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Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 08-11 March 2021

Chair: Sabine Straus – Vice-Chair: Martin Huber

08 March 2021, 10:30 – 19:30, via teleconference

09 March 2021, 08:30 – 19:30, via teleconference

10 March 2021, 08:30 – 19:30, via teleconference

11 March 2021, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

25 March 2021, 09:00 – 12:00, via teleconference

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

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 08-11 March 2021. See March 2021 PRAC minutes (to be published post April 2021 PRAC meeting).

1.2. Agenda of the meeting on 08-11 March 2021

Action: For adoption

1.3. Minutes of the previous meeting on 08-11 February 2021

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

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

Applicant: Bluebird bio (Netherlands) B.V.; ATMP¹

¹ Advanced therapy medicinal product

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

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

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

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

3.3.1. Ifosfamide² (NAP) - EMEA/H/A-31/1495

Applicant(s): various

PRAC Rapporteur: Martin Huber; PRAC Co-rapporteur: Nikica Mirošević Skvrce

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

Action: For adoption of a recommendation to CMDh

3.4. Re-examination procedures³

None

3.5. Others

None

4. Signals assessment and prioritisation⁴

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Coronavirus (COVID-19) mRNA⁵ vaccine (nucleoside-modified) - COMIRNATY (CAP)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

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

² Solution, concentrate for solution

³ Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC

⁴ 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

⁵ Messenger ribonucleic acid

Action: For adoption of PRAC recommendation

EPITT 19674 – New signal

Lead Member State(s): NL

4.1.2. [Coronavirus \(COVID-19\) mRNA⁶ vaccine \(nucleoside-modified\) - COMIRNATY \(CAP\)](#)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of immune thrombocytopenia

Action: For adoption of PRAC recommendation

EPITT 19680 – New signal

Lead Member State(s): NL

4.1.3. [Coronavirus \(COVID-19\) vaccine \(ChAdOx1-S \[recombinant\]\) - COVID-19 VACCINE ASTRAZENECA \(CAP\)](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Signal of anaphylactic reaction

Action: For adoption of PRAC recommendation

EPITT 19668 – New signal

Lead Member State(s): BE

4.1.4. [Coronavirus \(COVID-19\) vaccine \(ChAdOx1-S \[recombinant\]\) - COVID-19 VACCINE ASTRAZENECA \(CAP\)](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Signal of immune thrombocytopenia

Action: For adoption of PRAC recommendation

EPITT 19678 – New signal

Lead Member State(s): BE

4.1.5. [Coronavirus \(COVID-19\) mRNA⁷ vaccine \(nucleoside-modified\) - COVID-19 VACCINE MODERNA \(CAP\)](#)

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

⁶ Messenger ribonucleic acid

⁷ Messenger ribonucleic acid

Scope: Signal of immune thrombocytopenia

Action: For adoption of PRAC recommendation

EPITT 19679 – New signal

Lead Member State(s): DK

4.2. New signals detected from other sources

4.2.1. Donepezil (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of cardiac conduction disorders including QT prolongation and

Action: For adoption of PRAC recommendation

EPITT 19667 – New signal

Lead Member State(s): DE

4.2.2. Octreotide (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of pancreatic exocrine insufficiency

Action: For adoption of PRAC recommendation

EPITT 19661 – New signal

Lead Member State(s): IE

4.2.3. Tofacitinib - XELJANZ (CAP)

Applicant(s): Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Signal of major adverse cardiovascular events (MACE) and malignancies excluding non-melanoma skin cancer (NMSC) from a clinical trial⁸

Action: For adoption of PRAC recommendation

EPITT 19673 – New signal

Lead Member State(s): NL

⁸ Study A3921133: a phase 3b/4 randomised safety endpoint study of 2 doses of tofacitinib in comparison to a tumour necrosis fibrosis (TNF) inhibitor in subjects with rheumatoid arthritis

4.3. Signals follow-up and prioritisation

4.3.1. Anakinra - KINERET (CAP) - EMEA/H/C/000363/SDA/032.1; canakinumab - ILARIS (CAP) - EMEA/H/C/001109/SDA/054.1

Applicant(s): Novartis Europharm Limited (Ilaris), Swedish Orphan Biovitrum AB (publ) (Kineret)

PRAC Rapporteur: Anette Kirstine Stark

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

Action: For adoption of PRAC recommendation

EPITT 19566 – Follow-up to November 2020

4.3.2. Efavirenz - SUSTIVA (CAP) - EMEA/H/C/000249/SDA/084; STOCRIN (CAP) - EMEA/H/C/000250/SDA/073; NAP

Applicant(s): Bristol-Myers Squibb Pharma EEIG (Sustiva), Merck Sharp & Dohme B.V. (Stocrin), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Signal of microcephaly

Action: For adoption of PRAC recommendation

EPITT 19595 – Follow-up to October 2020

4.3.3. Trastuzumab emtansine - KADCYLA (CAP) - EMEA/H/C/002389/SDA/022

Applicant: Roche Registration GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of extravasation and epidermal necrosis

Action: For adoption of PRAC recommendation

EPITT 19611 – Follow-up to November 2020

4.4. Variation procedure(s) resulting from signal evaluation

None

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - EMEA/H/C/005737

Scope: Active immunisation for prevention of coronavirus disease-2019 (COVID-19) caused

by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in adults ≥ 18 years old

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

5.1.2. Eflornithine, sulindac - EMEA/H/C/005043, Orphan

Applicant: Cancer Prevention Pharma (Ireland) Limited

Scope: Treatment of adult patients with familial adenomatous polyposis (FAP)

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

5.1.3. Insulin human (rDNA) - EMEA/H/C/005331

Scope: Treatment of patients with diabetes mellitus who require intravenous insulin

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

5.1.4. Obeticholic acid - EMEA/H/C/005249

Scope: Improvement of liver fibrosis and resolution of steatohepatitis in adult patients with significant liver fibrosis due to non-alcoholic steatohepatitis (NASH)

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

5.1.5. Setmelanotide - EMEA/H/C/005089, Orphan

Applicant: Rhythm Pharmaceuticals Limited

Scope: Treatment of obesity and the control of hunger associated with deficiencies in the leptin-melanocortin pathway

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

5.1.6. Vericiguat - EMEA/H/C/005319

Scope: Treatment of symptomatic chronic heart failure

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. Alpelisib - PIQRAY (CAP) - EMEA/H/C/004804/II/0001

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 2.0) in order to replace the following studies (listed as category 3 studies in the RMP): 1) study CBYL719C2402: a retrospective cohort study to evaluate the risk of hyperglycaemia in patients with advanced breast cancer treated with Piqray (alpelisib) in the real world setting;;2) study CBYL719A0IC02: an open-label, multicentre, phase 3b study to evaluate the safety and tolerability of alpelisib in

combination with fulvestrant for the treatment of men and postmenopausal women with hormone receptor-positive (HR+), epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer with a PIK3CA⁹ mutation, after disease progression following an endocrine based regimen, with: 3) study CBYL719C2404: A non-interventional PASS of Piqray (alpelisib) in combination with fulvestrant in postmenopausal women, and men, with HR+, HER2 negative, locally advanced or metastatic breast cancer with a PIK3CA mutation in the real-world setting in European countries. Additionally, a separated healthcare professional (HCP) survey (CBYL719A0IC02) is proposed as part of the pharmacovigilance plan

Action: For adoption of PRAC Assessment Report

5.2.2. Cerliponase alfa - BRINEURA (CAP) - EMEA/H/C/004065/II/0027, Orphan

Applicant: BioMarin International Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 3.2) in order to change the final date for completion from July 2020 to May 2024 of the post-authorisation efficacy study (PAES) study 190-203: a phase 2, open-label, multicentre study to evaluate safety, tolerability, and efficacy of intra-cerebroventricular cerliponase alfa in paediatric patients < 18 years of age with neuronal ceroid lipofuscinosis type 2 (CLN2) disease

Action: For adoption of PRAC Assessment Report

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

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

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

Action: For adoption of PRAC Assessment Report

5.2.4. Lopinavir, ritonavir - LOPINAVIR/RITONAVIR MYLAN (CAP) - EMEA/H/C/004025/II/0016

Applicant: Mylan S.A.S

PRAC Rapporteur: Adrien Inoubli

⁹ Phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alfa

Scope: Submission of an updated RMP (version 4.0) in order to bring the RMP in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template) and revision 2 of GVP module V on 'Risk management systems' and to align the safety concerns with those of the reference medicinal product

Action: For adoption of PRAC Assessment Report

5.2.5. [Rasagiline - AZILECT \(CAP\) - EMEA/H/C/000574/WS2011/0087; RASAGILINE RATIOPHARM \(CAP\) - EMEA/H/C/003957/WS2011/0019](#)

Applicant: Teva B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of an updated RMP (version 3.0) following the completion of study TV1030-CNS-50024 (listed as a category 3 study in the RMP): a non-interventional retrospective cohort study which was conducted using the United States Medicare research database to assess the potential risk of melanoma associated with the use of rasagilline mesylate in patients with Parkinson's disease (as assessed and concluded in procedure WS/1749 finalised in September 2020). The MAH took the opportunity to introduce a minor update to the targeted follow-up questionnaire for the important potential risk of malignant melanoma and to revise the list of safety concerns in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.6. [Zoledronic acid - ACLASTA \(CAP\) - EMEA/H/C/000595/II/0076](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 13.0) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' including consequential removal/reclassification of a number of important potential risks; to remove the education material on renal dysfunction and use in patients with severe renal impairment; to remove 'post-dose symptoms' from the list of important identified risks as per the conclusions of LEG 037 adopted in September 2019 and variation II/74/G adopted in March 2020; to update the targeted questionnaire related to osteonecrosis of the jaw (ONJ) as per the conclusions of LEG 035 adopted in January 2017; to include the completed 5-year registry for study ZOL446H2422 (listed as a category 3 study in the RMP): a non-interventional post-authorisation safety study using health registries to compare safety of Aclasta (zoledronic acid) against oral bisphosphonates and untreated population controls as per the conclusions of variation II/69 adopted in January 2018. The additional risk minimisation measures in Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' are updated accordingly

Action: For adoption of PRAC Assessment Report

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

5.3.1. Andexanet alfa - ONDEXXYA (CAP) - EMEA/H/C/004108/II/0009/G

Applicant: Alexion Europe SAS

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations consisting of an update of section 5.2 of the SmPC in order to update pharmacokinetic (PK) information based on the clinical study results (CSR) from: 1) study 19-514 evaluating the PK comparability of generation 1 process 3 andexanet and generation 2 andexanet (PK comparability); 2) study 16-508: a phase 2 randomised, double-blind, placebo-controlled study to evaluate the efficacy, safety, tolerability and PK/pharmacodynamics (PD) of andexanet alfa administered to healthy Japanese and Caucasian subjects (Japanese ethnicity study). Annex II-D on 'Specific obligation to complete post-authorisation measures for the conditional marketing authorisation' is updated accordingly. The RMP (version 2.1) is updated in accordance

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

5.3.2. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/II/0080

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include treatment of lupus nephritis. 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 38) are updated in accordance

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

5.3.3. Ceritinib - ZYKADIA (CAP) - EMEA/H/C/003819/II/0034

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to reflect the results of study CLDK378A2112: a multicentre, randomized open label study to assess the systemic exposure, efficacy and safety of 450 mg ceritinib taken with a low-fat meal and 600 mg ceritinib taken with a low-fat meal as compared with that of 750 mg ceritinib taken in the fasted state in adult patients with anaplastic lymphoma kinase (ALK) rearranged (ALK-positive) metastatic non-small cell lung cancer (NSCLC). The package leaflet and the RMP (version 16.0) are updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1). The MAH also introduced other editorial changes including information on sodium content in line with the Annex to the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use' and the removal of the black triangle

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

5.3.4. [Deferasirox - EXJADE \(CAP\) - EMEA/H/C/000670/II/0075](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of the product information to remove discrepancies between SmPC and package leaflet in sections dedicated to pregnancy and breastfeeding. In addition, the product information is updated in line with the Annex to the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use' and in line with the latest quality review of documents (QRD) template (version 10.1). The MAH took the opportunity to update the details of local representatives in Estonia, Latvia and the Netherlands. The RMP (version 18.0) is updated to remove the important identified risk of 'severe cutaneous adverse reactions (including Stevens-Johnson syndrome, toxic epidermal necrolysis and drug reaction with eosinophilia and systemic symptoms)', to change the milestone for study CICL670E2422 (listed as a category 1 study in Annex II of the product information): an observational, multicentre study to evaluate the safety of deferasirox in the treatment of paediatric non transfusion dependant-thalassaemia (NTDT) patients over 10 years old for whom deferoxamine is contraindicated or inadequate; to change to RMP commitment deliverable and milestone for study CICL670F2202 (listed as a category 3 study in the RMP): a randomized, open-label, multicentre, two arm, phase 2 study to evaluate treatment compliance, efficacy and safety of an improved deferasirox formulation (granules) in paediatric patients with iron overload; and to remove study CICL670F2429 (listed as a category 1 study in Annex II): a single-arm interventional phase intravenous (IV), post-authorisation study evaluating the safety of paediatric patients with transfusional hemosiderosis treated with deferasirox crushed film coated tablets, due to fulfilment of the corresponding post-authorisation measure. Finally, the RMP is updated to remove the expedited reporting requirement for the serious adverse drug reactions (ADRs), 'increase in hepatic enzymes >10 x upper limit of normal (ULN)', 'serious rise in creatinine', 'results of renal biopsies', 'cataracts' and 'hearing loss' and 'gallstones as agreed in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00000939/201910) adopted in May 2020. Annex II of the product information is updated accordingly

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

5.3.5. [Dabrafenib - TAFINLAR \(CAP\) - EMEA/H/C/002604/II/0049](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Submission of the final report from study 201710 (listed as a category 3 study in the RMP): a non-interventional study to perform evaluation of secondary malignancies in patients treated with dabrafenib in randomized controlled trials. The RMP (version 10.0) is updated accordingly

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

5.3.6. [Evolocumab - REPATHA \(CAP\) - EMEA/H/C/003766/II/0048](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of the final report from study 20130286 (listed as a category 3 study in the RMP): a double blind, randomised, placebo controlled, multicentre study to evaluate safety, tolerability, and efficacy on low-density lipoprotein cholesterol (LDL-C) of evolocumab in human immunodeficiency virus (HIV) positive patients with hyperlipidemia and mixed dyslipidemia. The RMP (version 6.0) is updated accordingly

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

5.3.7. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/II/0095

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of section 4.2 of the SmPC to add a new posology for the rheumatoid arthritis indication that does not include intravenous (IV) induction doses prior subcutaneous use. The package leaflet and the RMP (version 13.1) are updated accordingly

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

5.3.8. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/II/0026, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Annika Folin

Scope: Update of Annex II-E on 'Specific obligation to complete post-authorisation measures for the conditional marketing authorisation' of the product information to reflect the completion of study C16014: a phase 3, randomized, double-blind, multicentre study comparing ixazomib plus lenalidomide and dexamethasone versus placebo plus lenalidomide and dexamethasone in adult patients with newly diagnosed multiple myeloma not eligible for stem cell transplantation (SCT) (in fulfilment of SOB 003). The RMP (version 5.1) is updated accordingly. In addition, a minor editorial change is proposed to section 4.2 of the SmPC in order to improve the consistency with other sections of the SmPC. Finally, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

5.3.9. Nilotinib - TASIGNA (CAP) - EMEA/H/C/000798/II/0107

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the 5 year data including data on late relapses from the following ongoing studies: 1) study CAMN107I2201 (ENESTfreedom): a phase 2, single-arm, open-label, multicentre nilotinib treatment-free remission (TFR) study in patients with breakpoint cluster region gene/Abelson proto-oncogene 1 (BCR-ABL1) positive chronic myeloid leukaemia in chronic phase (CML-CP), who had achieved durable minimal residual disease (MRD) status on first-line nilotinib treatment; 2) study CAMN107A2408 (ENESTop): a phase 2, single-arm, open-label, multicentre study, evaluating TFR in patients with BCR-ABL1-positive CML-CP who achieved a sustained molecular response of MR4.5 on nilotinib treatment after switching from imatinib to nilotinib. The RMP (version 23.0) is updated accordingly

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

5.3.10. [Ipilimumab - YERVOY \(CAP\) - EMEA/H/C/002213/WS1881/0085; nivolumab - OPDIVO \(CAP\) - EMEA/H/C/003985/WS1881/0091](#)

Applicant(s): Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include first-line treatment of adult patients with unresectable malignant pleural mesothelioma (MPM) for Opdivo (nivolumab) in combination with Yervoy (ipilimumab). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 20.0 for Opdivo, version 30.0 for Yervoy) are updated in accordance

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

5.3.11. [Ivacaftor - KALYDECO \(CAP\) - EMEA/H/C/002494/II/0089, Orphan](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to extend the indication of Kalydeco (ivacaftor) tablets in combination regimen with Kaftrio (ivacaftor/tezacaftor/elexacaftor) tablets for the treatment of adults and adolescents aged 12 years and older with cystic fibrosis (CF) who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. As a consequence, sections 4.1, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 9.2) are updated in accordance

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

5.3.12. [Ivacaftor, tezacaftor, elexacaftor - KAFTRIO \(CAP\) - EMEA/H/C/005269/II/0001, Orphan](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to patients with cystic fibrosis (CF) aged 12 years and older who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR gene), regardless of the second allele (F/any), based on efficacy data from study 104: a phase 3, randomized, double-blind, controlled study evaluating the efficacy and safety of elexacaftor (VX-445) combination therapy in subjects with CF who are heterozygous for the F508del mutation and a gating or residual function mutation (F/G and F/RF genotypes). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 1.1) are updated accordingly

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

5.3.13. [Migalastat - GALAFOLD \(CAP\) - EMEA/H/C/004059/II/0029, Orphan](#)

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include long-term treatment of adolescents 12 to < 16 years with a confirmed diagnosis of Fabry disease (α -galactosidase A deficiency) and who have an amenable mutation. As a consequence, sections 4.1, 4.2, 4.8 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 4.0) are updated accordingly

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

5.3.14. Migalastat - GALAFOLD (CAP) - EMEA/H/C/004059/II/0030, Orphan

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 5.1 of the SmPC based on final results from study AT1001-042 (listed as a category 3 study in the RMP: an open-label, non-comparative, long-term extension study to evaluate long term safety and efficacy of migalastat in monotherapy in subjects with Fabry disease. The RMP (version 5.0) is updated accordingly

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

5.3.15. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0095

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include adjuvant treatment of adult patients with resected oesophageal, or gastro-oesophageal junction cancer who have residual pathologic disease following prior neoadjuvant chemoradiotherapy based on study CA209-577: a randomized, multicenter, double blind, phase 3 study of adjuvant nivolumab or placebo in subjects with resected esophageal, or gastroesophageal junction cancer. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 22.0) are updated in accordance

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

5.3.16. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0096

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to use Opdivo (nivolumab) in combination with fluoropyrimidine- and platinum-based combination chemotherapy, in first-line treatment of adult patients with advanced or metastatic gastric, gastro-oesophageal junction (GEJ) or oesophageal adenocarcinoma based on study CA209-649: a randomized, multicentre, open-label, phase 3 study of nivolumab plus ipilimumab or nivolumab in combination with oxaliplatin plus fluoropyrimidine versus oxaliplatin plus fluoropyrimidine in subjects with previously untreated advanced or metastatic gastric or gastroesophageal junction cancer. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 21.0) are updated in accordance

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

5.3.17. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0098

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 5.1 of the SmPC in order to update overall survival (OS) information based on the final OS data for study CA209-238 (listed as an obligation in the Annex II and in the RMP): a Phase 3, randomised double-blind study of Opdivo (nivolumab) versus Yervoy (ipilimumab) in patients who have undergone complete resection of stage IIIb/c or stage IV melanoma. The MAH took also the opportunity to update section 4.8 of the SmPC to pull the safety data sets of nivolumab as monotherapy across advanced metastatic and adjuvant settings. The package leaflet and the RMP (version 17.2) are updated accordingly. Finally, the MAH took the opportunity to introduce minor editorial and formatting revisions throughout the product information

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

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

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

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

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

5.3.19. Parathyroid hormone - NATPAR (CAP) - EMEA/H/C/003861/II/0026, Orphan

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final results for study PAR-C10-008: a long-term open-label study investigating the safety and tolerability of a Natpar (parathyroid hormone) for the treatment of adults with hypoparathyroidism – a clinical extension study (RACE). As a consequence, section 5.1 of the SmPC is updated to reflect 72-month data from the study. The RMP (version 3.0) is updated accordingly and in line with revision 2 of GVP module V on 'Risk management systems'

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

5.3.20. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0099

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication for Keytruda (pembrolizumab) to include in combination with chemotherapy, treatment of locally recurrent unresectable or metastatic triple negative breast cancer in adults whose tumours express programmed death-ligand 1 (PD-L1) with a combined positive score (CPS) ≥ 10 and who have not received prior chemotherapy for metastatic disease. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 31.1) are updated in accordance

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

5.3.21. Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/II/0023/G, Orphan

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped variations consisting of an update of sections 4.2, 4.4, 4.5, 5.1 and 5.2 of the SmPC based on new clinical data from: 1) study P09-10 (HARMONY III): an open-label naturalistic pragmatic study to assess the long-term safety of pitolisant in the treatment of excessive daytime sleepiness (EDS) (with or without cataplexy) in narcolepsy; 2) study P16-02: a randomised, double-blind, active- and placebo-controlled, single-dummy, 4-way crossover study to determine the abuse potential of pitolisant compared to phentermine and placebo, in healthy, non-dependent recreational stimulant users. The proposed update also includes results of a post approval network meta-analysis which compares efficacy and safety of multiple treatments, multi-arm studies, and multi-criteria treatment decisions. The package leaflet and the RMP (version 6.0) are updated accordingly

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

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

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Extension of indication to include primary treatment of invasive aspergillosis in adults and adolescents from 13 years of age for Noxafil gastroresistant tablet and concentrate for solution for infusion based on the results of study P069: a phase 3 randomized study of the efficacy and safety of posaconazole versus voriconazole for the treatment of invasive aspergillosis. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 16.2) are updated in accordance

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

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

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Grouped applications consisting of: 1) extension application to introduce a new pharmaceutical form (gastro-resistant powder and solvent for oral suspension); 2) extension of indication to the paediatric population. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The package leaflet and the RMP (version 17.1) are updated in accordance

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

5.3.24. Saxagliptin, dapagliflozin - QTERN (CAP) - EMEA/H/C/004057/II/0031

Applicant: AstraZeneca AB

PRAC Rapporteur: Ilaria Baldelli

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to reflect new data based on final results from study D1693C00001 (DECLARE): a multi-centre, randomised, double-blind, placebo-controlled study to evaluate the effect of dapagliflozin on cardiovascular (CV) and renal outcomes in patients with type 2 diabetes mellitus (T2DM) with or without established CV disease. The labelling, package leaflet and the RMP (version 5.1) are updated accordingly. The MAH took the opportunity to introduce additional editorial changes to the product information

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

5.3.25. Tedizolid phosphate - SIVEXTRO (CAP) - EMEA/H/C/002846/II/0037

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of section 5.1 of the SmPC in order to update the description of the potential risk of emergence of drug resistance with tedizolid phosphate based on final results from study 'surveillance of tedizolid activity and resistance (STAR)' (listed as a category 3 study in the RMP): a surveillance study established in January 2014 to monitor tedizolid susceptibility activity and emergence of resistance across the US, 11 European Union countries, Russia and Turkey. The RMP (version 6.2) is updated accordingly

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

5.3.26. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/X/0024/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Grouped application consisting of: 1) extension application to introduce a new pharmaceutical form (oral solution, 1 mg/mL); 2) addition of a new indication as treatment of active polyarticular juvenile idiopathic arthritis (pJIA) in patients of 2 years of age and older. The RMP (version 12.1) is updated in accordance. The MAH took the opportunity to align the product information with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.27. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0027

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 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 active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have been intolerant to a prior disease modifying antirheumatic drug therapy; as an alternative to the immediate release film-coated tablets. Section 4.2 of the SmPC for Xeljanz (tofacitinib) film-coated tablets is also updated to include switching with the prolonged-release tablet in the treatment of PsA. The package leaflet and the RMP (version 13.1) are updated accordingly

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

5.3.28. Trametinib - MEKINIST (CAP) - EMEA/H/C/002643/II/0043

Applicant: Novartis Europharm Limited

PRAC Rapporteur: David Olsen

Scope: Submission of the final report from study 201711 (listed as a category 3 study in the RMP): a study to identify and characterize the risk of cardiomyopathy and subsequent sequelae, including safety evaluations of patient populations at highest risk for developing these toxicities, based on 7 randomized controlled clinical studies with trametinib monotherapy or in combination with other anti-cancer agents. The RMP (version 17.0) is updated accordingly

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

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

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

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

5.3.30. 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. Afibercept¹⁰ - ZALTRAP (CAP) - PSUSA/00010019/202008

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Apalutamide - ERLEADA (CAP) - PSUSA/00010745/202008

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Asenapine - SYCREST (CAP) - PSUSA/00000256/202008

Applicant: N.V. Organon

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Ataluren - TRANSLARNA (CAP) - PSUSA/00010274/202007

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁰ Oncological indication(s) only

6.1.5. Baricitinib - OLUMIANT (CAP) - PSUSA/00010578/202008

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Bempedoic acid - NILEMDO (CAP); bempedoic acid, ezetimibe - NUSTENDI (CAP) - PSUSA/00010841/202008

Applicant(s): Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Bictegravir, emtricitabine, tenofovir alafenamide - BIKTARVY (CAP) - PSUSA/00010695/202008

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Botulinum toxin type A - NUCEIVA (CAP) - PSUSA/00010796/202007

Applicant: Evolus Pharma Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Burosumab - CRYSVITA (CAP) - PSUSA/00010669/202008

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Catridecacog - NOVOTHIRTEEN (CAP) - PSUSA/00010034/202007

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Chlormethine - LEDAGA (CAP) - PSUSA/00010587/202008

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Cobicistat - TYBOST (CAP) - PSUSA/00010081/202008

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Cobicistat, elvitegravir, emtricitabine, tenofovir disoproxil - STRIBILD (CAP) - PSUSA/00010082/202008

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Cobimetinib - COTELLIC (CAP) - PSUSA/00010450/202008

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Corifollitropin alfa - ELONVA (CAP) - PSUSA/00000875/202007

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Daunorubicin, cytarabine - VYXEOS LIPOSOMAL (CAP) - PSUSA/00010701/202008

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Eliglustat - CERDELGA (CAP) - PSUSA/00010351/202008

Applicant: Genzyme Europe BV

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Eravacycline - XERAVA (CAP) - PSUSA/00010718/202008

Applicant: Tetrphase Pharmaceuticals Ireland Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - PSUSA/00010352/202008

Applicant: Holostem Therapie Avanzate s.r.l., ATMP¹¹

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.20. Ferric maltol - FERACCRU (CAP) - PSUSA/00010476/202008

Applicant: Norgine B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Hydrocortisone¹² - ALKINDI (CAP) - PSUSA/00010674/202008

Applicant: Diurnal Europe BV

¹¹ Advanced therapy medicinal product

¹² Centrally authorised product(s) for adrenal insufficiency, paediatric use only

PRAC Rapporteur: Annika Folin
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.22. Ibuprofen¹³ - PEDEA (CAP) - PSUSA/00001712/202007

Applicant: Recordati Rare Diseases
PRAC Rapporteur: Rhea Fitzgerald
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.23. Lamivudine¹⁴ - ZEFFIX (CAP) - PSUSA/00001824/202007

Applicant: GlaxoSmithKline (Ireland) Limited
PRAC Rapporteur: Adrien Inoubli
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.24. Lanadelumab - TAKHZYRO (CAP) - PSUSA/00010743/202008

Applicant: Shire Pharmaceuticals Ireland Limited
PRAC Rapporteur: Kirsti Villikka
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.25. Lefamulin - XENLETA (CAP) - PSUSA/00010872/202008

Applicant: Nabriva Therapeutics Ireland DAC
PRAC Rapporteur: Eva Jirsová
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.26. Lomitapide - LOJUXTA (CAP) - PSUSA/00010112/202007

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

¹³ Indicated for the treatment of ductus arteriosus only

¹⁴ Indicated for the treatment of chronic hepatitis B only

6.1.27. [Methoxy polyethylene glycol-epoetin beta - MIRCERA \(CAP\) - PSUSA/00002017/202007](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. [Natalizumab - TYSABRI \(CAP\) - PSUSA/00002127/202008](#)

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. [Nonacog alfa - BENEFIX \(CAP\) - PSUSA/00002183/202008](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. [Palbociclib - IBRANCE \(CAP\) - PSUSA/00010544/202008](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. [Panobinostat - FARYDAK \(CAP\) - PSUSA/00010409/202008](#)

Applicant: Secura Bio Limited

PRAC Rapporteur: Sofia Trantza

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. [Patisiran - ONPATTRO \(CAP\) - PSUSA/00010715/202008](#)

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. [Pyronaridine, artesunate - PYRAMAX \(Art 58¹⁵\) - EMEA/H/W/002319/PSUV/0022](#)

Applicant: Shin Poong Pharmaceutical Co., Ltd.

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.34. [Ropeginterferon alfa-2b - BESREMI \(CAP\) - PSUSA/00010756/202008](#)

Applicant: AOP Orphan Pharmaceuticals AG

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. [Sacubitril, valsartan - ENTRESTO \(CAP\); NEPARVIS \(CAP\) - PSUSA/00010438/202007](#)

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. [Saxagliptin - ONGLYZA \(CAP\) - PSUSA/00002685/202007](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. [Sitagliptin - JANUVIA \(CAP\); RISTABEN \(CAP\); TESAVEL \(CAP\); XELEVIA \(CAP\); sitagliptin, metformin hydrochloride - EFFICIB \(CAP\); JANUMET \(CAP\); RISTFOR \(CAP\); VELMETIA \(CAP\) - PSUSA/00010673/202008 \(with RMP\)](#)

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

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.1.38. [Smallpox vaccine \(live, modified vaccinia Ankara virus\) - IMVANEX \(CAP\) - PSUSA/00010119/202007](#)

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. [Telotristat - XERMELO \(CAP\) - PSUSA/00010639/202008](#)

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. [Tezacaftor, ivacaftor - SYMKEVI \(CAP\) - PSUSA/00010730/202008](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. [Tisagenlecleucel - KYMRIAHA \(CAP\) - PSUSA/00010702/202008 \(with RMP\)](#)

Applicant: Novartis Europharm Limited, ATMP¹⁶

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.42. [Tocofersolan - VEDROP \(CAP\) - PSUSA/00002981/202007](#)

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. [Upadacitinib - RINVOQ \(CAP\) - PSUSA/00010823/202008](#)

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

¹⁶ Advanced therapy medicinal product

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Zanamivir¹⁷ - DECTOVA (CAP) - PSUSA/00010763/202007

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. Buprenorphine¹⁸ - BUVIDAL (CAP); NAP - PSUSA/00000459/202007

Applicants: Camurus AB (Buvidal), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Duloxetine - CYMBALTA (CAP); DULOXETINE LILLY (CAP); NODETRIP (CAP); YENTREVE (CAP); NAP - PSUSA/00001187/202008

Applicants: Eli Lilly Nederland B.V. (Cymbalta, Duloxetine Lilly, Yentreve), Esteve Pharmaceuticals S.A. (Nodetrip), various

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Human protein C - CEPROTIN (CAP); NAP - PSUSA/00002563/202007

Applicants: Takeda Manufacturing Austria AG (Ceprotin), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁷ Centrally authorised product(s) only

¹⁸ All formulation(s) except implant(s)

6.2.4. Ribavirin¹⁹ - REBETOL (CAP); NAP - PSUSA/00010007/202007

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

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Temozolomide - TEMODAL (CAP); NAP - PSUSA/00002886/202007

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

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Aciclovir, hydrocortisone (NAP) - PSUSA/00009004/202007

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Cisatracurium (NAP) - PSUSA/00000777/202007

Applicant(s): various

PRAC Lead: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Dimetindene, phenylephrine (NAP) - PSUSA/00001102/202007

Applicant(s): various

PRAC Lead: Marek Juracka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

¹⁹ Oral formulation(s) only

6.3.4. Epinephrine (NAP) - PSUSA/00001232/202007

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Escherichia coli lysate (NAP) - PSUSA/00001263/202007

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Ezetimibe, rosuvastatin (NAP) - PSUSA/00010271/202007

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Fenofibrate (NAP) - PSUSA/00001362/202007

Applicant(s): various

PRAC Lead: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Fluocinolone acetonide²⁰ (NAP) - PSUSA/00010224/202008

Applicant(s): various

PRAC Lead: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Fosphenytoin (NAP) - PSUSA/00001476/202008

Applicant(s): various

PRAC Lead: Ronan Grimes

²⁰ Intravitreal implant(s) in applicator only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Glyceryl trinitrate (NAP) - PSUSA/00001552/202007

Applicant(s): various

PRAC Lead: Gabriela Jazbec

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Ibuprofen, levomenthol (NAP) - PSUSA/00001708/202007

Applicant(s): various

PRAC Lead: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Ifosfamide (NAP) - PSUSA/00001723/202007

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Imipramine (NAP) - PSUSA/00001728/202007

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Indium (¹¹¹In) pentetate (NAP) - PSUSA/00009191/202007

Applicant(s): various

PRAC Lead: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Indium (¹¹¹In) pentetate (NAP) - PSUSA/00009192/202007

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Indometacin (NAP) - PSUSA/00001738/202007

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Lidocaine hydrochloride, methylprednisolone acetate (NAP) - PSUSA/00001879/202008

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Naftifine (NAP) - PSUSA/00002109/202008

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Naproxen (NAP) - PSUSA/00002125/202008

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Niclosamide (NAP) - PSUSA/00002151/202008

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Oxymetazoline (NAP) - PSUSA/00002258/202008

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Pethidine (NAP) - PSUSA/00002357/202008

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Quetiapine (NAP) - PSUSA/00002589/202007

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Trimetazidine (NAP) - PSUSA/00003043/202008

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Typhoid polysaccharide vaccine (NAP) - PSUSA/00003065/202008

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Ziprasidone (NAP) - PSUSA/00003146/202007

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/LEG 015

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Martin Huber

Scope: Detailed review of cases of pancreatitis as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010077/202003) adopted in November 2020

Action: For adoption of advice to CHMP

6.4.2. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/LEG 014

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Detailed review of cases of pancreatitis as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010077/202003) adopted in November 2020

Action: For adoption of advice to CHMP

6.4.3. Choriogonadotropin alfa - OVITRELLE (CAP) - EMEA/H/C/000320/LEG 055.1

Applicant: Merck Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to LEG 055 [detailed review of criteria for classification of events as 'non-reactions' and methodology for causality assessment as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00000736/201909) adopted in April 2020] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/II/0114

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 6.6 of the SmPC in order to add a new warning that the medicine should be allowed to reach room temperature before use, based on cumulative reviews of post-marketing reports of medication errors with the on-body injector (OBI) following the

conclusions of MEA 060.3 adopted in September 2020

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews²¹

6.6.1. Coronavirus (COVID-19) mRNA²² vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 002.2

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

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

Action: For adoption of PRAC Assessment Report

6.6.2. Coronavirus (COVID-19) mRNA²³ vaccine (nucleoside-modified) - COVID-19 VACCINE MODERNA (CAP) - EMEA/H/C/005791/MEA 011.1

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

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

Action: For adoption of PRAC Assessment Report

6.6.3. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - COVID-19 VACCINE ASTRAZENECA (CAP) - EMEA/H/C/005675/MEA 027

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: First expedited monthly summary safety report for COVID-19 Vaccine AstraZeneca (COVID-19 vaccine vaccine (ChAdOx1-S [recombinant]))

Action: For adoption of PRAC Assessment Report

²¹ 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

²² Messenger ribonucleic acid

²³ Messenger ribonucleic acid

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)²⁴

7.1.1. Betibeglogene autotemcel - ZYNTGLO (CAP) - EMEA/H/C/PSP/S/0090

Applicant: Bluebird bio (Netherlands) B.V., ATMP²⁵

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Protocol for study REG-504: a non-interventional post-authorisation safety and efficacy study to further characterise and contextualise the long-term safety and efficacy of Zynteglo (betibeglogene autotemcel) in patients aged 12 years and older with transfusion-dependent β -thalassaemia (TDT) who do not have a β^0/β^0 genotype

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

7.1.2. Eliglustat - CERDELGA (CAP) - EMEA/H/C/PSA/S/0054.2

Applicant: Genzyme Europe BV

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to PSA/S/0054.1 [substantial amendment to a protocol previously agreed in December 2018 (PSA/S/0035) for a prospective multicentre observational post authorisation safety sub-registry to characterise the long-term safety profile of commercial use of Cerdelga (eliglustat) in adult patients with Gaucher disease] as per the request for supplementary information (RSI) adopted in November 2020

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

7.1.3. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/PSA/S/0067

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Substantial amendment to a protocol previously agreed in September 2016 (PSP/0020.3) for study CC-5013-MM-034: a prospective non-interventional PASS of lenalidomide in previously untreated adult multiple myeloma patients who are not eligible for transplant (Revlimid TNE NDMM PASS)

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

7.1.4. Voretigene neparovvec - LUXTURNA (CAP) - EMEA/H/C/PSA/S/0066

Applicant: Novartis Europharm Limited; ATMP²⁶

PRAC Rapporteur: Brigitte Keller-Stanislawski

²⁴ In accordance with Article 107n of Directive 2001/83/EC

²⁵ Advanced therapy medicinal product

²⁶ Advanced therapy medicinal product

Scope: Substantial amendment to a protocol previously agreed in July 2019 (PSP/S/0078.1) for a post-authorisation multicentre, multinational, longitudinal, observational safety registry study to collect long-term safety information associated with voretigene neparvovec (vector and/or transgene), its subretinal injection procedure, the concomitant use of corticosteroids, or a combination of these procedures and products

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)²⁷

7.2.1. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - COVID-19 VACCINE ASTRAZENECA (CAP) - EMEA/H/C/005675/MEA 006.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to MEA 006 [protocol for study AZD1222: a pregnancy registry of women exposed to AZD1222 (COVID-19 Vaccine AstraZeneca (COVID-19 vaccine)) immediately before or during pregnancy (C-VIPER) (from initial opinion/marketing authorisation(s) (MA))] as per the request for supplementary information (RSI) adopted in February 2021

Action: For adoption of advice to CHMP

7.2.2. Coronavirus (COVID-19) mRNA²⁸ vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 011

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study C4591010: assessment of occurrence of safety events in real-world use of COVID-19 mRNA vaccine [final clinical study report (CSR) expected in March 2024] (from initial opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.2.3. Coronavirus (COVID-19) mRNA²⁹ vaccine (nucleoside-modified) - COVID-19 VACCINE MODERNA (CAP) - EMEA/H/C/005791/MEA 003

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

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

²⁷ 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

²⁸ Messenger ribonucleic acid

²⁹ Messenger ribonucleic acid

Action: For adoption of advice to CHMP

7.2.4. [Coronavirus \(COVID-19\) mRNA³⁰ vaccine \(nucleoside-modified\) - COVID-19 VACCINE MODERNA \(CAP\) - EMEA/H/C/005791/MEA 005](#)

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

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

Action: For adoption of advice to CHMP

7.2.5. [Dimethyl fumarate - TECFIDERA \(CAP\) - EMEA/H/C/002601/MEA 008.5](#)

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Amendment to a protocol previously agreed in September 2020 for study 109MS402: Biogen multiple sclerosis (MS) pregnancy exposure registry to prospectively evaluate pregnancy outcomes in women with MS who were exposed to a registry-specified Biogen MS product during the eligibility window for that product

Action: For adoption of advice to CHMP

7.2.6. [Esketamine - SPRAVATO \(CAP\) - EMEA/H/C/004535/MEA 002.1](#)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Kirsti Villikka

Scope: MAH's response to MEA 002 [protocol for a pregnancy registry study (listed as a category 3 study in the RMP) using the National Pregnancy Registry for Psychiatric Medications (NPRPM) in order to further characterise the impact of the missing information of use during pregnancy on the safety profile of esketamine nasal spray and obtain information on the frequency of major malformations (from initial opinion/marketing authorisation) [final report expected in Q4 2024]] as per the request for supplementary information (RSI) adopted in October 2020

Action: For adoption of advice to CHMP

7.2.7. [Gilteritinib - XOSPATA \(CAP\) - EMEA/H/C/004752/MEA 004.1](#)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 004 [protocol for study 2215-PV-0001: a cross-sectional survey study among healthcare professionals (HCPs) to assess awareness and knowledge,

³⁰ Messenger ribonucleic acid

an evaluation of the effectiveness of a Xospata (gilteritinib) routine risk minimisation measures (RMM) and an additional risk minimisation measure (aRMM)] as per the request for supplementary information (RSI) adopted in October 2020

Action: For adoption of advice to CHMP

7.2.8. Isatuximab - SARCLISA (CAP) - EMEA/H/C/004977/MEA 002

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: 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)

Action: For adoption of advice to CHMP

7.2.9. Ixekizumab - TALTZ (CAP) - EMEA/H/C/003943/MEA 005

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Protocol for study I1F-MC-B015: an observational post-marketing safety study of ixekizumab and other systemic and non-systemic treatments for paediatric psoriasis to further characterise the long-term safety of ixekizumab in paediatric patients with psoriasis with a focus on the important identified risks of inflammatory bowel disease (IBD) and serious infections

Action: For adoption of advice to CHMP

7.2.10. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 002.7

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Substantial amendment to a protocol previously agreed in July 2020 for study D3820R00006: a post-marketing observational drug utilisation study (DUS) of Moventig (naloxegol) conducted in selected European populations in order to describe demographic, clinical, and treatment characteristics in the baseline of patients treated with naloxegol as well as to describe treatment pattern characteristics of naloxegol utilisation at initiation and follow-up

Action: For adoption of advice to CHMP

7.2.11. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 006.9

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Substantial amendment to a protocol previously agreed in December 2018 for study D3820R00009 (previously study D2288R00084): an observational PASS of Moventig

(naloxegol) among patients aged 18 years and older treated with opioids chronically

Action: For adoption of advice to CHMP

7.2.12. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/MEA 002.3

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 002.2 [protocol for study PUMA-NER-6202: a randomised study to characterise the incidence and severity of diarrhoea in patients with early stage epidermal growth factor receptor 2 + (HER2+) breast cancer treated with neratinib and intensive loperamide prophylaxis versus neratinib and intensive loperamide prophylaxis plus a bile acid sequestrant in the first month of treatment [final study results expected in December 2021]] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.2.13. Netarsudil - RHOKIINSA (CAP) - EMEA/H/C/004583/MEA 001.1

Applicant: Aerie Pharmaceuticals Ireland Limited

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 001 [Protocol for study AR-13324-OBS02: a non-interventional, observational cohort study to investigate the long-term safety of netarsudil beyond 12 months treatment [final clinical study report (CSR) expected in June 2026]] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.2.14. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/MEA 001

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 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] (from initial marketing authorisation/opinion)

Action: For adoption of advice to CHMP

7.2.15. Semaglutide - OZEMPIC (CAP) - EMEA/H/C/004174/MEA 002.2

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: MAH's response to MEA 002.1 [substantial amendment to a protocol previously agreed in September 2018 (MEA 002) for study NN9535-4447: an epidemiological database study to estimate the risk of pancreatic cancer in patients with type 2 diabetes mellitus

(T2DM) taking semaglutide - a cohort study based on Nordic registry data [final study report expected 5 years after start of study]] as per the request for supplementary information (RSI) adopted in November 2020

Action: For adoption of advice to CHMP

7.2.16. Semaglutide - RYBELSUS (CAP) - EMEA/H/C/004953/MEA 001

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Protocol for study MTC-22341: a medullary thyroid carcinoma surveillance study, a case-series registry of at least 15 years duration to systematically monitor the annual incidence of medullary thyroid carcinoma in the US and to identify any increase related to the introduction of semaglutide into the marketplace [final study report expected in February 2037] (from initial opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.2.17. Semaglutide - RYBELSUS (CAP) - EMEA/H/C/004953/MEA 002.1

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: MAH's response to MEA 002 [substantial amendment to a protocol previously agreed in September 2018 (MEA 002) for study NN9535-4447: an epidemiological database study to estimate the risk of pancreatic cancer in patients with type 2 diabetes mellitus (T2DM) taking semaglutide - a cohort study based on Nordic registry data [final study report expected 5 years after start of study]] as per the request for supplementary information (RSI) adopted in November 2020

Action: For adoption of advice to CHMP

7.2.18. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 044.10

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 044.9 [substantial amendment to a protocol previously agreed in October 2019 for study CNTO1275PSO4056: an observational PASS of ustekinumab in the treatment of paediatric patients aged 12 years and older with moderate to severe plaque psoriasis (adolescent registry)] as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)³¹

7.3.1. Iron^{32 33} (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 for 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 October 2020

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

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

Applicant: Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Final study report comprising the pharmaco-epidemiological study programme of rivaroxaban use and potential adverse outcomes in routine clinical practice in the UK, Germany, the Netherlands and Sweden

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

7.4. Results of PASS non-imposed in the marketing authorisation(s)³⁴

7.4.1. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/II/0068

Applicant: Bayer AG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of the final study report for the study (listed as a category 3 study in the RMP) evaluating physician knowledge of safety and safe use information for aflibercept in Europe: a follow-up physician survey. The RMP (version 27.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

³¹ In accordance with Article 107p-q of Directive 2001/83/EC

³² Intravenous (IV)

³³ Iron(III)-hydroxide dextran complex, iron sucrose complex/iron(III)-hydroxide sucrose complex, ferric carboxymaltose complex, iron(III) isomaltoside complex, sodium ferric gluconate complex

³⁴ In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

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

Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

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

Action: For adoption of PRAC Assessment Report

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of the final clinical study report (CSR) for study B1781044 (listed as a category 3 study in the RMP): a study to estimate the incidence and to compare the risks of endometrial hyperplasia and endometrial cancer in postmenopausal women initiating either Duavive (estrogens conjugated/bazedoxifene) or estrogen + progestin (E+P) combination hormone replacement therapy (HRT)

Action: For adoption of PRAC Assessment Report

7.4.4. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0039, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Submission of the final report from study 20180138 (listed as a category 3 study in the RMP: a long-term follow-up of adult Philadelphia chromosome-negative acute lymphoblastic leukaemia (ALL) relapsed refractory patients enrolled in study 00103311: a phase 3, randomized, open label study investigating the efficacy of the blinatumomab versus standard of care chemotherapy in adult subjects with relapsed/refractory B-precursor ALL (TOWER Study), in order to update the overall survival (OS) Kaplan-Meier probability estimates

Action: For adoption of PRAC Assessment Report

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

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

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

Action: For adoption of PRAC Assessment Report

7.4.6. [Epoetin zeta - RETACRIT \(CAP\) - EMEA/H/C/000872/II/0100](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

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

Action: For adoption of PRAC Assessment Report

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

Applicant: Stada Arzneimittel AG

PRAC Rapporteur: Martin Huber

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

Action: For adoption of PRAC Assessment Report

7.4.8. [Ivacaftor - KALYDECO \(CAP\) - EMEA/H/C/002494/II/0094, Orphan](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final report from study VX15-770-122 (listed as a category 3 study in the RMP): a study in US cystic fibrosis patients with the R117H-CFTR mutation to confirm the long-term safety and effectiveness of Kalydeco (ivacaftor) including patients <18 years of age, combining data captured in the cystic fibrosis foundation patient registry from an interventional cohort and a non-interventional cohort. In addition, the MAH took the opportunity to propose a change of due date for study 126 (listed as a category 3 in the RMP): a phase 3, 2-arm, open-label study to evaluate the safety and pharmacodynamics of long-term ivacaftor treatment in subjects with cystic fibrosis who are less than 24 months of age at treatment initiation and have an approved ivacaftor-responsive mutation. The RMP (version 10.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.9. [Lipegfilgrastim - LONQUEX \(CAP\) - EMEA/H/C/002556/II/0062](#)

Applicant: Teva B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Submission of the final report from study XM22-ONC-5002 (listed as a category 3 study in the RMP): a drug utilisation study (DUS) on the prescribing patterns of lipegfilgrastim in the EU. The RMP (version 13.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.10. Lurasidone - LATUDA (CAP) - EMEA/H/C/002713/II/0033

Applicant: Aziende Chimiche Riunite Angelini Francesco A.C.R.A.F. S.p.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final study report for a non-interventional PASS on the evaluation of the safety profile of lurasidone: a PASS using United States administrative claims databases in order to compare the incidence of important identified risks and important potential risks in patients treated with lurasidone to patients treated with other second-generation oral atypical antipsychotics (OAAs)

Action: For adoption of PRAC Assessment Report

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

7.5.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.10

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

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

Action: For adoption of advice to CHMP

7.5.2. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 024.14

Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: Annual report 2020 on adverse events and/or lack of efficacy, immunological data, follow-up growth disturbances in children and data on urinary hexose tetrasaccharide (Hex4) from the Pompe registry: a global, multicentre, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease irrespective of treatment status [final clinical study report expected in Q4 2021]

Action: For adoption of advice to CHMP

7.5.3. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 025.14

Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: Annual report 2020 on data on patients with renal or hepatic insufficiency from the Pompe registry: a global, multicentre, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease irrespective of treatment status [final clinical study report expected in Q4 2021]

Action: For adoption of advice to CHMP

7.5.4. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/MEA 017.7

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Fourth interim report for study ALIROC07997: a non-interventional safety study using healthcare databases to monitor the safety of Praluent (alirocumab) in patients affected with human immunodeficiency virus (HIV)]

Action: For adoption of advice to CHMP

7.5.5. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/MEA 006.5

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Five-year interim results for the UK clinical practice research datalink (CPRD) database data analysis for psoriatic arthritis (PsA) and psoriasis [due date: CPRD data analysis at years 1, 3 and 5 starting from the date of first commercial availability in the UK. Final clinical study report (CSR) expected in June 2021]

Action: For adoption of advice to CHMP

7.5.6. Cinacalcet - MIMPARA (CAP) - EMEA/H/C/000570/MEA 035.2

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: First interim report for study 20180204: a registry study to evaluate the incidence and risk of hypocalcaemia in paediatric patients treated with cinacalcet with secondary hyperparathyroidism receiving maintenance dialysis within the International Pediatric Dialysis Network (IPDN) registry

Action: For adoption of advice to CHMP

7.5.7. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/LEG 041.1

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual interim report year for study 20090522: a PASS on denosumab global safety assessment among women with postmenopausal osteoporosis (PMO) and men with osteoporosis in multiple observational databases [final report expected in 2023]

Action: For adoption of advice to CHMP

7.5.8. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/MEA 053.4

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Biennial interim report for study M07-001: a prospective registry for an observational, multicentre, multinational study of patients with paroxysmal nocturnal haemoglobinuria (PNH) including MAH's response to MEA 051.1 as per the request for supplementary information (RSI) adopted in March 2019

Action: For adoption of advice to CHMP

7.5.9. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 005.3

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Fourth interim report for enhanced pharmacovigilance study 1245.146 to evaluate the risk of diabetic ketoacidosis (DKA) in patients treated with empagliflozin-containing product(s) as discussed with the FDA and requested in the conclusions of the referral procedure on sodium-glucose cotransporter-2 (SGLT2) inhibitors under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA) (EMEA/H/A-20/1419) finalised in 2016 [final clinical study report (CSR) expected in Q4/2021], including MAH's responses to MEA 005.2 as per the request for supplementary information (RSI) adopted in March 2020

Action: For adoption of advice to CHMP

7.5.10. Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/MEA 005.3

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Fourth interim report for enhanced pharmacovigilance study 1245.146 to evaluate the risk of diabetic ketoacidosis (DKA) in patients treated with empagliflozin-containing product(s) as discussed with the FDA and requested in the conclusions of the referral procedure on sodium-glucose cotransporter-2 (SGLT2) inhibitors under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA) (EMEA/H/A-20/1419) finalised in 2016 [final clinical study report (CSR) expected in Q4/2021], including MAH's responses to MEA 005.2 as per the request for supplementary information (RSI) adopted in March 2020

Action: For adoption of advice to CHMP

7.5.11. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 002.3

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Fourth interim report for enhanced pharmacovigilance study 1245.146 to evaluate the risk of diabetic ketoacidosis (DKA) in patients treated with empagliflozin-containing product(s) as discussed with the FDA and requested in the conclusions of the referral procedure on sodium-glucose cotransporter-2 (SGLT2) inhibitors under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA) (EMA/H/A-20/1419) finalised in 2016 [final clinical study report (CSR) expected in Q4/2021], including MAH's responses to MEA 002.2 as per the request for supplementary information (RSI) adopted in March 2020

Action: For adoption of advice to CHMP

7.5.12. Imatinib - GLIVEC (CAP) - EMEA/H/C/000406/ANX 191.9

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Seventh progress report for study CSTI571I2201: a European observational registry collecting efficacy and safety data in newly diagnosed paediatric Philadelphia positive (Ph+) acute lymphoblastic leukaemia (ALL) patients treated with chemotherapy + imatinib ± haematopoietic stem cell treatment (±HSCT)

Action: For adoption of advice to CHMP

7.5.13. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58³⁵) - EMEA/H/W/002300/MEA 003.4

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Third annual progress report for study EPI-MAL-003 (listed as a category 3 study in the RMP): a phase 4 prospective observational study to evaluate the safety, effectiveness and impact of Mosquirix (plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted)) in young children in sub-Saharan Africa in order to estimate the incidence of potential adverse events of special interest (AESI) and other adverse events leading to hospitalisation or death, in children vaccinated with the vaccine

Action: For adoption of advice to CHMP

7.5.14. Nonacog beta pegol - REFIXIA (CAP) - EMEA/H/C/004178/LEG 006.1

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

Scope: Yearly progress report for PASS NN7999-4031 (Pardigm 8): a non-interventional study in male haemophilia B patients receiving nonacog beta pegol (N9-GP) prophylaxis treatment to investigate the potential effects of PEG accumulation in the choroid plexus of the brain and other tissues/organs

Action: For adoption of advice to CHMP

7.5.15. Romiplostim - NPLATE (CAP) - EMEA/H/C/000942/MEA 003.8

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Interim report for surveillance study 20070797: a population based prospective study evaluating the short and long term safety of romiplostim treatment in real-life clinical practice in adult patients with chronic idiopathic (immune) thrombocytopenic purpura (ITP) based on national health registry systems in Denmark, Sweden, and Norway (Nordic Country Patient Registry for Romiplostim [NCPRR])

Action: For adoption of advice to CHMP

7.5.16. Teduglutide - REVESTIVE (CAP) - EMEA/H/C/002345/ANX 003.6

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Third biennial interim results for study TED-R-13-002: an international short bowel syndrome registry - a prospective, long-term observational cohort study of patients with short bowel syndrome

Action: For adoption of advice to CHMP

7.5.17. Tezacaftor, ivacaftor - SYMKEVI (CAP) - EMEA/H/C/004682/MEA 002.3

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Annual interim report for study VX17-661-117 (study 117) (listed as a category 3 study in the RMP): an observational cohort study on utilisation patterns and real-world effects of tezacaftor and ivacaftor combination therapy (TEZ/IVA) in patients with cystic fibrosis (CF) [final report expected in December 2023]

Action: For adoption of advice to CHMP

7.5.18. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/MEA 003.3

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual progress report 2020 for study M-14745-40: a European psoriasis registry to collect long-term safety data for tildrakizumab and to further characterise the long-term safety profile of tildrakizumab in the treatment of psoriasis under conditions of routine

clinical practice

Action: For adoption of advice to CHMP

7.5.19. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 002.7

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Third annual study progress report for study P16-562 (listed as a category 3 study in the RMP): a prospective observational study to assess the long-term safety profile of venetoclax in a Swedish cohort of chronic lymphocytic leukaemia (CLL) patients [final clinical study report expected in December 2025]

Action: For adoption of advice to CHMP

7.5.20. Vonicog alfa - VEYVONDI (CAP) - EMEA/H/C/004454/MEA 001.3

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim report for study VON (BAX0111) VWF-500 COL (also called ATHN-9 study) (listed as a category 3 study in the RMP): a real world safety and effectiveness study of factor replacement for clinically severe von Willebrand disease (VWD) [final report expected in 2022]

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Coronavirus (COVID-19) mRNA³⁶ vaccine (nucleoside-modified) - COVID-19 VACCINE MODERNA (CAP) - EMEA/H/C/005791/MEA 004

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

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

Action: For adoption of advice to CHMP

7.6.2. Ertugliflozin - STEGLATRO (CAP) - EMEA/H/C/004315/MEA 002.2

Applicant: Merck Sharp & Dohme B.V.

³⁶ Messenger ribonucleic acid

PRAC Rapporteur: Menno van der Elst

Scope: Feasibility assessment for study 8835-062/000: a PASS to assess the risk of diabetic ketoacidosis (DKA) among patients with type 2 diabetes mellitus (T2DM) treated with ertugliflozin compared to patients treated with other antihyperglycemic agents [final study report due date: December 2023]

Action: For adoption of advice to CHMP

7.6.3. [Ertugliflozin, metformin hydrochloride - SEGLUROMET \(CAP\) - EMEA/H/C/004314/MEA 002.2](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Feasibility assessment for study 8835-062/000: a PASS to assess the risk of diabetic ketoacidosis (DKA) among patients with type 2 diabetes mellitus (T2DM) treated with ertugliflozin compared to patients treated with other antihyperglycemic agents [final study report due date: December 2023]

Action: For adoption of advice to CHMP

7.6.4. [Ertugliflozin, sitagliptin - STEGLUJAN \(CAP\) - EMEA/H/C/004313/MEA 002.2](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Feasibility assessment for study 8835-062/000: a PASS to assess the risk of diabetic ketoacidosis (DKA) among patients with type 2 diabetes mellitus (T2DM) treated with ertugliflozin compared to patients treated with other antihyperglycemic agents [final study report due date: December 2023]

Action: For adoption of advice to CHMP

7.6.5. [Fingolimod - GILENYA \(CAP\) - EMEA/H/C/002202/MEA 038.2](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: First interim report for open-label extension phase of study CFTY720D2311: a phase 3, two-year, double-blind, double dummy, randomised, multicentre, active controlled study evaluating efficacy and safety of fingolimod once daily versus interferon β -1a once weekly in paediatric patients with multiple sclerosis (MS) aged 10 to <18 years old

Action: For adoption of advice to CHMP

7.7. **New Scientific Advice**

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Histamine dihydrochloride - CEPLENE (CAP) - EMEA/H/C/000796/S/0042

Applicant: Noventia Pharma S.r.l.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/S/0023 (without RMP)

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Susoctocog alfa - OBIZUR (CAP) - EMEA/H/C/002792/S/0039 (without RMP)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Tafamidis - VYNDALIQ (CAP) - EMEA/H/C/002294/S/0065 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

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. Entrectinib - ROZLYTREK (CAP) - EMEA/H/C/004936/R/0002 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Onasemnogene abeparvovec - ZOLGENSMA (CAP) - EMEA/H/C/004750/R/0012 (without RMP)

Applicant: Novartis Gene Therapies EU Limited, ATMP³⁷

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

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

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Cemiplimab - LIBTAYO (CAP) - EMEA/H/C/004844/R/0017 (without RMP)

Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Glycopyrronium - SIALANAR (CAP) - EMEA/H/C/003883/R/0018 (without RMP)

Applicant: Proveca Pharma Limited

PRAC Rapporteur: Zane Neikena

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

³⁷ Advanced therapy medicinal product

8.3.3. Lenvatinib - KISPLYX (CAP) - EMEA/H/C/004224/R/0043 (without RMP)

Applicant: Eisai GmbH

PRAC Rapporteur: David Olsen

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Saxagliptin, dapagliflozin - QTERN (CAP) - EMEA/H/C/004057/R/0030 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Ilaria Baldelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Zentiva k.s.

PRAC Rapporteur: Adrien Inoubli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Gabapentin (NAP) - DE/H/XXXX/WS/691

Applicant: Pfizer Pharma (Gabapentin Pfizer, Neurontin)

PRAC Lead: Martin Huber

Scope: PRAC consultation on a worksharing variation procedure evaluating an analysis of cases of suicidality and feasibility assessment for an epidemiological study investigating the suicidal risk of gabapentin/gabapentinoids as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure (PSUSA/00001499/201902) concluded in October 2019, on request of Germany

Action: For adoption of advice to Member States

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

12.3.1. Scientific Advisory Groups (SAG) - launch of public call for expression of interests for renewal of mandate of all therapeutic SAGs: preparation

Action: For information

12.3.2. Scientific Advisory Groups (SAG) - renewal of the mandate of the Inter-Committee SAG Oncology (SAG-O) - request for nominations

Action: For discussion

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

Action: For discussion

12.4.2. Safety communication – relevant aspects for European regulators

PRAC Lead: Sabine Straus

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

None

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

12.13.2. EudraVigilance - annual report 2020

Action: For discussion

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Advanced therapy medicinal products (ATMPs) - EU data sources for long-term safety and efficacy follow-up

Action: For adoption

12.15.2. Post-authorisation Safety Studies - imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. Commission implementing Regulation (EU) No 520/2012 - scoping paper

Action: For adoption

12.20.2. EMA-funded studies - new call for framework contractors

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/