11 January 2021
EMA/PRAC/17329/2021
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 11-14 January 2021

Chair: Sabine Straus – Vice-Chair: Martin Huber

11 January 2021, 10:30 – 19:30, via teleconference

12 January 2021, 08:30 – 19:30, via teleconference

13 January 2021, 08:30 – 19:30, via teleconference

14 January 2021, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

28 January 2021, 09:00 – 12:00, via teleconference

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 11-14 January 2021. See January 2021 minutes (to be published post February 2021 PRAC meeting).

1.2. Agenda of the meeting on 11-14 January 2021

Action: For adoption

1.3. Minutes of the previous meeting on 23-26 November 2020

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Eliglustat – CERDELGA (CAP)

Applicant(s): Genzyme Europe BV

PRAC Rapporteur: Eva Segovia

Scope: Signal of erectile dysfunction

Action: For adoption of PRAC recommendation

EPITT 19644 – New signal

Lead Member State(s): ES

4.1.2. Labetalol (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of nipple pain and suppressed lactation

Action: For adoption of PRAC recommendation

EPITT 19639 – New signal

Lead Member State(s): NO

4.1.3. Rituximab – MABTHERA (CAP)

Applicant(s): Roche Registration GmbH

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

PRAC Rapporteur: Hans Christian Siersted

Scope: Signal of sarcoidosis

Action: For adoption of PRAC recommendation

EPITT 19642 – New signal

Lead Member State(s): DK

4.1.4. Romosozumab – EVENITY (CAP)

Applicant(s): UCB Pharma S.A.

PRAC Rapporteur: Adrien Inoubli

Scope: Signal of cardiac arrhythmia

Action: For adoption of PRAC recommendation

EPITT 19629 – New signal

Lead Member State(s): FR

4.1.5. Secukinumab – COSENTYX (CAP)

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Signal of Henoch-Schonlein purpura

Action: For adoption of PRAC recommendation

EPITT 19640 – New signal

Lead Member State(s): ES

4.1.6. Secukinumab – COSENTYX (CAP)

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Signal of facial paralysis

Action: For adoption of PRAC recommendation

EPITT 19653 – New signal

Lead Member State(s): ES

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

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of acute respiratory distress syndrome

Action: For adoption of PRAC recommendation

EPITT 19625 – New signal

Lead Member State(s): HR

4.1.8. Sulfametoxazole, trimethoprim (co-trimoxazole) (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of haemophagocytic lymphohistiocytosis (HLH)

Action: For adoption of PRAC recommendation

EPITT 19655 – New signal

Lead Member State(s): HR

4.1.9. Tramadol (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of serotonin syndrome

Action: For adoption of PRAC recommendation

EPITT 19635 – New signal

Lead Member State(s): FR

4.1.10. Warfarin (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of anticoagulant-related nephropathy

Action: For adoption of PRAC recommendation

EPITT 19652 – New signal

Lead Member State(s): DK

4.2. New signals detected from other sources

4.2.1. Alemtuzumab – LEMTRADA (CAP)

Applicant(s): Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of sarcoidosis

Action: For adoption of PRAC recommendation

EPITT 19638 – New signal

Lead Member State(s): DK

4.2.2. Clindamycin (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of acute renal failure

Action: For adoption of PRAC recommendation

EPITT 19647 – New signal

Lead Member State(s): AT

4.2.3. Hydrocortisone – ALKINDI (CAP)

Applicant(s): Diurnal Europe BV

PRAC Rapporteur: Annika Folin

Scope: Signal of adrenal crisis

Action: For adoption of PRAC recommendation

EPITT 19656 – New signal

Lead Member State(s): SE

4.3. Signals follow-up and prioritisation

4.3.1. Adalimumab - AMGEVITA (CAP); AMSPARITY (CAP), HALIMATOZ (CAP); HEFIYA (CAP); HULIO (CAP); HUMIRA (CAP) - EMEA/H/C/000481/SDA/118.1; HYRIMOZ (CAP); IDACIO (CAP); IMRALDI (CAP)

Applicant(s): AbbVie Deutschland GmbH & Co. KG (Humira), Amgen Europe B.V. (Amgevita), Fresenius Kabi Deutschland GmbH (Idacio), Mylan S.A.S (Hulio), Pfizer Europe MA EEIG (Amsparity), Samsung Bioepis NL B.V. (Imraldi), Sandoz GmbH (Halimatoz, Hefiya, Hyrimoz)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of abnormal weight gain

Action: For adoption of PRAC recommendation

EPITT 19520 – Follow-up to July 2020

4.3.2. Anastrozole (NAP)

Applicant(s): various

PRAC Rapporteur: Zane Neikena

Scope: Signal of depressed mood disorders

Action: For adoption of PRAC recommendation

EPITT 19592 – Follow-up to September 2020

4.3.3. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/SDA/027

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Signal of systemic scleroderma

Action: For adoption of PRAC recommendation

EPITT 19591 – Follow-up to September 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. Autologous glioma tumour cells (inactivated), autologous glioma tumour cell lysates (inactivated), allogeneic glioma tumour cells (inactivated), allogeneic glioma tumour cell lysates (inactivated) - EMEA/H/C/003693, Orphan

Applicant: Epitopoietic Research Corporation-Belgium (E.R.C.), ATMP[3]

Scope: Treatment of glioma

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

5.1.2. 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

5.1.3. Dexamethasone phosphate - EMEA/H/C/005740

Scope: Treatment for cerebral oedema, post-traumatic shock-lung syndrome, asthma, skin diseases, autoimmune diseases, rheumatoid arthritis, prophylaxis and treatment of post-operative or cytostatic-induced vomiting, treatment of coronavirus (COVID-19), eye inflammation and infection

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

[3] Advanced therapy medicinal product

5.1.4. Elivaldogene autotemcel - EMEA/H/C/003690, Orphan

Applicant: bluebird bio (Netherlands) B.V, ATMP[4]

Scope (accelerated assessment): Treatment of adenosine triphosphate (ATP) binding cassette subfamily D member 1 (ABCD1) genetic mutation and cerebral adrenoleukodystrophy

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

5.1.5. Hydrocortisone - EMEA/H/C/005105, Orphan

Applicant: Diurnal Europe BV

Scope: Replacement therapy for congenital adrenal hyperplasia (CAH) in adolescents aged 12 years and over and adults

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

5.1.6. Ponesimod - EMEA/H/C/005163

Scope: Treatment of adult patients with relapsing forms of multiple sclerosis (RMS) with active disease defined by clinical or imaging features

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

5.1.7. Pralsetinib - EMEA/H/C/005413

Scope: Treatment of non-small cell lung cancer (NSCLC)

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

5.1.8. Relugolix, estradiol, norethisterone acetate - EMEA/H/C/005267

Scope: Treatment of uterine fibroids

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

5.1.9. Salmeterol xinafoate, fluticasone propionate - EMEA/H/C/005591

Scope: Treatment of asthma

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

5.1.10. Salmeterol xinafoate, fluticasone propionate - EMEA/H/C/004881

Scope: Treatment of asthma

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

[4] Advanced therapy medicinal product

5.1.11. Tanezumab - EMEA/H/C/005189

Scope: Treatment of moderate to severe chronic pain associated with osteoarthritis (OA) in adult patients for whom treatment with non-steroidal anti-inflammatory drugs (NSAIDs) and/or an opioid is ineffective, not tolerated or inappropriate

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

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

Action: For adoption of PRAC Assessment Report

5.2.2. Cetrorelix - CETROTIDE (CAP) - EMEA/H/C/000233/II/0075

Applicant: Merck Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 5.2) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' including the consequential removal of a number of important identified risks and important potential risk of congenital anomalies, as well as the removal of missing information on infertile premenopausal women. The MAH also revised the RMP based on the most recent data and post-marketing exposure

Action: For adoption of PRAC Assessment Report

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

Applicant: Merck Europe B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Submission of an updated RMP (version 1.4) in order to bring it in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template). In addition, the MAH took the opportunity to include long-term safety data from the completed PREMIERE registry: a prospective observational long-term safety registry of multiple sclerosis patients who have participated in cladribine clinical studies; and to remove it from the pharmacovigilance plan. Furthermore, the status of the post-approval safety study MS 700568-0002: a long term, prospective, observational cohort study evaluating the safety profile in patients with highly active relapsing multiple sclerosis (RMS) newly started on oral cladribine (CLARION); and study MS 700568-0004: pregnancy outcomes in women exposed to oral cladribine: a multi-country cohort database study (CLEAR). Finally, the RMP is updated in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010634/201907)

adopted in January 2020

Action: For adoption of PRAC Assessment Report

5.2.4. Elosulfase alfa - VIMIZIM (CAP) - EMEA/H/C/002779/II/0034, Orphan

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of an updated RMP (version 5) in order to update the safety specifications and the pharmacovigilance plan, and to add healthcare provider educational materials and process indicator to evaluate the distribution of the educational materials. The RMP is also brought in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.5. Influenza vaccine (surface antigen, inactivated, adjuvanted) - FLUAD TETRA (CAP) - EMEA/H/C/004993/II/0008

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of an updated RMP (version 1.9) in order to provide a consolidated RMP for adjuvanted trivalent influenza vaccine (aTIV) and adjuvanted quadrivalent influenza vaccine (aQIV), including an alignment of safety concerns for aTIV and aQIV

Action: For adoption of PRAC Assessment Report

5.2.6. Mannitol - BRONCHITOL (CAP) - EMEA/H/C/001252/II/0042, Orphan

Applicant: Pharmaxis Europe Limited

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of an updated RMP (version 9.0) brought in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template). The MAH took the opportunity to review the safety information and proposed to reclassify 'cough' from an important potential risk to an important identified risk; to remove the important identified risks of 'bronchospasm during and after the initiation dose assessment' and 'bronchospasm during long term use'; to remove the important potential risk of 'cough-related sequelae', 'off label use in non-cystic fibrosis (CF) bronchiectasis', 'off label use in paediatric/adolescent CF patients (aged 6-17 years)', 'administration of Bronchitol via the wrong inhaler device' and 'starting Bronchitol treatment without completing the full Bronchitol initiation dose assessment (BIDA) dose'; to remove the missing information of 'patients requiring home oxygen or needing assisted ventilation', 'children <6 years of age', 'pregnancy and lactation', 'risks associated with long-term use' from the list of safety concerns; to add 'increased risk of respiratory or systemic infection' as an important potential risk replacing 'pulmonary abscess on continued use', 'septicaemia on continued use', 'increased risk of bacteria sputum identified or infections with extended use of Bronchitol' and 'microbial infection via a contaminated inhaler device' previously classified as important potential risks. In addition, the pharmacovigilance plan is updated with completed studies. Finally,

the RMP is updated as requested as per the conclusions of the periodic safety update report single assessment (PSUSA) procedure (PSUSA/00009226/201904) adopted at the November 2019 PRAC meeting

Action: For adoption of PRAC Assessment Report

5.2.7. Melatonin - CIRCADIN (CAP) - EMEA/H/C/000695/II/0061

Applicant: RAD Neurim Pharmaceuticals EEC SARL

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of an updated RMP (version 7.0) to remove the following risks from the list of potential risks: drug interaction with levothyroxine, panic attacks, potential interaction with warfarin, sperm motility decreased/spermatozoa morphology abnormal and withdrawal. Furthermore, the MAH took the opportunity to introduce minor corrections throughout the RMP

Action: For adoption of PRAC Assessment Report

5.2.8. Saxagliptin - ONGLYZA (CAP) - EMEA/H/C/001039/WS1975/0051; saxagliptin, metformin hydrochloride - KOMBOGLYZE (CAP) - EMEA/H/C/002059/WS1975/0049

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 15.1 for Onglyza; version 16.1 for Komboglyze) in order to change the milestones to Q1 2021 of the final study report for study D1680C00016 (MEASURE-HF) (listed as a category 3 study in the RMP): a 24-week, multicentre, randomised, double-blind, parallel group, placebo-controlled study to investigate the effects of saxagliptin and sitagliptin in patients with type 2 diabetes mellitus (T2DM) and heart failure. The MAH took the opportunity to introduce minor changes throughout the RMP

Action: For adoption of PRAC Assessment Report

5.2.9. Sildenafil - REVATIO (CAP) - EMEA/H/C/000638/II/0091

Applicant: Upjohn EESV

PRAC Rapporteur: Menno van der Elst

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

Action: For adoption of PRAC Assessment Report

5.2.10. Tolvaptan - JINARC (CAP) - EMEA/H/C/002788/II/0029

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of an updated RMP (version 14.4) to include dehydration and the pregnancy prevention programme as additional risk minimisation measures (aRMM) in order to align the RMP with Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product'

Action: For adoption of PRAC Assessment Report

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

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

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

Action: For adoption of PRAC Assessment Report

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

5.3.1. Apalutamide - ERLEADA (CAP) - EMEA/H/C/004452/II/0009

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section 5.3 of the SmPC in order to include non-clinical information based on final results from a 26-week study TOX13540 (listed as a category 3 study in the RMP): a carcinogenicity study of JNJ-56021927-AAA (apalutamide) by oral gavage in CByB6F1/TgrasH2 hemizygous mice. The RMP (version 3.2) is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to bring the product information in line with the latest quality review of (QRD) template (version 10.1)

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. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0038, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include the use of blinatumomab as monotherapy for the treatment of paediatric patients aged 1 year or older with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-precursor acute lymphoblastic leukaemia (ALL) as consolidation therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 13.0) are updated in accordance

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

5.3.4. Cannabidiol - EPIDYOLEX (CAP) - EMEA/H/C/004675/II/0005, Orphan

Applicant: GW Pharma (International) B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication for use as adjunctive therapy of seizures associated with tuberous sclerosis complex (TSC) for patients 1 year of age and older. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 1.1) are updated accordingly. The MAH took the opportunity to correct typographic errors in the product information, to introduce editorial updates and to implement the updated ethanol statement in compliance with the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'

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

5.3.5. Cholera vaccine (recombinant, live, oral) - VAXCHORA (CAP) - EMEA/H/C/003876/II/0003/G

Applicant: Emergent Netherlands B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Grouped variations consisting of: 1) extension of indication for the active immunisation against disease caused by *Vibrio cholerae* serogroup O1, from the currently approved age range 'adults and children aged 6 years and older' to 'adults and children aged 2 years and older'. 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 2.0) are updated in accordance; 2) update section 5.1 of the SmPC to include long-term immunogenicity data supporting Vaxchora (cholera vaccine (recombinant, live, oral)) effectiveness at generating a protective immune response that persists for 2 years following vaccination; based on the final results from study PXVX-VC-200-006: a randomised, double-blind, placebo-controlled trial aimed to assess the safety and immunogenicity of Vaxchora (cholera vaccine (recombinant, live, oral)) in children 2 to <18 years of age. The MAH took the opportunity to include editorial changes throughout the SmPC and Annex II

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

5.3.6. 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 list of 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 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 category 3 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 (category 1): a single-arm interventional phase 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

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

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

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

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

5.3.8. Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA[5]), poliomyelitis (inactivated) and haemophilus type B conjugate vaccine (adsorbed) - HEXACIMA (CAP) - EMEA/H/C/002702/WS1965/0110/G; HEXYON (CAP) - EMEA/H/C/002796/WS1965/0114/G

Applicant: Sanofi Pasteur

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of: 1) update of section 5.1 of the SmPC in order to describe the persistence of anti-surface antigens of the hepatitis B virus (HBs) antibodies in subjects 6 years of age having received a hexavalent vaccine based on the final results from study A3L00052: a phase 4, open-label, multicentre study in children previously vaccinated in study A3L38a with 3 doses of either Hexacima/Hexyon (group 1) or Infanrix Hexa (group 2); 2) update of sections 4.4 and 5.1 of the SmPC in order to reword safety and immunogenicity information regarding individuals with immunodeficiency based on the final results from study A3L44: a phase 3, single centre, open-label, two-arm study including human immunodeficiency virus (HIV)-exposed infected and uninfected infants vaccinated with a 3-dose infant primary series (at 6, 10, and 14 weeks of age) and a booster dose (at 15 to 18 months of age) with Hexacima/Hexyon in Republic of South Africa; 3) update of section 4.4 of the SmPC in order to include syncope within the precautions for use. The package leaflet and the RMP (version 13.0) are updated accordingly. In addition, the MAH/Scientific Opinion holder (SOH) 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. Eltrombopag - REVOLADE (CAP) - EMEA/H/C/001110/II/0063

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.2, 4.8 and 5.2 of SmPC to clarify dosing recommendations to ensure accurate treatment of patients of 'East-/Southeast-Asian' ancestry and to correct the adverse drug reactions (ADR) list based on currently available data, which was previously submitted and reviewed. In addition, section 4.4 of the SmPC is updated in line with the 'Excipients in the labelling and package leaflet of medicinal products for human use'. The package leaflet is updated accordingly. The RMP (version 53) is also updated accordingly and to reflect the updated date for the provision of the primary study report of CETB115E2201 (listed as a category 3 study in the RMP): a phase 2 dose-escalation study characterising the pharmacokinetic (PK) of eltrombopag in paediatric patients with previously untreated or relapsed severe aplastic anaemia or recurrent aplastic anaemia as well as to update it in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001205/201809) adopted in April 2019

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

[5] Ribosomal deoxyribonucleic acid

5.3.10. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/II/0055

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include treatment of adult patients with heart failure and reduced ejection fraction. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 4.9 and 5.1 of the SmPC are updated based on final results from study EMPEROR-Reduced: a phase 3 randomised, double-blind trial to evaluate efficacy and safety of once daily empagliflozin 10 mg compared to placebo in patients with chronic heart failure with reduced ejection fraction (HFrEF). The package leaflet, labelling and the RMP (version 15.0) are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

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

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nikica Mirošević Skvrce

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

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

5.3.12. Follitropin delta - REKOVELLE (CAP) - EMEA/H/C/003994/II/0022

Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 4.2 of the SmPC in order to introduce a new anti-Müllerian hormone (AMH) assay to determine the dose of follitropin delta, following an agreed recommendation. The RMP (version 5.0) is updated accordingly and in line with revision 2 of GVP module V on 'Risk management systems'. The MAH took the opportunity to amend section 4.4 of the SmPC to introduce traceability information. Finally, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.13. Meningococcal group B vaccine (recombinant, adsorbed) - TRUMENBA (CAP) - EMEA/H/C/004051/II/0032

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.8 and 5.1 of the SmPC following the interim data from the

primary vaccination phase (stage 1) of study B1971057: a phase 3, randomised, active-controlled, observer-blinded study to assess the immunogenicity, safety and tolerability of bivalent rLP2086 vaccine (Trumenba (meningococcal group B vaccine)) when administered as a 2-dose regimen and a first-in-human study to describe the immunogenicity, safety and tolerability of a bivalent rLP2086 containing pentavalent vaccine (MenABCWY) in healthy subjects ⩾10 to <26 years of age. The RMP (version 5.0) is updated accordingly. The MAH took the opportunity to implement some editorial changes in section 4.4 of the SmPC and in the package leaflet to introduce information on sodium content in line with the Annex to the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'

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

5.3.14. Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/II/0035

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include chronic rhinosinusitis with nasal polyps (CRSwNP). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 7) are updated in accordance. In addition, the MAH took the opportunity to update the local representative for Italy in the package leaflet

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

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

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of: 1) extension of indication to include eosinophilic granulomatosis with polyangiitis (EGPA). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 7) are updated in accordance. In addition, the MAH took the opportunity to update the local representative for Italy in the package leaflet; 2) addition of a new pack size of 9x100mg/mL multipack for pre-filled pens 100 mg/mL solution for injection and another pack size of 9x100mg/mL multipack for pre-filled syringes100 mg/mL solution for injection. As a consequence, sections 6.5 and 8 of the SmPC and the package leaflet are updated accordingly. Annex III-A on 'labelling' is also updated to include information relating to the new pack sizes

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

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

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include hypereosinophilic syndrome (HES). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. In addition, section 6.6 of the SmPC for the powder for solution for injection presentations is updated. The package leaflet and the RMP (version 7) are updated in accordance. The MAH took the

opportunity to update the local representative for Italy in the package leaflet

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

5.3.17. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/X/0116

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension application to introduce a new pharmaceutical form (solution for injection), associated with a new strength (150 mg) and a new route of administration (subcutaneous use). The RMP (version 26.1) is updated accordingly

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

5.3.18. Netupitant, palonosetron - AKYNZEO (CAP) - EMEA/H/C/003728/X/0031

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: Extension application to introduce a new pharmaceutical form (concentrate for solution for infusion). The RMP (version 2.8) is updated accordingly

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

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

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of the 5 year data including data on late relapses from the 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

5.3.20. Nintedanib - VARGATEF (CAP) - EMEA/H/C/002569/II/0035/G

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Agni Kapou

Scope: Grouped variations consisting of: 1) update of sections 4.5, 4.6 and 5.2 of the SmPC to reflect the results of study 1199-0340 conducted in female patients with systemic sclerosis associated interstitial lung disease (SSc-ILD) to investigate a potential interaction

between nintedanib and a combined oral contraceptive (COC) containing ethinylestradiol/levonorgestrel; 2) update of sections 4.3 and 4.6 of the SmPC to introduce a new contraindication of pregnancy. This follows the update for Ofev (nintedanib) on SSc-ILD introduced in the context of variation II/0026 finalised in February 2020 and as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010318/201910) adopted in May 2020. The package leaflet and the RMP (version 7.0) are updated accordingly

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

5.3.21. Nintedanib - VARGATEF (CAP) - EMEA/H/C/002569/II/0037

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Agni Kapou

Scope: Submission of the final report from study LUME BioNIS (listed as an obligation in the Annex II of the product information): a non-interventional study in patients eligible for treatment with Vargatef (nintedanib) to explore whether genetic or genomic markers (alone or combined with clinical covariates) could be used to predict overall survival. Annex II and the RMP (version 8.0) are updated accordingly

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

5.3.22. Pegvisomant - SOMAVERT (CAP) - EMEA/H/C/000409/II/0098/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Adrien Inoubli

Scope: Grouped variations consisting of: 1) update of section 4.4 of the SmPC to remove the warning on growth hormone secreting tumours, consequential to the removal of pituitary tumour growth as a potential risk from the RMP. The package leaflet is updated accordingly; 2) update of the RMP (version 2.0) to reflect the evaluation of the final results of study A6291010 (ACROSTUDY) (listed as a category 3 study in the RMP): an open-label, global, multicentre, non-interventional PASS performed to monitor the long-term safety and outcomes of pegvisomant treatment in clinical practice as per the conclusions of variation II/0089 adopted in July 2019. The RMP is also brought 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

5.3.23. Pertuzumab - PERJETA (CAP) - EMEA/H/C/002547/II/0054

Applicant: Roche Registration GmbH

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of the final report from study MO28047 (PERUSE) (listed as an obligation in Annex II): a multicentre, open-label, single-arm study of pertuzumab in combination with trastuzumab and taxane in first line treatment of patients with human epidermal growth factor receptor 2 (HER2)-positive advanced (metastatic or locally recurrent) breast cancer. The RMP (version 13.0) is updated accordingly

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

5.3.24. 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

5.3.25. Pyronaridine, artesunate - PYRAMAX (Art 58[6]) - EMEA/H/W/002319/II/0023/G

Applicant: Shin Poong Pharmaceutical Co., Ltd.

PRAC Rapporteur: Adrien Inoubli

Scope: Grouped variations consisting of the submission of the final clinical study reports (CSR) of two completed studies: 1) study SP-C-021-15 (listed as a category 3 study in the RMP): a phase 3b/4 cohort event monitoring study conducted in Central Africa to evaluate the safety in patients after the local registration of Pyramax (pyronaridine/artesunate) (CANTAM study); 2) study SP-C-026-18: a randomized open-label exploratory study to determine the efficacy of different treatment regimens of Pyramax (pyronaridine/artesunate) in asymptomatic carriers of Plasmodium falciparum mono-infections. This non-imposed study was conducted in Gambia and Zambia and compared asymptomatic subjects with parasitaemia dosed according to the approved label of 3-day dosing with 2-day and 1-day dosing. As a consequence, sections 4.2, 4.4, 4.6, 4.8 and 5.1 are updated. The package leaflet is updated in accordance. The RMP (version 17) is also updated accordingly and in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template)

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

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

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Update of section 4.6 of the SmPC in order to update safety information following

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

pregnancy outcome data for raltegravir 400 mg film-coated tablet from prospective reports of pregnancy data with known outcome and time of raltegravir exposure. The RMP (version 15.1) is updated accordingly. In addition, the MAH took the opportunity to introduce some minor changes agreed in previous procedures in the product information and to update the list of local representatives for Germany. Finally, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.27. Rurioctocog alfa pegol - ADYNOVI (CAP) - EMEA/H/C/004195/II/0017

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.8 and 5.1 of the SmPC to provide results from the further analysis of the continuation study 261302: a phase 3b, prospective, open label, multicentre continuation study of safety and efficacy of BAX 855 (rurioctocog alfa pegol) in the prophylaxis of bleeding; and the pharmacokinetics (PK)-guided dosing study 261303: a phase 3, prospective, randomised, multicentre clinical study comparing the safety and efficacy of rurioctocog alfa pegol following PK-guided prophylaxis targeting two different factor VIII (FVIII) trough levels in subjects with severe haemophilia A. The package leaflet and the RMP (version 2.0) are updated accordingly. The MAH took the opportunity to update the product information to introduce information on sodium content in line with the Annex to the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'

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

5.3.28. Ruxolitinib - JAKAVI (CAP) - EMEA/H/C/002464/II/0050

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Update of section 4.2 and 5.1 of the SmPC to include the final results of study CINC424A2201 (EXPAND study) (listed as a category 3 study in the RMP):a phase 1b open-label, dose-finding study intended to establish the maximum safe starting dose (MSSD) of ruxolitinib tablets administered orally to patients with myelofibrosis (MF) in previous unstudied population of patients who had baseline platelet counts ≥50×109/L and <100×109/L. The package leaflet and the RMP (version 12.0) are updated accordingly. The RMP is also brought in line with revision 2 of GVP module V on 'Risk management systems' and in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010015/202002) adopted in October 2020

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

5.3.29. 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 multicentre, 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

5.3.30. Tegafur, gimeracil, oteracil - TEYSUNO (CAP) - EMEA/H/C/001242/II/0045

Applicant: Nordic Group B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include treatment of metastatic colorectal cancer in adult patients where it is not possible to initiate or continue treatment with another fluoropyrimidine. As a consequence, sections 4.1, 4.2, 4.3, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 10.0) are updated in accordance

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

5.3.31. Ticagrelor - BRILIQUE (CAP) - EMEA/H/C/001241/II/0049

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include, in co-administration with acetylsalicylic acid (ASA), the prevention of stroke in adult patients with acute ischaemic stroke or transient ischaemic attack (TIA), based on the final results of study D5134C00003 (THALES): a phase 3, international, multicentre, randomised, double-blind, placebo-controlled study to investigate the efficacy and safety of ticagrelor and ASA compared with ASA in the prevention of stroke and death in patients with acute ischaemic stroke or transient ischaemic attack. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 13.0) are updated in accordance

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

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

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

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

5.3.33. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/II/0081/G

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Grouped variations consisting of: 1) update of section 4.2 of the SmPC solution for injection presentations in order to change posology recommendations for patients with ulcerative colitis, and section 5.1 of the SmPC to update efficacy information based on 2-year results from study 3001 (listed as a category 3 study in the RMP): a phase 3, randomized, double blind, placebo controlled, parallel-group, multicentre protocol to evaluate the safety and efficacy of ustekinumab induction and maintenance therapy in subjects with moderately to severely active ulcerative colitis; 2) update of section 5.1 of the SmPC in order to update efficacy information based on 5-year results from study 3003 (listed as a category 3 study in the RMP): a phase 3, randomized, double blind, placebo controlled, parallel-group, multicentre trial to evaluate the safety and efficacy of ustekinumab maintenance therapy in adult patients with moderately to severely active Crohn's disease. The RMP (version 18.1) is updated accordingly

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

5.3.34. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/II/0030

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication in combination with hypomethylating agents (HMAs) or low dose cytarabine (LDAC) for the treatment of adult patients with newly-diagnosed acute myeloid leukaemia (AML) who are ineligible for intensive chemotherapy. As a consequence, sections 4.2, 4.3, 4.4, 4.5, 4.7, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and RMP (version 6.1) are updated accordingly

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Afamelanotide - SCENESSE (CAP) - PSUSA/00010314/202006

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Angiotensin II - GIAPREZA (CAP) - PSUSA/00010785/202006

Applicant: La Jolla Pharmaceutical II B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Apixaban - ELIQUIS (CAP) - PSUSA/00000226/202005

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Atezolizumab - TECENTRIQ (CAP) - PSUSA/00010644/202005

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Avatrombopag - DOPTELET (CAP) - PSUSA/00010779/202005

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Betibeglogene autotemcel - ZYNTEGLO (CAP) - PSUSA/00010769/202005

Applicant: bluebird bio (Netherlands) B.V, ATMP[7]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.7. Binimetinib - MEKTOVI (CAP) - PSUSA/00010717/202006

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

[7] Advanced therapy medicinal product

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Blinatumomab - BLINCYTO (CAP) - PSUSA/00010460/202006

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Buprenorphine[8] - SIXMO (CAP) - PSUSA/00010778/202005

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

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Cannabidiol[9] - EPIDYOLEX (CAP) - PSUSA/00010798/202006

Applicant: GW Pharma (International) B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Chlorhexidine - UMBIPRO (Art 58[10]) - EMEA/H/W/003799/PSUV/0006

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.12. Cholera vaccine (inactivated, oral) - DUKORAL (CAP) - PSUSA/00000730/202004

Applicant: Valneva Sweden AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[8] Implant(s) only
[9] Centrally authorised product(s) only
[10] 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)

6.1.13. Cholera vaccine (oral, live) - VAXCHORA (CAP) - PSUSA/00010862/202006

Applicant: Emergent Netherlands B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Crisaborole - STAQUIS (CAP) - PSUSA/00010842/202006

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Darunavir, cobicistat - REZOLSTA (CAP) - PSUSA/00010315/202005

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Dasatinib - SPRYCEL (CAP) - PSUSA/00000935/202006

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Decitabine - DACOGEN (CAP) - PSUSA/00009118/202005

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Delafloxacin - QUOFENIX (CAP) - PSUSA/00010822/202006

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

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Dengue tetravalent vaccine (live, attenuated) - DENGVAXIA (CAP) - PSUSA/00010740/202006

Applicant: Sanofi Pasteur

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Dimethyl fumarate[11] - SKILARENCE (CAP) - PSUSA/00010647/202006

Applicant: Almirall S.A

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Dolutegravir, rilpivirine - JULUCA (CAP) - PSUSA/00010689/202005

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Efmoroctocog alfa - ELOCTA (CAP) - PSUSA/00010451/202006

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Emedastine - EMADINE (CAP) - PSUSA/00001207/202005

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[11] Indicated for the treatment of psoriasis

6.1.24. Emicizumab - HEMLIBRA (CAP) - PSUSA/00010668/202005

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Encorafenib - BRAFTOVI (CAP) - PSUSA/00010719/202006

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Erenumab - AIMOVIG (CAP) - PSUSA/00010699/202005

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Fidaxomicin - DIFICLIR (CAP) - PSUSA/00001390/202005

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Fluciclovine (^{18}F) - AXUMIN (CAP) - PSUSA/00010594/202005

Applicant: Blue Earth Diagnostics Ireland Limited

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Follitropin beta - PUREGON (CAP) - PSUSA/00001465/202005

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Fulvestrant - FASLODEX (CAP) - PSUSA/00001489/202004

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Galsulfase - NAGLAZYME (CAP) - PSUSA/00001515/202005

Applicant: BioMarin International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Gemtuzumab ozogamicin - MYLOTARG (CAP) - PSUSA/00010688/202005

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Givosiran - GIVLAARI (CAP) - PSUSA/00010839/202005

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Glibenclamide[12] - AMGLIDIA (CAP) - PSUSA/00010690/202005

Applicant: Ammtek

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[12] Centrally authorised product(s) only

6.1.35. Human fibrinogen, human thrombin - EVICEL (CAP); TACHOSIL (CAP); VERASEAL (CAP) - PSUSA/00010297/202006

Applicant(s): Instituto Grifols, S.A. (VeraSeal), Omrix Biopharmaceuticals N. V. (Evicel), Takeda Austria GmbH (TachoSil)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Human papillomavirus 9-valent vaccine (recombinant, adsorbed) - GARDASIL 9 (CAP) - PSUSA/00010389/202006

Applicant: MSD Vaccins

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Hydroxycarbamide[13] - SIKLOS (CAP); XROMI (CAP) - PSUSA/00001692/202006

Applicant(s): Addmedica S.A.S. (Siklos), Nova Laboratories Ireland Limited (Xromi)

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Insulin glargine, lixisenatide - SULIQUA (CAP) - PSUSA/00010577/202005

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Larotrectinib - VITRAKVI (CAP) - PSUSA/00010799/202005

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[13] Centrally authorised product(s) only

6.1.40. Levodopa - INBRIJA (CAP) - PSUSA/00107800/202006

Applicant: Acorda Therapeutics Ireland Limited

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Lumacaftor, ivacaftor - ORKAMBI (CAP) - PSUSA/00010455/202005

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - PSUSA/00010643/202006

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Methylthioninium chloride - METHYLTHIONINIUM CHLORIDE PROVEBLUE (CAP) - PSUSA/00002029/202005

Applicant: Provepharm SAS

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Mexiletine[14] - NAMUSCLA (CAP) - PSUSA/00010738/202006

Applicant: Lupin Europe GmbH

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Migalastat - GALAFOLD (CAP) - PSUSA/00010507/202005

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Ulla Wändel Liminga

[14] Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Mitotane - LYSODREN (CAP) - PSUSA/00002075/202004

Applicant: HRA Pharma Rare Diseases

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Netarsudil - RHOKIINSA (CAP) - PSUSA/00107812/202006

Applicant: Aerie Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Nonacog beta pegol - REFIXIA (CAP) - PSUSA/00010608/202005

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Nonacog gamma - RIXUBIS (CAP) - PSUSA/00010320/202006

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Nusinersen - SPINRAZA (CAP) - PSUSA/00010595/202005

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Obeticholic acid - OCALIVA (CAP) - PSUSA/00010555/202005

Applicant: Intercept Pharma International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Onasemnogene abeparvovec - ZOLGENSMA (CAP) - PSUSA/00010848/202005

Applicant: Novartis Gene Therapies EU Limited, ATMP[15]

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.53. Opicapone - ONGENTYS (CAP) - PSUSA/00010516/202006

Applicant: Bial - Portela & Cª, S.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) - PSUSA/00010501/202005

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.55. Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - ADJUPANRIX (CAP); prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) – PREPANDRIX[16] - PSUSA/00002281/202005

Applicant(s): GlaxoSmithKline Biologicals SA

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.56. Pegvaliase - PALYNZIQ (CAP) - PSUSA/00010761/202005

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

[15] Advanced therapy medicinal product
[16] European Commission (EC) Decision dated 17 December 2020 on the withdrawal of the marketing authorisation(s)

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.57. Pentosan polysulfate sodium[17] - ELMIRON (CAP) - PSUSA/00010614/202006

Applicant: Bene-Arzneimittel GmbH

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.58. Pertuzumab - PERJETA (CAP) - PSUSA/00010125/202006

Applicant: Roche Registration GmbH

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.59. Polatuzumab vedotin - POLIVY (CAP) - PSUSA/00010817/202006

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.60. Prasterone[18] - INTRAROSA (CAP) - PSUSA/00010672/202005

Applicant: Endoceutics S.A.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.61. Ravulizumab - ULTOMIRIS (CAP) - PSUSA/00010787/202006

Applicant: Alexion Europe SAS

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[17] Centrally authorised product(s) only
[18] Pessary, vaginal use only

6.1.62. Rucaparib - RUBRACA (CAP) - PSUSA/00010694/202006

Applicant: Clovis Oncology Ireland Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.63. Semaglutide - OZEMPIC (CAP); RYBELSUS (CAP) - PSUSA/00010671/202005

Applicant(s): Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.64. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - PSUSA/00010524/202006

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.65. Sonidegib - ODOMZO (CAP) - PSUSA/00010408/202006

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.66. Tafamidis - VYNDAQEL (CAP) - PSUSA/00002842/202005

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.67. Tedizolid phosphate - SIVEXTRO (CAP) - PSUSA/00010369/202006

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.68. Tilmanocept - LYMPHOSEEK (CAP) - PSUSA/00010313/202005

Applicant: Navidea Biopharmaceuticals Europe Ltd.

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.69. Tolvaptan[19] - JINARC (CAP) - PSUSA/00010395/202005

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.70. Tolvaptan[20] - SAMSCA (CAP) - PSUSA/00002994/202005

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.71. Trametinib - MEKINIST (CAP) - PSUSA/00010262/202005

Applicant: Novartis Europharm Limited

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.72. Treosulfan[21] - TRECONDI (CAP) - PSUSA/00010777/202006

Applicant: medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[19] Indicated for adults with autosomal dominant polycystic kidney disease (ADPKD)
[20] Indicated for adults with hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH)
[21] Centrally authorised product(s) only

6.1.73. Turoctocog alfa pegol - ESPEROCT (CAP) - PSUSA/00010782/202006

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.74. Varenicline - CHAMPIX (CAP) - PSUSA/00003099/202005

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.75. Vedolizumab - ENTYVIO (CAP) - PSUSA/00010186/202005

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.76. Vonicog alfa - VEYVONDI (CAP) - PSUSA/00010714/202006

Applicant: Baxalta Innovations GmbH

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. Fentanyl[22] - EFFENTORA (CAP); INSTANYL (CAP); PECFENT (CAP); NAP - PSUSA/00001369/202004

Applicant(s): Kyowa Kirin Holdings B.V. (PecFent), Takeda Pharma A/S (Instanyl), Teva B.V. (Effentora), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[22] Transmucosal route of administration only

6.2.2. Human normal immunoglobulin (IgG) - FLEBOGAMMA DIF (CAP); HIZENTRA (CAP); HYQVIA (CAP); KIOVIG (CAP); PRIVIGEN (CAP); NAP - PSUSA/00001633/202005

Applicant(s): Baxalta Innovations GmbH (HyQvia), CSL Behring GmbH (Hizentra, Privigen), Instituto Grifols, S.A. (Flebogamma DIF), Takeda Manufacturing Austria AG (Kiovig), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Ivabradine - CORLENTOR (CAP); IVABRADINE ANPHARM (CAP); PROCORALAN (CAP); NAP - PSUSA/00001799/202004

Applicant(s): Anpharm Przedsiebiorstwo Farmaceutyczne S.A. (Ivabradine Anpharm), Les Laboratoires Servier (Corlentor, Procoralan), various

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Topotecan - HYCAMTIN (CAP); TOPOTECAN HOSPIRA (CAP); NAP - PSUSA/00002997/202005

Applicant(s): Novartis Europharm Limited (Hycamtin), Pfizer Europe MA EEIG (Topotecan Hospira), various

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Treprostinil - TREPULMIX (CAP); NAP - PSUSA/00003013/202005

Applicants: SciPharm Sarl, various

PRAC Rapporteur: Zane Neikena

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. Amfepramone (NAP) - PSUSA/00000138/202006

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Azithromycin[23] (NAP) - PSUSA/00010492/202004

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Azithromycin[24] (NAP) - PSUSA/00010491/202004

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Chlorpromazine (NAP) - PSUSA/00000715/202005

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Cidofovir (NAP) - PSUSA/00010558/202006

Applicant(s): various

PRAC Lead: Rugilė Pilvinienė

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Ciprofloxacin hydrochloride, dexamethasone acetate[25] (NAP) - PSUSA/00010012/202004

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[23] Formulation(s) for ocular use only
[24] Formulation(s) for systemic use only
[25] Ear drops, suspension only

6.3.7. Clevidipine (NAP) - PSUSA/00010288/202005

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Clotiazepam (NAP) - PSUSA/00000827/202005

Applicant(s): various

PRAC Lead: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Cyproterone, ethinylestradiol (NAP) - PSUSA/00000906/202005

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Dexpanthenol, xylometazoline (NAP) - PSUSA/00010030/202005

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Diphtheria vaccine (adsorbed) (NAP); diphtheria, tetanus vaccine (adsorbed) (NAP) - PSUSA/00001128/202005

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Fluorescein[26] (NAP) - PSUSA/00009153/202004

Applicant(s): various

PRAC Lead: Martin Huber

[26] Systemic use only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Formoterol (NAP) - PSUSA/00001469/202005

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Gadobenic acid (NAP) - PSUSA/00001500/202004

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Gadobutrol (NAP) - PSUSA/00001502/202004

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Gadodiamide (NAP) - PSUSA/00001503/202004

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Gadopentetic acid (NAP) - PSUSA/00001504/202004

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Gadoteric acid[27] (NAP) – PSUSA/00001505/202004

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Gadoteric acid[28] (NAP) - PSUSA/00001506/202004

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Gadoteridol (NAP) - PSUSA/00001507/202004

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Gadoxetic acid disodium (NAP) - PSUSA/00001509/202004

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Human hemin (NAP) - PSUSA/00001629/202005

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Indobufen (NAP) - PSUSA/00001736/202005

Applicant(s): various

PRAC Lead: Amelia Cupelli

[27] Intra-articular formulation(s) only
[28] Intravenous (IV) and intravascular formulation(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Iodixanol (NAP) - PSUSA/00001766/202004

Applicant(s): various

PRAC Lead: Karen Pernille Harg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Iomeprol (NAP) - PSUSA/00001769/202004

Applicant(s): various

PRAC Lead: Karen Pernille Harg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Irinotecan[29] (NAP) - PSUSA/00001783/202005

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.27. Ivabradine, metoprolol (NAP) - PSUSA/00010381/202004

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.28. Ketobemidone (NAP) - PSUSA/00001807/202005

Applicant(s): various

PRAC Lead: Karen Pernille Harg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[29] All formulation(s) except liposomal

6.3.29. Lanreotide (NAP) - PSUSA/00001826/202005

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.30. Methoxyflurane (NAP) - PSUSA/00010484/202005

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.31. Mifepristone (NAP) - PSUSA/00002060/202005

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.32. Mifepristone, misoprostol (NAP) - PSUSA/00010378/202005

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.33. Misoprostol[30] (NAP) - PSUSA/00010291/202006

Applicant(s): various

PRAC Lead: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.34. Misoprostol[31] (NAP) - PSUSA/00010353/202005

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

[30] Gastrointestinal indication(s) only
[31] Gynaecological indication(s) only - labour induction

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.35. Misoprostol[32] (NAP) - PSUSA/00010354/202005

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.36. Mometasone (NAP) - PSUSA/00002085/202005

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.37. Nicergoline (NAP) - PSUSA/00002150/202005

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.38. Ozenoxacin (NAP) - PSUSA/00010651/202005

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.39. Peppermint oil (NAP) - PSUSA/00010436/202005

Applicant(s): various

PRAC Lead: Gudrun Stefansdottir

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[32] Gynaecological indication(s) only - termination of pregnancy

6.3.40. Solifenacin (NAP) - PSUSA/00002769/202006

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.41. Tamoxifen (NAP) - PSUSA/00002846/202004

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.42. Ticlopidine (NAP) - PSUSA/00002952/202005

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.43. Tramadol (NAP) - PSUSA/00003002/202005

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.44. Valsartan (NAP); hydrochlorothiazide, valsartan (NAP) - PSUSA/00010396/202004

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.45. Xylometazoline (NAP) - PSUSA/00003134/202005

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/LEG 066

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Cumulative review of cases of pancreatitis as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00000013/201912) adopted in September 2020

Action: For adoption of advice to CHMP

6.4.2. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/LEG 031

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Cumulative review of cases of acute pancreatitis as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00009204/202001) adopted in September 2020

Action: For adoption of advice to CHMP

6.4.3. Methotrexate - JYLAMVO (CAP) - EMEA/H/C/003756/LEG 002

Applicant: Therakind (Europe) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Comprehensive review of the value of performing liver biopsies as a diagnostic tool to monitor hepatotoxicity of methotrexate in non-oncologic indications as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002014/201910) adopted in May 2020

Action: For adoption of advice to CHMP

6.4.4. Methotrexate - NORDIMET (CAP) - EMEA/H/C/003983/LEG 003

Applicant: Nordic Group B.V.

PRAC Rapporteur: Martin Huber

Scope: Comprehensive review of the value of performing liver biopsies as a diagnostic tool to monitor hepatotoxicity of methotrexate in non-oncologic indications as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002014/201910) adopted in May 2020

Action: For adoption of advice to CHMP

6.4.5. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/LEG 049

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Cumulative review of cases of major adverse cardiovascular events (MACE), including fatal cases, as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00003085/201912) adopted in July 2020

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Ceftaroline fosamil - ZINFORO (CAP) - EMEA/H/C/002252/II/0055

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Maia Uusküla

Scope: Update of sections 4.4 and 5.2 of the SmPC in order to include information on the use of ceftaroline in patients with cystic fibrosis, based on a pooled population pharmacokinetic (pop PK) analysis that included data from cystic fibrosis patients treated with ceftaroline fosamil as requested in the conclusions of LEG 016 adopted in June 2020, initially requested in the conclusions of periodic safety update single assessment (PSUSA) procedure (PSUSA/00010013/201810) adopted in May 2019. The MAH took the opportunity to make minor editorial changes in the product information

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews[33]

6.6.1. COVID-19 mRNA vaccine (nucleoside-modified) BNT162b1 - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 002

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: First 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

[33] 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

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[34]

7.1.1. Betibeglogene autotemcel – ZYNTEGLO (CAP) - EMEA/H/C/PSA/S/0059.1

Applicant: Bluebird bio (Netherlands) B.V, ATMP[35]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to PSA/S/0059 [substantial amendment to a protocol previously agreed in the framework of the initial marketing authorisation(s) for a non-interventional PASS to collect longitudinal data on clinical outcomes of patients with transfusion-dependent β-thalassaemia (TDT) who have received treatment with Zynteglo (betibeglogene autotemcel) in the post-marketing setting] as per the request for supplementary information (RSI) adopted in November 2020[36]

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

7.1.2. Blinatumomab – BLINCYTO (CAP) - EMEA/H/C/PSA/S/0057.1

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: MAH's response to PSA/S/0057 [substantial amendment to a protocol previously agreed in February 2020 for study 20180130: an observational PASS to describe the long-term safety profile of first-relapse B-precursor acute lymphocytic leukaemia (ALL) paediatric patients who have been treated with blinatumomab or chemotherapy prior to undergoing haematopoietic stem cell transplant (HSCT)] as per the request for supplementary information (RSI) adopted in September 2020

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

7.1.3. Elosulfase alfa – VIMIZIM (CAP) - EMEA/H/C/PSA/S/0062

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Substantial amendment to a protocol previously agreed in the framework of the initial marketing authorisation(s) for a multicentre, multinational, observational Morquio A Registry Study (MARS) to characterise and describe the mucopolysaccharidosis IV type A (MPS IVA) population as a whole, including the heterogeneity, progression, and natural history of MPS IVA and to track the safety and clinical outcomes of patients with MPS IVA patients treated with Vimizim (elosulfase alfa)

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

[34] In accordance with Article 107n of Directive 2001/83/EC
[35] Advanced therapy medicinal product
[36] Held 26-29 October 2020

7.1.4. Turoctocog alfa pegol – ESPEROCT (CAP) - EMEA/H/C/PSA/S/0061

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Substantial amendment to a protocol previously agreed in April 2020 for a multinational, prospective, open labelled, non-controlled, non-interventional post-authorisation study to investigate the long-term safety of turoctocog alfa pegol (N8-GP) including the polyethylene glycol (PEG) moiety of the substance during routine prophylaxis in patients with haemophilia A

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[37]

7.2.1. Botulinum toxin type A - NUCEIVA (CAP) - EMEA/H/C/004587/MEA 002.2

Applicant: Evolus Pharma Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA 002.1 [protocol for study EV-010: a non-interventional post-authorisation safety study of Nuceiva (botulinum toxin type A) for the treatment of moderate-to-severe glabellar lines] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.2.2. Fremanezumab - AJOVY (CAP) - EMEA/H/C/004833/MEA 003.2

Applicant: Teva GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: MAH's response to MEA 003.1 [protocol for observational cohort study TV48125-MH-50038: a pregnancy database study assessing pregnancy outcomes in patients treated with Ajovy (fremanezumab)] as per the request for supplementary information (RSI) adopted in March 2020

Action: For adoption of advice to CHMP

7.2.3. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 033.4

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Substantial amendment to a protocol previously agreed in December 2017 for study MK-8259-050 (version 2.0) (listed as a category 3 study in the RMP): an observational PASS for golimumab in the treatment of poly-articular juvenile idiopathic arthritis (pJIA) using the German Biologics JIA registry (BiKeR)

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

Action: For adoption of advice to CHMP

7.2.4. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/MEA 020.2

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: MAH's response to MEA 020.1 [protocol for study CT-P13 4.8: an observational, prospective cohort study to evaluate the safety of Remsima (infliximab) subcutaneous in patients with rheumatoid arthritis (RA)] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.2.5. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/MEA 002

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Protocol for study VX20-445-120: a five year-registry based study to assess real-world effects and utilisation patterns of elexacaftor/tezacaftor/ivacaftor combination therapy (ELX/TEZ/IVA) in patients with cystic fibrosis (CF)

Action: For adoption of advice to CHMP

7.2.6. Loxapine - ADASUVE (CAP) - EMEA/H/C/002400/MEA 001.7

Applicant: Ferrer Internacional s.a.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 001.5 [substantial amendment to a protocol previously agreed in May 2018 for study AMDC-204-401: a post-authorisation observational study to evaluate the safety of Adasuve (loxapine for inhalation) in agitated persons in routine clinical care] as per the request for supplementary information (RSI) adopted in July 2020

Action: For adoption of advice to CHMP

7.2.7. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/MEA 001.5

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

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

Action: For adoption of advice to CHMP

7.2.8. Naldemedine - RIZMOIC (CAP) - EMEA/H/C/004256/MEA 001.3

Applicant: Shionogi B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 001.2 [protocol for an observational PASS of patients with chronic opioid use for non-cancer and cancer pain who have opioid-induced constipation (OIC) [final clinical study report (CSR) expected in January 2026]] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.2.9. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/MEA 004.6

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Substantial amendment to a protocol previously agreed in April 2018 for study NB-452: a cross-sectional survey to evaluate the effectiveness of the physician prescribing checklist (PPC) among physicians in the European Union (EU) as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010366/201909) adopted in April 2020

Action: For adoption of advice to CHMP

7.2.10. Patisiran - ONPATTRO (CAP) - EMEA/H/C/004699/MEA 003.1

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 003 [protocol for non-interventional study ALN-TTR02-010: patisiran-lipid nanoparticle (LNP) observational pregnancy surveillance programme] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.2.11. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[38]) - EMEA/H/W/002300/MEA 003.3

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Scientific Opinion Holder (SOH)'s response to MEA 003.2 [amended protocol previously agreed in May 2018 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

[38] 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)

hospitalisation or death, in children vaccinated with the vaccine] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.2.12. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/MEA 001.3

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 001.2 [protocol for study P19-633: a post-marketing registry-based prospective cohort study of long-term safety of risankizumab in real world setting in Denmark and Sweden [final study report expected in December 2031]] as per the request for supplementary information (RSI) adopted in September 2020

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[39]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[40]

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

Action: For adoption of PRAC Assessment Report

7.4.2. Agalsidase beta - FABRAZYME (CAP) - EMEA/H/C/000370/II/0120

Applicant: Genzyme Europe BV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of the final study report of the Fabry pregnancy sub-registry (listed as a category 3 study in the RMP): a multicentre, international, longitudinal, observational study on pregnancy outcomes for any pregnant woman enrolled in the MAH's Fabry registry who also consented to participate in the sub-registry, regardless of whether she was receiving disease therapy and irrespective of the commercial medicinal product with which she may have been be treated

Action: For adoption of PRAC Assessment Report

[39] In accordance with Article 107p-q of Directive 2001/83/EC
[40] 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

7.4.3. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0048

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Submission of the results of study WO41486 evaluating the effectiveness of the healthcare professional (HCP) brochure designed to mitigate important immune-related risks in patients receiving atezolizumab in the European Union. As a consequence, section 4.4 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 RMP (version 17.0) is updated accordingly. In addition, a delay until 31 August 2021 in the due date for the submission of the final clinical safety report (CSR) for IMvigor210: a phase 2, multicentre, single-arm study of atezolizumab in patients with locally advanced or metastatic urothelial bladder cancer, is introduced

Action: For adoption of PRAC Assessment Report

7.4.4. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/WS1810/0061; dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/WS1810/0082; dolutegravir, rilpivirine - JULUCA (CAP) - EMEA/H/C/004427/WS1810/0028

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report for study 201177 (EuroSIDA) (listed as a category 3 study in the RMP): a prospective observational cohort study to monitor and compare the occurrence of hypersensitivity reactions (HSR) and hepatotoxicity in patients receiving dolutegravir (with or without abacavir) and other integrase inhibitors (with or without abacavir)

Action: For adoption of PRAC Assessment Report

7.4.5. Follitropin alfa - OVALEAP (CAP) - EMEA/H/C/002608/II/0034

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Menno van der Elst

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

Action: For adoption of PRAC Assessment Report

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

Applicant: Ferrer Internacional s.a.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of the final clinical study report (CSR) for study AMDC-204-401: a post-

authorisation observational study to evaluate the safety of Adasuve/Staccato (loxapine for inhalation) in agitated persons in routine clinical care (EU PASS). The RMP (version 9.3) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

7.5.1. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/MEA 019.5

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Second interim report for drug utilisation survey OBS14697: a drug utilisation study to assess the effectiveness of dosing recommendation of Praluent (alirocumab) as per the product information to avoid very low-density lipoprotein (LDL)-C levels [final results expected in Q3 2021]

Action: For adoption of advice to CHMP

7.5.2. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/ANX 002.1

Applicant: Kite Pharma EU B.V., ATMP[41]

PRAC Rapporteur: Anette Kirstine Stark

Scope: First quarterly safety data report for study KT-EU-471-0117: a long-term non-interventional registry study of Yescarta (axicabtagene ciloleucel) to evaluate the incidence rate and severity of adverse drug reactions (ADRs) and further evaluate and characterise the identified risks, potential risks and missing information (from initial opinion/marketing authorisation)

Action: For adoption of advice to CAT and CHMP

7.5.3. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/MEA 024.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Fifth interim report for study A8081062 (listed as category 3 study in the RMP): a descriptive study evaluating the frequency of risk factors for and sequelae of potential sight threatening event and severe visual loss among patients following exposure to Xalkori (crizotinib) and measuring the effectiveness of the crizotinib therapeutic management guide in communicating risks, and recommended actions to minimize risks, among physicians prescribing crizotinib in Europe

Action: For adoption of advice to CHMP

[41] Advanced therapy medicinal product

7.5.4. Ketoconazole - KETOCONAZOLE HRA (CAP) - EMEA/H/C/003906/ANX 002.7

Applicant: HRA Pharma Rare Diseases

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Third interim annual report for a prospective, multi-country, observational registry study to collect clinical information on patients with endogenous Cushing's syndrome exposed to ketoconazole using the existing European registry on Cushing's syndrome (ERCUSYN) to assess drug utilisation pattern and to document the safety (e.g. hepatotoxicity, QT prolongation) and effectiveness of ketoconazole

Action: For adoption of advice to CHMP

7.5.5. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/MEA 001.1

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study PUMA-NER-6201: an open-label study to characterize the incidence and severity of diarrhoea in patients with early stage human epidermal growth factor receptor 2 positive (HER2+) breast cancer treated with neratinib and intensive loperamide prophylaxis, with/without anti-inflammatory treatment (budesonide) and with/without a bile acid sequestrant (colestipol) [final study results expected in March 2021]

Action: For adoption of advice to CHMP

7.5.6. Nomegestrol acetate, estradiol - ZOELY (CAP) - EMEA/H/C/001213/ANX 011.7

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Adrien Inoubli

Scope: Fifth interim report for study P08291 (PRO-E2): a prospective observational controlled cohort study to assess the risk of venous thromboembolic events (VTE) and arterial thromboembolic events (ATE) in nomegestrel/estradiol users compared with the VTE risk in users of combined oral contraceptives containing levonorgestrel

Action: For adoption of advice to CHMP

7.5.7. Ospemifene - SENSHIO (CAP) - EMEA/H/C/002780/ANX 001.10

Applicant: Shionogi B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Fifth annual interim report for a PASS (ENCEPP/SDPP/8585) (listed as a category 1 study in Annex II and the RMP): an observational retrospective cohort study of ospemifene utilising existing databases in Germany, Italy, Spain and the United States to evaluate the incidence of venous thromboembolism and other adverse events in vulvar and vaginal atrophy (VVA) patients treated with ospemifene as compared to: 1) patients newly prescribed selective oestrogen receptor modulators (SERM) for oestrogen-deficiency conditions or breast cancer prevention and; 2) the incidence in untreated VVA patients [final report expected in February 2021]

Action: For adoption of advice to CHMP

7.5.8. Rotavirus vaccine (live, oral) - ROTARIX (CAP) - EMEA/H/C/000639/MEA 094.2

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Second annual report for study EPI-ROTA-052 BOD EU SUPP (201433) (EuroRotaNet): an observational community-based strain surveillance study to monitor the potential emergence and spread of novel rotavirus strains throughout Europe [study extended until December 2020]

Action: For adoption of advice to CHMP

7.5.9. Sebelipase alfa - KANUMA (CAP) - EMEA/H/C/004004/ANX 001.4

Applicant: Alexion Europe SAS

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fifth interim report for study ALX-LALD-501: a non-interventional, multicentre, prospective disease and clinical outcome registry of patients with lysosomal acid lipase deficiency (LAL-D) to further understand the disease, its progression and any associated complication, and to evaluate the long-term efficacy and safety of Kanuma (sebelipase alfa)

Action: For adoption of advice to CHMP

7.5.10. Somatropin - OMNITROPE (CAP) - EMEA/H/C/000607/MEA 039

Applicant: Sandoz GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Second interim report for study EP00-502 – PATRO Adults: a non-interventional post-marketing surveillance in adult patients with growth hormone deficiency treated with Omnitrope (somatropin) within routine clinical practice in Europe

Action: For adoption of advice to CHMP

7.5.11. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/ANX 003.3

Applicant: Novartis Europharm Limited, ATMP[42]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Second 6-monthly interim report for a study based on disease registry CCTL019B2401 (listed as a category 1 study in Annex II and the RMP): a non-interventional PASS in acute lymphoblastic leukaemia (ALL) and diffuse large B-cell lymphoma (DLBCL) patients in order to further characterise the safety, including long-term safety, of Kymriah (tisagenlecleucel). The procedure also includes the MAH's response to ANX 003.2 [final study report expected in December 2038]

[42] Advanced therapy medicinal product

Action: For adoption of advice to CAT and CHMP

7.6. Others

7.6.1. Apalutamide - ERLEADA (CAP) - EMEA/H/C/004452/MEA 004.2

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to MEA 004.1 [feasibility study for a prospective, observational safety study to characterise the risks of the use of apalutamide in non-metastatic castration-resistant prostate cancer (NM-CRPC) patients on androgen deprivation therapy (ADT) with clinically significant cardiovascular conditions [final report expected in 2023]] as per the request for supplementary information (RSI) adopted in February 2020

Action: For adoption of advice to CHMP

7.6.2. Avatrombopag - DOPTELET (CAP) - EMEA/H/C/004722/MEA 002.2

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 002.1 [feasibility assessment for study AVA-CLD-402: evaluation of the feasibility of conducting a PASS of Doptelet (avatrombopag) in patients with severe chronic liver disease (CLD) and of the use of potential European electronic health care databases] as per the request for supplementary information (RSI) adopted in July 2020

Action: For adoption of advice to CHMP

7.6.3. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/LEG 028.2

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Tiphaine Vaillant

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

Action: For adoption of advice to CHMP

7.6.4. Lopinavir, ritonavir - KALETRA (CAP) - EMEA/H/C/000368/LEG 121.3

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Adrien Inoubli

Scope: Annual safety review of the PENTA - European Pregnancy and Paediatric human immunodeficiency virus (HIV) Cohort Collaboration (EPPICC) cohort study conducted in children from 14 days to 2 years of age as regards to chronic exposure to propylene glycol and ethanol and toxicity, medication errors and lack of efficacy/resistance in relation to

potentially suboptimal pharmacokinetic (PK) parameters

Action: For adoption of advice to CHMP

7.6.5. Lusutrombopag - MULPLEO (CAP) - EMEA/H/C/004720/MEA 002.1

Applicant: Shionogi B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Feasibility study report for study VV-REG-090246: a PASS exploring the hepatic safety of lusutrombopag Shionogi in patients with Child-Pugh class C liver disease (from initial opinion/MA) [final study report expected in December 2025]

Action: For adoption of advice to CHMP

7.6.6. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/MEA 064.1

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Interim report for study 101MS411 (listed as a category 3 study in the RMP): an observational cohort study utilising the Tysabri outreach unified commitment to health (TOUCH) prescribing programme and certain EU multiple sclerosis (MS) registries to estimate the risk of progressive multifocal leukoencephalopathy (PML) and other serious opportunistic infections among patients who were exposed to an MS disease modifying therapies prior to treatment with Tysabri (natalizumab) [final clinical study report expected in Q2 2024]

Action: For adoption of advice to CHMP

7.6.7. Trastuzumab emtansine - KADCYLA (CAP) - EMEA/H/C/002389/MEA 016

Applicant: Roche Registration GmbH

PRAC Rapporteur: Hans Christian Siersted

Scope: Primary interim clinical study report (CSR) (report No. 1100510) for study BO28407 (KAITLIN): a randomised, multicentre, open-label, phase 3 trial comparing trastuzumab plus pertuzumab plus a taxane following anthracyclines versus trastuzumab emtansine plus pertuzumab following anthracyclines as adjuvant therapy in patients with operable human epidermal growth factor receptor 2 (HER2)-positive primary breast cancer

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. 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

8.1.2. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/S/0043 (without RMP)

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Metreleptin - MYALEPTA (CAP) - EMEA/H/C/004218/S/0014 (without RMP)

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Tocofersolan - VEDROP (CAP) - EMEA/H/C/000920/S/0039 (without RMP)

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Melinda Palfi

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. Betibeglogene autotemcel - ZYNTEGLO (CAP) - EMEA/H/C/003691/R/0018 (without RMP)

Applicant: bluebird bio (Netherlands) B.V, ATMP[43]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.2.2. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/R/0047 (without RMP)

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Laurence de Fays

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Lorlatinib - LORVIQUA (CAP) - EMEA/H/C/004646/R/0011 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Novartis Gene Therapies EU Limited, ATMP[44]

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.2.5. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) - EMEA/H/C/003963/R/0040 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Hrabcik

Scope: Conditional renewal of the marketing authorisation

[43] Advanced therapy medicinal product
[44] Advanced therapy medicinal product

Action: For adoption of advice to CHMP

8.2.6. Rucaparib - RUBRACA (CAP) - EMEA/H/C/004272/R/0025 (without RMP)

Applicant: Clovis Oncology Ireland Limited

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/R/0018 (with RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Elbasvir, grazoprevir - ZEPATIER (CAP) - EMEA/H/C/004126/R/0026 (with RMP)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Human coagulation factor X - COAGADEX (CAP) - EMEA/H/C/003855/R/0031 (with RMP)

Applicant: BPL Bioproducts Laboratory GmbH

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Nomegestrol acetate, estradiol - ZOELY (CAP) - EMEA/H/C/001213/R/0055 (without RMP)

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Adrien Inoubli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. 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

8.3.6. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/R/0054 (without RMP)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

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. Ethinylestradiol; ethinylestradiol, levonorgestrel (NAP) - FR/H/0516/001/II/016

Applicant(s): Theramex Ireland Limited (Seasonique)

PRAC Lead: Adrien Inoubli

Scope: PRAC consultation on a national procedure evaluating results of an imposed PASS: a retrospective longitudinal cohort study to assess the risk of venous thromboembolic events (VTE) in women exposed to Seasonique conducted in the USA and results of a drug utilisation study (DUS) conducted in Europe: France, Italy and Belgium, on request of France

Action: For adoption of advice to Member States

11.2. Other requests

11.2.1. Methotrexate[45] (NAP) - DE/H/PSUFU/00002014/201910

Applicant(s): Addenda Pharma, Especialidades Farmacéuticas Centrum S.A., Gebro Pharma, medac, Morningside Healthcare Limited, Mylan, Nordic Group, Orion Pharma, Pfizer, Remedica, Rompharm, Sandoz, Teva

PRAC Lead: Martin Huber

Scope: PRAC consultation on a PSUR follow-up (PSU FU) procedure evaluating comprehensive reviews of the value of performing liver biopsies as a diagnostic tool to monitor hepatotoxicity of methotrexate in non-oncologic indications, as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure (PSUSA/00002014/201910) concluded in May 2020, on request of Germany

Action: For adoption of advice to Member States

[45] In non-oncology indication(s)

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

Action: For discussion

12.5. Cooperation with International Regulators

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

12.7.1. PRAC work plan 2021

PRAC lead: Sabine Straus, Martin Huber

Action: For adoption

12.8. Planning and reporting

12.8.1. EMA Executive Director - introduction to PRAC

Action: For discussion

12.8.2. Marketing authorisation applications (MAA) 2021 - initial MAA submissions with eligibility request to CP and forecast for 2020 – planning update dated Q4 2020

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.13.2. EU individual case safety report (ICSR) implementation guide – revision 2

Action: For adoption

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.14.3. EU RMP Annex 1 tool update - suspension of submission

Action: For discussion

12.14.4. Good pharmacovigilance practice (GVP) module XVI on 'Risk minimisation measures: selection of tools and effectiveness indicators' – revision 3 and new Addendum II

PRAC lead: Sabine Straus

Action: For adoption

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. 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. EMA policy on handling of competing interests for scientific committees' members and experts – revision of policy 0044

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/