 [protocol for study AR-13324-OBS02: a non-interventional, observational cohort study of 2-year of treatment with Rhokiinsa (netarsudil) compared with non-Rhokiinsa (netarsudil) ocular hypotensive therapy in patients with elevated intraocular pressure due to primary open angle glaucoma or ocular hypertension [final clinical study report (CSR) expected in June 2026]] as per the request for supplementary information (RSI) adopted in March 2021

Action: For adoption of advice to CHMP

7.2.17. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/MEA 001.1

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA 001 [protocol for study RPC-1063-MS-004 (listed as a category 3 study in the RMP): a post authorisation multinational long-term non-interventional study (ORION) study on ozanimod real world safety [final clinical study report (CSR) expected in December 2031] as per the request for supplementary information (RSI) adopted in March 2021

Action: For adoption of advice to CHMP

7.2.18. Somapacitan - SOGROYA (CAP) - EMEA/H/C/005030/MEA 002

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Martin Huber

Scope: Protocol for study NN8640-4515: a multinational, multicentre, prospective, open label, single-arm, observational, non-interventional PASS to investigate long-term safety of somapacitan in adults with growth hormone deficiency (AGHD) under normal clinical practice conditions (from initial marketing authorisation/opinion)

Action: For adoption of advice to CHMP

7.2.19. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 017

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study A3921352: an active surveillance, post-authorisation study to characterise the safety of tofacitinib in patients with moderately to severely active ulcerative colitis in the real-world setting using data from the united registries for clinical assessment and research (UR-CARE) in the European Union (EU)

Action: For adoption of advice to CHMP

7.2.20. Trastuzumab deruxtecan - ENHERTU (CAP) - EMEA/H/C/005124/MEA 003

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Protocol for an EU survey of relevant healthcare professionals on the understanding of key risk minimisation measures pertaining to interstitial lung disease (ILD)/pneumonitis with trastuzumab deruxtecan treatment (from initial marketing authorisation/opinion)

Action: For adoption of advice to CHMP

7.2.21. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 002.8

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Amendment to a protocol previously agreed in September 2019 for study P16-562 (listed as a category 3 study in the RMP): a prospective observational study to assess the long-term safety profile of venetoclax in a Swedish cohort of chronic lymphocytic leukaemia (CLL) patients

Action: For adoption of advice to CHMP

7.2.22. Zanamivir - DECTOVA (CAP) - EMEA/H/C/004102/MEA 003

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Protocol for study 208140: an intravenous (IV) zanamivir pregnancy registry to evaluate pregnancy outcomes among women exposed to IV zanamivir at any time during pregnancy (from initial marketing authorisation/opinion)

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[46]

7.3.1. Aprotinin (NAP) - EMEA/H/N/PSR/S/0030

Applicant: Nordic Group BV (Trasylol)

PRAC Rapporteur: Laurence de Fays

Scope: MAH's response to PSR/S/0030 [results for a Nordic aprotinin patient registry to record utilisation information on patients at cardiac surgery centres] as per the request for supplementary information (RSI) adopted in April 2021

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

7.3.2. Dexamfetamine (NAP) - EMEA/H/N/PSR/S/0028

Applicant: Medice Arzneimittel Pütter GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to PSR/S/0028 [results of a PASS to evaluate the long-term safety of dexamfetamine to assess the incidence proportion and incidence rate for cardiovascular, psychiatric, growth and sexual maturity related adverse events in children with a diagnosis of attention deficit hyperactivity disorder (ADHD) who have been treated with dexamfetamine, methylphenidate or lisdexamfetamine as recorded in healthcare databases of three countries. The study also compares the risk of long-term cardiovascular, psychiatric, growth and sexual maturity-related adverse events of dexamfetamine versus methylphenidate or lisdexamfetamine in each database] as per the request for supplementary information (RSI) adopted in April 2021

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

7.3.3. Dexamfetamine (NAP) - EMEA/H/N/PSR/S/0029

Applicant: Medice Arzneimittel Pütter GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to PSR/S/0029 [Results of a drug utilisation study (DUS) to collect data on abuse, misuse, overdose, diversion and dependence related to dexamfetamine in five European countries] as per the request for supplementary information (RSI) adopted in April 2021

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

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

7.3.4. Iron[47] [48] (NAP) - EMEA/H/N/PSR/J/0026

Applicant(s): Mesama Consulting (on behalf of a consortium) (CosmoFer, Diafer, Fer Arrow Ferinject, FerMed, Fer Mylan, Fer Panpharma, Ferracin, Ferrisat, Ferrlecit, Fer Sandoz, IJzerhydroxide saccharose complex Teva, Järnsackaros Rechon, Monofer, Venofer)

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to PSR/J/0026 [results of a joint study on intravenous iron: evaluation of the risk of severe hypersensitivity reactions, as imposed in the conclusions of the referral under Article 31 of Directive 2001/83/EC (EMEA/H/A-31/1322) for intravenous (IV) iron-containing medicines in 2013]] as per the request for supplementary information (RSI) adopted in March 2021

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

7.3.5. Lisdexamfetamine dimesylate (NAP) - EMEA/H/N/PSR/S/0033

Applicant(s): Shire Pharmaceuticals Ireland Limited (Elvanse Adult)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Results of study SPD489-825 to evaluate the long-term cardiovascular safety of lisdexamfetamine (LDX) in adults in order to estimate in real-world settings the incidence rate and the adjusted incidence rate ratios of the composite major adverse cardiovascular events (MACE) endpoint in a cohort of adult patients who are current new users of LDX (LDX cohort) as compared with a cohort of remote users of other attention-deficit hyperactivity disorder (ADHD) treatments

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)[49]

7.4.1. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/II/0040, Orphan

Applicant: Kite Pharma EU B.V., ATMP[50]

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final study report for non-interventional study KT-EU-471-0116 (listed as category 3 study in the RMP): a quantitative testing of healthcare provider knowledge about Yescarta (axicabtagene ciloleucel) risk minimisation measures

Action: For adoption of PRAC Assessment Report

[47] Intravenous (IV)
[48] Iron (III)-hydroxide dextran complex, iron sucrose complex/iron(III)-hydroxide sucrose complex, ferric carboxymaltose complex, iron(III) isomaltoside complex, sodium ferric gluconate complex
[49] 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
[50] Advanced therapy medicinal product

7.4.2. Dapivirine - DAPIVIRINE VAGINAL RING 25 MG (Art 58[51]) - EMEA/H/W/002168/II/0011

Applicant: International Partnership for Microbicides Belgium AISBL

PRAC Rapporteur: Jan Neuhauser

Scope: Submission of the final report from study MTN-16 (EMBRACE) (listed as a category 3 study in the RMP): an observational cohort study in women with exposure to active and non-active investigational product who became pregnant in phase 3 trial MTN-020 (ASPIRE) and open-label extension study MTN-025 (HOPE) and who subsequently enrolled in study MTN-016. This study assessed pregnancy and delivery outcomes in these women and infant follow up for the first year of life. The RMP (version 0.8) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.3. Dibotermin alfa - INDUCTOS (CAP) - EMEA/H/C/000408/II/0100

Applicant: Medtronic BioPharma B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final study report from study EUPAS32916 (listed as a category 3 study in the RMP): an observational study to evaluate the effectiveness of additional risk minimisation measures for InductOs (dibotermin alfa). The product information and the RMP (version 2.1) are updated accordingly. In addition, the MAH took the opportunity to submit study protocol for study EUPAS32916 as suggested by PRAC

Action: For adoption of PRAC Assessment Report

7.4.4. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/II/0244

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Eva Segovia

Scope: Submission of the final report from study B1801310 (BIKER) (listed as a category 3 study in the RMP): an observational PASS of etanercept and methotrexate in the treatment of juvenile idiopathic arthritis (JIA) using data obtained from participants in the German Biologics JIA registry (BIKER) to monitor long-term safety and effectiveness of etanercept in the treatment of JIA in regular clinical practice

Action: For adoption of PRAC Assessment Report

7.4.5. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - EMEA/H/C/004336/II/0045

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Update of section 4.4 of the SmPC in order to add a new warning on an increased risk of Guillain-Barré syndrome (GBS) after vaccination with Shingrix (herpes zoster

[51] 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)

vaccine) observed in a post-marketing observational study in individuals aged 65 years or older. The package leaflet and the RMP (version 5.1) are updated accordingly. In addition, the MAH took the opportunity to make some editorial changes to the SmPC and to update the list of local representatives in the package leaflet

Action: For adoption of PRAC Assessment Report

7.4.6. Human normal immunoglobulin - HYQVIA (CAP) - EMEA/H/C/002491/II/0070/G

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of: 1) update of section 4.6 of the SmPC in order to update information on pregnancy and breast-feeding based on the final results from study 161301 (listed as a category 3 study in the RMP): an observational pregnancy registry study to collect long-term safety data from women treated with HyQvia (human normal immunoglobulin). The package leaflet and the RMP (version 12.0) are updated accordingly. In addition, the MAH took the opportunity to implement minor corrections and editorial changes to the SmPC; 2) submission of an updated RMP (version 12.0) to update the educational material (additional risk minimisation measures) as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001633/202005) finalised in January 2021

Action: For adoption of PRAC Assessment Report

7.4.7. Insulin glargine, lixisenatide - SULIQUA (CAP) - EMEA/H/C/004243/II/0023

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final study report from study EUPAS 19769 (listed as a category 3 study in the RMP): a registry to monitor the occurrence of events of interest including acute pancreatitis, pancreatic cancer and thyroid cancer, especially medullary carcinoma of the thyroid (MCT), among adult type 2 diabetes patients treated with lixisenatide using data from national registers and databases in Italy and Belgium (in fulfilment of post-authorisation measure (PAM) MEA 005.3)

Action: For adoption of PRAC Assessment Report

7.4.8. Lixisenatide - LYXUMIA (CAP) - EMEA/H/C/002445/II/0033

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Annika Folin

Scope: Submission of the final report of study EUPAS 19769 (listed as a category 3 study in the RMP): a registry to monitor the occurrence of events of interest including acute pancreatitis, pancreatic cancer and thyroid cancer, especially medullary carcinoma of the thyroid, among adult type 2 diabetes patients treated with lixisenatide using data from national registers and databases in Italy and Belgium. The RMP (version 7.0) is updated accordingly (in fulfilment of post-authorisation measure (PAM) MEA 008.5)

Action: For adoption of PRAC Assessment Report

7.4.9. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/II/0116

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study 20170701 (listed as a category 3 study in the RMP): an observational study to assess the effectiveness of the Neulasta (pegfilgrastim) patient alert card and to measure medication errors related to the use of the on-body injector. The RMP (version 8.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

Applicant: Amgen Europe B.V., ATMP[52]

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

Action: For adoption of PRAC Assessment Report

7.4.11. Trastuzumab - ONTRUZANT (CAP) - EMEA/H/C/004323/II/0036

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report from clinical study SB3-G31-BC-E (listed as a category 3 study in the RMP): an observational cohort study assessing the long-term cardiac safety (for cardiac safety and survival cohort) and survival (survival only cohort and cardiac safety and survival cohort) in patients who received treatment with trastuzumab. The RMP (version 5.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

7.5.1. Aclidinium - BRETARIS GENUAIR (CAP) - EMEA/H/C/002706/ANX 001.9

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Third interim report for study D6560R00004, formerly M/34273/44, (listed as a category 1 in Annex II and the RMP): an observational study evaluating the risk of

[52] Advanced therapy medicinal product

cardiovascular endpoints of aclidinium bromide-containing products versus other chronic obstructive pulmonary disease (COPD) medications in COPD patients - sub-study report addressing the acute myocardial infarction (AMI) report and stroke components of the PASS programme

Action: For adoption of advice to CHMP

7.5.2. Aclidinium - EKLIRA GENUAIR (CAP) - EMEA/H/C/002211/ANX 001.9

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Third interim report for study D6560R00004, formerly M/34273/44, (listed as a category 1 in Annex II and the RMP): an observational study evaluating the risk of cardiovascular endpoints of aclidinium bromide-containing products versus other chronic obstructive pulmonary disease (COPD) medications in COPD patients - sub-study report addressing the acute myocardial infarction (AMI) report and stroke components of the PASS programme

Action: For adoption of advice to CHMP

7.5.3. Aclidinium, formoterol fumarate dihydrate - BRIMICA GENUAIR (CAP) - EMEA/H/C/003969/ANX 003.6

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Third interim report for study D6560R00004, formerly M/34273/44, (listed as a category 1 in Annex II and the RMP): an observational study evaluating the risk of cardiovascular endpoints of aclidinium bromide-containing products versus other chronic obstructive pulmonary disease (COPD) medications in COPD patients - sub-study report addressing the acute myocardial infarction (AMI) report and stroke components of the PASS programme

Action: For adoption of advice to CHMP

7.5.4. Aclidinium, formoterol fumarate dihydrate - DUAKLIR GENUAIR (CAP) - EMEA/H/C/003745/ANX 003.6

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Third interim report for study D6560R00004, formerly M/34273/44, (listed as a category 1 in Annex II and the RMP): an observational study evaluating the risk of cardiovascular endpoints of aclidinium bromide-containing products versus other chronic obstructive pulmonary disease (COPD) medications in COPD patients - sub-study report addressing the acute myocardial infarction (AMI) report and stroke components of the PASS programme

Action: For adoption of advice to CHMP

7.5.5. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/MEA 008.1

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Second yearly report for study CC 10004 PSA-012: evaluation of the long-term safety and safety outcomes for psoriatic arthritis patients treated with Otezla (apremilast) in the British Society for Rheumatology Psoriatic Arthritis Register (BSRBR-PsA) [final clinical study report (CSR) expected in Q2 2026]

Action: For adoption of advice to CHMP

7.5.6. Brodalumab - KYNTHEUM (CAP) - EMEA/H/C/003959/MEA 002.5

Applicant: LEO Pharma A/S

PRAC Rapporteur: Eva Segovia

Scope: Second study progress report for study NIS-KYNTHEUM-1345: an observational PASS investigating the risk of suicidal behaviour, serious infections, major adverse cardiovascular events (MACE) and malignancy in psoriasis patients treated with brodalumab. The brodalumab assessment of hazards: a multinational safety (BRAHMS) study in electronic healthcare databases [final report expected in Q3 2030]

Action: For adoption of advice to CHMP

7.5.7. Coronavirus (COVID-19) mRNA[53] vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 010

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study C4591012: a post-emergency use authorisation active safety surveillance study among individuals in the veteran's affairs health system receiving Comirnaty (COVID-19 mRNA vaccine) in real-world use [final clinical study report (CSR) expected in December 2023]

Action: For adoption of advice to CHMP

7.5.8. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/MEA 002.4

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Laurence de Fays

Scope: MAH's response to MEA 002.3 [fourth annual progress report for study 242-12-402 (listed as a category 3 study in the RMP): a multicentre EU-wide observational non-interventional post-authorisation study to assess the safety and drug usage of delamanid (OPC-67683) in routine medical practice in multidrug-resistant tuberculosis patients (Delamanid registry)] as per the request for supplementary information (RSI) adopted in February 2021

[53] Messenger ribonucleic acid

Action: For adoption of advice to CHMP

7.5.9. Dimethyl fumarate - SKILARENCE (CAP) - EMEA/H/C/002157/MEA 001.5

Applicant: Almirall S.A

PRAC Rapporteur: Annika Folin

Scope: Third annual interim results for study M-41008-40 (listed as a category 3 study in the RMP): an observational PASS in European psoriasis registers to evaluate the long-term safety of Skilarence (dimethyl fumarate) used for the treatment of patients with moderate to severe psoriasis [future due date(s): end of data collection: Q1 2027; final study report expected within a year of availability of the final data set]

Action: For adoption of advice to CHMP

7.5.10. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/MEA 007.3

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 007.2 [amendment to a protocol previously agreed in November 2017 for study 109MS401 (ESTEEM): a multicentre, global, observational study to collect information on safety and to document the drug utilisation of Tecfidera (dimethyl fumarate) when used in routine medical practice in the treatment of relapsing multiple sclerosis] as per the request for supplementary information (RSI) adopted in April 2021, together with the sixth annual progress report for the study

Action: For adoption of advice to CHMP

7.5.11. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/MEA 008.7

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Fifth annual progress report for study 109MS402 (listed as a category 3 study in the RMP): Biogen multiple sclerosis (MS) pregnancy exposure registry to prospectively evaluate pregnancy outcomes in women with MS who were exposed to a registry-specified Biogen MS product during the eligibility window for that product

Action: For adoption of advice to CHMP

7.5.12. Fenofibrate, pravastatin sodium - PRAVAFENIX (CAP) - EMEA/H/C/001243/MEA 007.9

Applicant: Laboratoires SMB s.a.

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to MEA 007.7 [interim results for study POSE (Pravafenix Observational Study in Europe) (EUPAS13661): a European, observational, three-year cohort comparative study on the safety of the fixed dose combination pravastatin 40 mg/ fenofibrate 160 mg (Pravafenix) versus statin alone in real clinical practice] as per the

request for supplementary information (RSI) adopted in April 2021

Action: For adoption of advice to CHMP

7.5.13. Filgrastim - FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/MEA 007.11

Applicant: Hexal AG

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 007.11 [tenth annual report for study EP06-501 (SMART): a non-interventional, prospective, long-term safety data collection of Zarzio/Filgrastim Hexal (filgrastim) in healthy unrelated stem cell donors undergoing peripheral blood progenitor cell (PBPC) mobilisation [final clinical study report (CSR) expected in December 2024]] as per the request for supplementary information (RSI) adopted in June 2021

Action: For adoption of advice to CHMP

7.5.14. Filgrastim - ZARZIO (CAP) - EMEA/H/C/000917/MEA 007.11

Applicant: Sandoz GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 007.11 [tenth annual report for study EP06-501 (SMART): a non-interventional, prospective, long-term safety data collection of Zarzio/Filgrastim Hexal (filgrastim) in healthy unrelated stem cell donors undergoing peripheral blood progenitor cell (PBPC) mobilisation [final clinical study report (CSR) expected in December 2024]] as per the request for supplementary information (RSI) adopted in June 2021

Action: For adoption of advice to CHMP

7.5.15. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/MEA 012.10

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Tenth annual interim report for study D2404: a multinational pregnancy exposure registry in patients with multiple sclerosis (MS) taking Gilenya (fingolimod) from the pregnancy intensive monitoring programme (PRIM)

Action: For adoption of advice to CHMP

7.5.16. Flutemetamol (^{18}F) - VIZAMYL (CAP) - EMEA/H/C/002557/MEA 003.3

Applicant: GE Healthcare AS

PRAC Rapporteur: Martin Huber

Scope: First study progress report for study GE-067-028: a post-authorisation survey of nuclear medicine physicians and radiologists in Europe to evaluate trends and patterns in Vizamyl (flutemetamol (^{18}F)) use in everyday clinical practice in the EU

Action: For adoption of advice to CHMP

7.5.17. Guanfacine - INTUNIV (CAP) - EMEA/H/C/003759/MEA 005.5

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Third annual progress report for a drug utilisation study (DUS) of Intuniv (guanfacine extended release) in European countries: a non-imposed, non-interventional, multi-country DUS using retrospective database analysis (DUS-database: EUPAS18735) and a prescriber survey (DUS-survey: EUPAS18739) [final report expected in June 2022] together with MAH's response to MEA 005.4 as adopted in October 2020

Action: For adoption of advice to CHMP

7.5.18. Influenza vaccine (live attenuated, nasal) - FLUENZ TETRA (CAP) - EMEA/H/C/002617/MEA 004.12

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Annual report for the passive enhanced safety surveillance (ESS) D2560C00008: a post-marketing non-interventional cohort study of the safety of live attenuated influenza vaccine (LAIV) in subjects 2 through 17 years of age for the 2020-2021 influenza season

Action: For adoption of advice to CHMP

7.5.19. Insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/MEA 028.8

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Annika Folin

Scope: Eighth interim report (batches released to the market between 01 April 2020 to 31 March 2021 [period 2]): a post-approval safety surveillance for monthly lot-specific adverse event review and analysis to evaluate any potential change in the frequency of hypersensitivity, local site injection reactions, immunogenicity, hypoglycaemia and lack of drug effect events comparing events from the new manufacturing process with events reported using drug substance from both the historic and concurrent process

Action: For adoption of advice to CHMP

7.5.20. Insulin lispro - LIPROLOG (CAP) - EMEA/H/C/000393/MEA 021.8

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Annika Folin

Scope: Eighth interim report (batches released to the market between 01 April 2020 to 31 March 2021 [period 2]): a post-approval safety surveillance for monthly lot-specific adverse event review and analysis to evaluate any potential change in the frequency of hypersensitivity, local site injection reactions, immunogenicity, hypoglycaemia and lack of drug effect events comparing events from the new manufacturing process with events reported using drug substance from both the historic and concurrent process

Action: For adoption of advice to CHMP

7.5.21. Luspatercept - REBLOZYL (CAP) - EMEA/H/C/004444/MEA 002

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Laurence de Fays

Scope: First annual report for study ACE-536-LTFU-001: a study to evaluate the long-term safety, including thromboembolic events (TEEs) and progression to acute myeloid leukaemia (AML) and/or other malignancies/pre malignancies of luspatercept in patients who have participated in company-sponsored luspatercept clinical trials [final clinical study report (CSR) expected in Q2 2029]

Action: For adoption of advice to CHMP

7.5.22. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/MEA 001.7

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

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

Action: For adoption of advice to CHMP

7.5.23. Octocog alfa - KOVALTRY (CAP) - EMEA/H/C/003825/MEA 005.3

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual interim report 2020 for epidemiological study 15689: an evaluation of adverse events of special interest (AESI) in the European PEDiatric NETwork (PedNet) for haemophilia management registry

Action: For adoption of advice to CHMP

7.5.24. Ravulizumab - ULTOMIRIS (CAP) - EMEA/H/C/004954/MEA 008

Applicant: Alexion Europe SAS

PRAC Rapporteur: Kimmo Jaakkola

Scope: First interim analysis safety report (biennial interim report) for study M07-001 (listed as a category 3 study in the RMP): a prospective registry for an observational, multicentre, multinational study of patients with paroxysmal nocturnal haemoglobinuria (PNH)

Action: For adoption of advice to CHMP

7.5.25. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 026.3

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Second annual update for an observational study (listed as a category 3 study in the RMP) using EU registries (Spanish drug-induced liver injury (DILI) registry and Prospective European DILI Network (Pro-Euro DILI registry)) with biomarker data, as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in May 2018 (EMEA/H/A-20/1460)

Action: For adoption of advice to CHMP

7.5.26. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 027.3

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Second annual update for a genetic analysis (HLA) study (listed as a category 3 study in the RMP) from EU registries (Spanish drug-induced liver injury (DILI) registry and Prospective European DILI Network (Pro-Euro DILI registry)) with biomarker data in patients with severe DILI, as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in May 2018 (EMEA/H/A-20/1460)

Action: For adoption of advice to CHMP

7.5.27. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 045.6

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Second interim report for study RRA-20745: an observational PASS to describe the safety of ustekinumab and other Crohn’s disease treatments in a cohort of patients with Crohn’s disease

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Cabazitaxel - CABAZITAXEL ACCORD (CAP) - EMEA/H/C/005178/MEA 001

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Six-monthly review of cases of ‘medication error’ for cabazitaxel reported during routine signal management activities

Action: For adoption of advice to CHMP

7.6.2. Radium (^{223}Ra) dichloride - XOFIGO (CAP) - EMEA/H/C/002653/MEA 016

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Interim status report for study NCT03574571 (DoRA) (listed as a category 3 study in the RMP): a phase 3 open-label, 1:1 randomised trial of docetaxel vs. docetaxel and radium-223 dichloride for metastatic castration-resistant prostate cancer (mCRPC) sponsored by the prostate Cancer Clinical Trials Consortium (PCCTC) to address the important identified risk of bone fractures [final clinical study report (CSR) expected in Q4 2023] as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMEA/H/A-20/1459) completed in 2018

Action: For adoption of advice to CHMP

7.6.3. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 024.3

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Second yearly report on the feasibility report for study PGL18-002: a retrospective, multi-national, comparative, non-interventional cohort study to investigate the risk of liver injury possibly associated with Esmya (ulipristal acetate) use based on data from various national electronic health record based databases in Europe, as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in 2018 (EMEA/H/A-20/1460)

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

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

7.8. Ongoing Scientific Advice

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. Zanamivir - DECTOVA (CAP) - EMEA/H/C/004102/S/0011 (without RMP)

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Autologous peripheral blood T cells CD[54]4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - TECARTUS (CAP) - EMEA/H/C/005102/R/0010 (without RMP)

Applicant: Kite Pharma EU B.V., ATMP[55]

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.2.2. Coronavirus (COVID-19) mRNA[56] vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/R/0046 (without RMP)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Coronavirus (COVID-19) mRNA[57] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/R/0025 (without RMP)

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Conditional renewal of the marketing authorisation

[54] Cluster of differentiation
[55] Advanced therapy medicinal product
[56] Messenger ribonucleic acid
[57] Messenger ribonucleic acid

Action: For adoption of advice to CHMP

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

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.5. Obeticholic acid - OCALIVA (CAP) - EMEA/H/C/004093/R/0027 (without RMP)

Applicant: Intercept Pharma International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.7. Trastuzumab deruxtecan - ENHERTU (CAP) - EMEA/H/C/005124/R/0006 (without RMP)

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/R/0025 (without RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Chlormethine - LEDAGA (CAP) - EMEA/H/C/002826/R/0030 (with RMP)

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Daptomycin - DAPTOMYCIN HOSPIRA (CAP) - EMEA/H/C/004310/R/0018 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Pernille Harg

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Edotreotide - SOMAKIT TOC (CAP) - EMEA/H/C/004140/R/0019 (with RMP)

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Ronan Grimes

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Methotrexate - JYLAMVO (CAP) - EMEA/H/C/003756/R/0015 (without RMP)

Applicant: Therakind (Europe) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Miglustat - YARGESA (CAP) - EMEA/H/C/004016/R/0011 (with RMP)

Applicant: Piramal Critical Care B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Pregabalin - PREGABALIN ZENTIVA K.S. (CAP) - EMEA/H/C/004277/R/0019 (with RMP)

Applicant: Zentiva k.s.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Rituximab - TRUXIMA (CAP) - EMEA/H/C/004112/R/0047 (without RMP)

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Anette Kirstine Stark

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Tadalafil - TADALAFIL LILLY (CAP) - EMEA/H/C/004666/R/0008 (without RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Mylan S.A.S

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

Disclosure of information on results of pharmacovigilance inspections could undermine the protection of the purpose of these inspections, investigations and audits. Therefore such information is not reported in the agenda.

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

10.3.1. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/A-5(3)/1507

Applicant: AstraZeneca AB

PRAC Lead: Jean-Michel Dogné, Brigitte Keller-Stanislawski

Scope: PRAC consultation on possible further characterisation of the risk of thrombosis with thrombocytopenia syndrome (TTS) considering the results of the study 'natural history of coagulopathy and use of anti-thrombotic agents in patients and persons vaccinated against SARS-COV-2' (EUPAS40414) in the context of the ongoing procedure under Article 5(3) of Regulation (EC) No 726/2004, on request of CHMP

Action: For adoption of advice to CHMP

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Azathioprine (NAP) - DK/H/0843/001/II/021, DK/H/0843/001/II/023

Applicant: Ebewe Pharma Ges.m.b.H (Azathioprin Ebewe 50 mg film-coated tablets)

PRAC Lead: Hans Christian Siersted

Scope: PRAC consultation on national variations proposing to update the product information on concomitant use of intrauterine devices (IUDs) and azathioprine therapy, on request of Denmark

Action: For adoption of advice to Member States

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. Mandate of PRAC Vice-Chairperson - prolongation

Action: For discussion

12.1.2. PRAC Rules of Procedure - revision

Action: For discussion

12.1.3. Relaunch of face to face scientific Committee meetings - pilot

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh-v

12.2.1. Advanced therapy medicinal products (ATMP) - Evaluation and grading of neurotoxicities for chimeric antigen receptor-T (CAR-T) cells ATMPs - proposal

Action: For adoption

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

Action: For discussion

12.4.2. PRAC strategic review and learning meeting (SRLM) under the Slovenian presidency of the European Union (EU) Council – Remote meeting, 22 September 2021 - agenda

PRAC lead: Polona Golmajer

Action: For discussion

12.5. Cooperation with International Regulators

12.5.1. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) - Pharmacoepidemiology discussion group (PEpiDG) - new guideline on 'general principles on planning and designing pharmaco-epidemiological studies that utilise real-world data (RWD) for safety assessment of a medicine - call for nomination of PRAC expert

Action: For adoption

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

12.6.1. Coronavirus (COVID-19)-medicines monitoring - COVID-19 infection and medicines in pregnancy - update

PRAC lead: Sabine Straus, Ulla Wändel Liminga

Action: For discussion

12.7. PRAC work plan

12.7.1. PRAC work plan 2021 - update

PRAC lead: Sabine Straus, Martin Huber

Action: For discussion

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system - quarterly workload measures and performance indicators - Q2 2021 and predictions

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC Lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.14.3. Good pharmacovigilance practice (GVP) module XVI on 'Risk minimisation measures: selection of tools and effectiveness indicators' - Addendum III on

'Pregnancy prevention programme and other pregnancy-specific risk minimisation measures'

PRAC lead: Sabine Straus

Action: For adoption

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies - imposed PASS

None

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

None

12.15.3. Registry-based studies - guideline - update

PRAC lead: Sabine Straus, Ulla Wändel Liminga, Patricia McGettigan

Action: For discussion

12.15.4. Coronavirus (COVID-19) pandemic - observational COVID-19 vaccine safety studies - progress overview and dashboard introduction

Action: For discussion

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

None

12.21. Others

12.21.1. Lifecycle regulatory submissions raw data project (LRSR) - presentation

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/