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Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 28 September - 01 October 2020

Chair: Sabine Straus – Vice-Chair: Martin Huber

28 September 2020, 10:30 – 19:30, via teleconference

29 September 2020, 08:30 – 19:30, via teleconference

30 September 2020, 08:30 – 19:30, via teleconference

01 October 2020, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

15 October 2020, 09:00 – 12:00, via teleconference

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

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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 28 September – 01 October 2020. See October 2020 PRAC minutes (to be published post November 2020 meeting).

1.2. Agenda of the meeting on 28 September-01 October 2020

Action: For adoption

1.3. Minutes of the previous meeting on 31 August-03 September 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 procedures¹

None

3.5. Others

None

4. Signals assessment and prioritisation²

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Isatuximab – SARCLISA (CAP)

Applicant(s): Sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: Signal of anaphylactic reaction

Action: For adoption of PRAC recommendation

EPITT 19598 – New signal

Lead Member State(s): ES

4.1.2. Prednisolone (NAP); prednisone (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of bradycardia

Action: For adoption of PRAC recommendation

EPITT 19613 – New signal

Lead Member State(s): DK

4.1.3. Remdesivir - VEKLURY (CAP)

Applicant(s): Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Signal of acute kidney injury

Action: For adoption of PRAC recommendation

EPITT 19605 – New signal

Lead Member State(s): CZ

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

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

4.2. New signals detected from other sources

4.2.1. Efavirenz – SUSTIVA (CAP), STOCRIN (CAP); NAP

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

PRAC Rapporteur: Ana Sofia Martins

Scope: Signal of microcephaly

Action: For adoption of PRAC recommendation

EPITT 19595 – New signal

Lead Member State(s): PT

4.3. Signals follow-up and prioritisation

4.3.1. Amitriptyline (NAP); bupropion (NAP); citalopram (NAP); escitalopram (NAP); fluoxetine (NAP); mirtazapine (NAP); paroxetine (NAP); sertraline (NAP); trazodone (NAP); venlafaxine (NAP)

Applicant(s): various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of post-partum haemorrhage

Action: For adoption of PRAC recommendation

EPITT 19552 – Follow-up to June 2020

4.3.2. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/SDA/026

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

PRAC Rapporteur: Menno van der Elst

Scope: Signal of Sjogren's syndrome

Action: For adoption of PRAC recommendation

EPITT 19564 – Follow-up to May 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. Abiraterone acetate - EMEA/H/C/005408

Scope: Treatment of metastatic prostate cancer

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

5.1.2. Azathioprine - EMEA/H/C/005055

Scope: Prophylaxis of transplant rejection and treatment of chronic inflammatory bowel disease (IBD) (Crohn's disease or ulcerative colitis), relapsing multiple sclerosis and generalised myasthenia gravis

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

5.1.3. Bevacizumab - EMEA/H/C/005286

Scope: Treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer; first-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer; first line treatment of patients with advanced and/or metastatic renal cell cancer

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

5.1.4. Bevacizumab - EMEA/H/C/005556

Scope: Treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer; first-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer; first line treatment of patients with advanced and/or metastatic renal cell cancer

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

5.1.5. 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 COVID-19, eye inflammation and infection

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

5.1.6. Fedratinib - EMEA/H/C/005026, Orphan

Applicant: Celgene Europe BV

Scope: Treatment of primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis

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

5.1.7. Fostemsavir - EMEA/H/C/005011

Scope: Treatment in combination with other antiretrovirals of adults with multidrug resistant human immunodeficiency virus-1 (HIV-1) infection for whom it is otherwise not possible to construct a suppressive anti-viral regimen due to resistance, intolerance or safety considerations

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

5.1.8. Hepatitis b surface antigen - EMEA/H/C/005063

Scope: Prevention of hepatitis B virus infection

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

5.1.9. Insulin aspart - EMEA/H/C/004965

Scope: Treatment of diabetes mellitus

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

5.1.10. Ioflupane (¹²³I) - EMEA/H/C/005135

Scope: Detection of loss of functional dopaminergic neuron terminals in the striatum

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

5.1.11. Lenalidomide - EMEA/H/C/005348

Scope: Treatment of multiple myeloma

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

5.1.12. Lenalidomide - EMEA/H/C/005734

Scope: Treatment of multiple myeloma and follicular lymphoma

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

5.1.13. Lenalidomide - EMEA/H/C/005729

Scope: Treatment of multiple myeloma, myelodysplastic syndromes and follicular lymphoma

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

5.1.14. Moxetumomab pasudotox - EMEA/H/C/005322, Orphan

Applicant: AstraZeneca AB

Scope: Treatment of relapsed or refractory hairy cell leukaemia (HCL) after receiving at least two prior systemic therapies

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

5.1.15. Ofatumumab – EMEA/H/C/005410

Scope: Treatment of relapsing forms of multiple sclerosis

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

5.1.16. Pertuzumab, trastuzumab - EMEA/H/C/005386

Scope: Treatment of early breast cancer, metastatic breast cancer

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

5.1.17. Potassium - EMEA/H/C/005407, Orphan

Applicant: Advicenne S.A.

Scope: Treatment of distal renal tubular acidosis (dRTA) in patients aged 6 months and older

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

5.1.18. Remimazolam - EMEA/H/C/005246

Scope: Induction and maintenance of procedural sedation

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

5.1.19. Risperidone - EMEA/H/C/005406

Scope: Treatment of schizophrenia

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

5.1.20. 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

5.1.21. 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

5.1.22. Selpercatinib - EMEA/H/C/005375

Scope: Treatment of adults with advanced rearranged during transfection (RET) fusion-positive non-small cell lung cancer (NSCLC) who require systemic therapy; treatment of adults with advanced RET fusion-positive thyroid cancer who require systemic therapy and who have progressed following prior treatment; treatment of adults and adolescents 12 years and older with advanced RET-mutant medullary thyroid cancer (MTC) who require systemic therapy

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

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

Applicant: TMC Pharma (EU) Limited

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

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

5.1.24. Sunitinib - EMEA/H/C/005419

Scope: Treatment of gastrointestinal stromal tumour (GIST) and metastatic renal cell carcinoma (MRCC) and pancreatic neuroendocrine tumours (pNET)

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

5.1.25. [Tucatinib - EMEA/H/C/005263](#)

Scope: Treatment of metastatic breast cancer or brain metastases

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. [Aprepitant - EMEND \(CAP\) - EMEA/H/C/000527/II/0063](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Annika Folin

Scope: Submission of an updated RMP (version 5.1) in order to remove all safety concerns and information related to both 40 mg and 165 mg capsules strengths and the postoperative nausea and vomiting indication (PONV), as well as to update data in the post-authorisation exposure and epidemiology section following the removal of the two capsule strengths (40 mg and 165 mg) and the removal of the PONV indication as approved in variation IB/0062/G finalised at CHMP in June 2020

Action: For adoption of PRAC Assessment Report

5.2.2. [Dapagliflozin - EDISTRIDE \(CAP\) - EMEA/H/C/004161/WS1844/0039; FORXIGA \(CAP\) - EMEA/H/C/002322/WS1844/0057](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Re-categorisation of study D169C00011: a retrospective cohort study on the risk of diabetic ketoacidosis (DKA) to determine the effectiveness of additional risk minimisation measures (aRMMs) in place for DKA by assessing the impact of the risk minimisation measures (RMMs) on the risk of DKA in type 1 diabetes mellitus (T1DM) patients who are treated with dapagliflozin in Europe, from a category 1 to a category 3 study in the RMP (version 20). Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated accordingly

Action: For adoption of PRAC Assessment Report

5.2.3. [Filgrastim - RATIOGRASTIM \(CAP\) - EMEA/H/C/000825/II/0069](#)

Applicant: Ratiopharm GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Submission of an updated RMP (version 10.0) in order to remove the additional pharmacovigilance activity on 'cooperation with the Severe Chronic Neutropenia International Registry (SCNIR) and analysis of corresponding Ratiograstim/Tevagrastim (filgrastim)-SCNIR data

Action: For adoption of PRAC Assessment Report

5.2.4. Filgrastim - TEVAGRASTIM (CAP) - EMEA/H/C/000827/II/0077

Applicant: Teva GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Submission of an updated RMP (version 10.0) in order to remove the additional pharmacovigilance activity on `cooperation with the Severe Chronic Neutropenia International Registry (SCNIR) and analysis of corresponding Ratiograstim/Tevagrastim (filgrastim)-SCNIR data

Action: For adoption of PRAC Assessment Report

5.2.5. Fosaprepitant - IVEMEND (CAP) - EMEA/H/C/000743/II/0043

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Annika Folin

Scope: Submission of an updated RMP (version 5.1) to remove all safety concerns and to update data in the post-authorisation exposure and epidemiology sections

Action: For adoption of PRAC Assessment Report

5.2.6. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0061, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Submission of an updated RMP (version 16.2) in order to introduce changes to safety concerns following the conclusions of renewal procedure R/049 finalised in April 2019. The MAH took the opportunity to include additional changes related to two post-authorisation measures, namely the postponement of the completion date of study PCI-32765MCL3002 (listed as a category 3 study in the RMP): a randomized, double-blind, placebo-controlled phase 3 study of the Bruton's tyrosine kinase (BTK) inhibitor, PCI-32765 (ibrutinib), in combination with bendamustine and rituximab (BR) in subjects with newly diagnosed mantle cell lymphoma and the removal of study 54179060CLL1017 on drug-drug interaction (DDI) in line with the conclusions of variation II/058 finalised in April 2020

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. Pregabalin - LYRICA (CAP) - EMEA/H/C/000546/WS1919/0109; PREGABALIN PFIZER (CAP) - EMEA/H/C/003880/WS1919/0038

Applicant: Upjohn EESV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of an updated RMP (version 13.0) to include results from recently completed PASS studies, namely: 1) study A0081359: a population-based cohort study of pregabalin to characterize pregnancy outcomes; 2) study A0081106: a 12-month open-label study to evaluate the safety and tolerability of pregabalin as adjunctive therapy in paediatric subjects 1 month to 16 years of age with partial onset seizures and paediatric and adult subjects 5 to 65 years of age with primary generalized tonic-clonic seizures; 3) study A0081042: a double-blind, placebo-controlled, parallel-group, multicentre study of the efficacy and safety of pregabalin as adjunctive therapy in children 1 month through <4 years of age with partial onset seizures; 4) study A0081105: a randomized, double-blind, placebo-controlled, parallel group, multicentre trial of pregabalin as adjunctive therapy in paediatric and adult subjects with primary generalized tonic-clonic seizures. In addition, information on study A0081096: a prospective randomized 12-week controlled study of visual field change in subjects with partial seizures receiving pregabalin or placebo has been updated as well as study A0081365: a phase 4, randomised, double-blind, double-dummy, placebo- and active-controlled, single-dose, six-way crossover study to evaluate the potential for abuse with pregabalin (added as a new FDA³-imposed PASS). The clinical study report (CSR) for study A0081359 is included in the submission

Action: For adoption of PRAC Assessment Report

5.2.9. Zoledronic acid - ACLASTA (CAP) - EMEA/H/C/000595/II/0076

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

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

Action: For adoption of PRAC Assessment Report

³ United States Food and Drug Administration

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

5.3.1. Adalimumab - HULIO (CAP) - EMEA/H/C/004429/X/0016

Applicant: Mylan S.A.S

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application to add a new strength of 20 mg solution for injection. The RMP (version 3.1) is updated in accordance

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

5.3.2. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/II/0198

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include treatment of moderately to severely active ulcerative colitis in paediatric patients. As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC for the 40mg/0.8mL, 40mg/0.4mL and 80mg/0.8mL presentations are updated. Furthermore, sections 5.1 and 5.2 of the SmPC for the 20mg/0.2mL presentation are updated. The package leaflet and the RMP (version 15.0) are updated in accordance

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

5.3.3. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/II/0033, Orphan

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC to revise the frequencies of adverse drug reactions (ADRs) based on safety reports and to add new ADRs based on post-marketing spontaneous reports as requested in the conclusions of the renewal procedure (R/0026) finalised in September 2019. The package leaflet and the RMP (version 9.0) are updated accordingly. The RMP is also brought 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 introduce minor editorial changes in section 2 of the SmPC and Annex III-A on labelling

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

5.3.4. Apalutamide - ERLEADA (CAP) - EMEA/H/C/004452/II/0008

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: 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 ARN-509-003 (SPARTAN) (listed as a post-authorisation efficacy study (PAES)) in Annex II): a multicentre, randomised, double-blind, placebo-controlled, phase 3 study of apalutamide (ARN-509) in men with non-metastatic (M0) castration-resistant prostate cancer. The package leaflet, Annex II and the RMP (version 3.1) are updated accordingly. The MAH took also 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

5.3.5. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/II/0028, Orphan

Applicant: Kite Pharma EU B.V., ATMP⁴

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC to update the safety information based on updates from study KTE-C19-101: a phase 1/2 multicentre study evaluating the safety and efficacy of Yescarta (axicabtagene ciloleucel (KTE-C19)) in subjects with refractory aggressive non-Hodgkin lymphoma (ZUMA-1). The updates include data from: 1) phase 2 safety management ZUMA-1 cohort 4 intended to assess the impact of earlier interventions on the rate and severity of cytokine release syndrome (CRS) and neurologic events; 2) a 36-month analysis from ZUMA-1 cohorts 1 and 2. The RMP (version 3.1) is updated accordingly

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

5.3.6. 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

5.3.7. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0030, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include the treatment of Philadelphia chromosome positive CD19⁵ positive B-cell precursor acute lymphoblastic leukaemia (ALL) in adult and paediatric patients with relapsed or refractory ALL and adult patients in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%. 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 10.0) are updated accordingly

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

5.3.8. Botulinum toxin type A - NUCEIVA (CAP) - EMEA/H/C/004587/X/0005

Applicant: Evolus Pharma Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to add a new strength of 50 U for botulinum toxin type A for powder for solution for injection in vial (glass) for intramuscular administration. The RMP

⁴ Advanced therapy medicinal product

⁵ Cluster of differentiation 19

(version 3.0) is updated accordingly

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

5.3.9. Budesonide, formoterol - BIRESPIROMAX (CAP) - EMEA/H/C/003890/II/0033/G

Applicant: Teva Pharma B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Grouped variation consisting of: 1) extension of indication to include adolescents of 12 years and older for the regular treatment of asthma, where the use in combination of an inhaled corticosteroid and long-acting β_2 adrenoceptor agonist is appropriate, either in patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting β_2 adrenoceptor agonists, or in patients already adequately controlled on both inhaled corticosteroids and long-acting β_2 adrenoceptor agonists. The extension to the indication is based upon data from the literature. As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 3.0) are updated accordingly. In addition, the MAH took the opportunity to make an administrative update to the Greek, Islandic, Irish and Maltese local representatives. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1); 2) update of sections 4.2, 5.1 and 5.2 of the SmPC to update the information on paediatric data and section 4.4 of the SmPC to remove the warning regarding the risk of growth retardation in children and the guidance on how to address this risk as agreed during the assessment of the initial application for Budesonide/Formoterol Teva Pharma B.V finalised in January 2020

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

5.3.10. Budesonide, formoterol - DUORESP SPIROMAX (CAP) - EMEA/H/C/002348/II/0033/G

Applicant: Teva Pharma B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Grouped variation consisting of: 1) extension of indication to include adolescents of 12 years and older for the regular treatment of asthma, where the use in combination of an inhaled corticosteroid and long-acting β_2 adrenoceptor agonist is appropriate, either in patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting β_2 adrenoceptor agonists, or in patients already adequately controlled on both inhaled corticosteroids and long-acting β_2 adrenoceptor agonists. The extension to the indication is based upon data from the literature. As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 3.0) are updated accordingly. In addition, the MAH took the opportunity to make an administrative update to the Greek, Islandic, Irish and Maltese local representatives. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1); 2) update of sections 4.2, 5.1 and 5.2 of the SmPC to update the information on paediatric data and section 4.4 of the SmPC to remove the warning regarding the risk of growth retardation in children and the guidance on how to address this risk as agreed during the assessment of the initial application for Budesonide/Formoterol Teva Pharma B.V finalised in January 2020

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

5.3.11. [Buprenorphine - BUVIDAL \(CAP\) - EMEA/H/C/004651/X/0008/G](#)

Applicant: Camurus AB

PRAC Rapporteur: Tiphaine Vaillant

Scope: Grouped applications consisting of: 1) line extension to add a new strength of 160 mg for prolonged-release solution for injection pharmaceutical form. The MAH took the opportunity to align the product information with the latest quality review of documents (QRD) template (version 10.1) and to implement new text regarding the content of ethanol in accordance with the EMA document on 'information for the package leaflet regarding ethanol used as an excipient in medicinal products for human use' in the package leaflet; 2) quality/manufacturing aspect related variations.

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

5.3.12. [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

5.3.13. [Clopidogrel - ISCOVER \(CAP\) - EMEA/H/C/000175/WS1820/0142; PLAVIX \(CAP\) - EMEA/H/C/000174/WS1820/0140](#)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Update of section 4.2 of the SmPC in order to add 600 mg as an alternative loading dose to the existing 300 mg to be used at initiation of treatment in the indication of secondary prevention of atherothrombotic events in adult patients suffering from acute coronary syndrome. This update is based on a bibliographic review of published studies. The package leaflet and the RMP (version 2.0) are updated accordingly

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

5.3.14. [Dabigatran etexilate - PRADAXA \(CAP\) - EMEA/H/C/000829/X/0122/G](#)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Grouped applications consisting of: 1) extension application to add two new pharmaceutical forms coated granules (20 mg, 30 mg, 40 mg, 50 mg, 110 mg, 150 mg) and powder and solvent for oral solution (6.25 mg/mL); 2) extension of indication to include

treatment of venous thromboembolic events (VTE) and prevention of recurrent VTE in paediatric patients from birth to less than 18 years of age for Pradaxa (dabigatran etexilate) 75 mg, 110 mg, 150 mg capsules based on paediatric trials, namely study 1160.106: an open-label, randomized, parallel-group, active-controlled, multi-centre non-inferiority study of dabigatran etexilate versus standard of care for venous thromboembolism treatment in children from birth to less than 18 years of age, and study 1160.108: an open label, single arm safety prospective cohort study of dabigatran etexilate for secondary prevention of venous thromboembolism in children from 0 to less than 18 years. As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and labelling are updated in accordance. The RMP (version 37.0) is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

5.3.15. [Dacomitinib - VIZIMPRO \(CAP\) - EMEA/H/C/004779/II/0003/G](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations to update sections 4.2 and 5.2 of the SmPC in order to revise the dosing recommendation for patients with hepatic impairment and to include relevant pharmacokinetics data based on results of study A7471058: a phase 1, open-label, single-dose, parallel-group study to evaluate the plasma pharmacokinetics and safety of dacomitinib in participants with severely impaired hepatic function relative to participants with normal hepatic function. As a consequence, the MAH proposed to remove 'safety in patient with severe hepatic impairment' as missing information from the list of safety concerns in the RMP. In addition, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1). The MAH took also the opportunity to update the RMP to include study A7471064: a single arm study to evaluate the safety of dacomitinib for the first-line treatment of participants in India with metastatic non-small-cell lung carcinoma (NSCLC) with epidermal growth factor receptor (EGFR)-activating mutations as a category 3 study. The RMP (version 1.1) is updated accordingly

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

5.3.16. [Dolutegravir - TIVICAY \(CAP\) - EMEA/H/C/002753/X/0058/G](#)

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Grouped application consisting of: 1) extension application to add a new pharmaceutical form associated with a new strength (5 mg dispersible tablet). The new presentation is indicated for the treatment of human immunodeficiency virus (HIV) infected children from 4 weeks of life and weighing at least 3 kg; 2) update of the currently approved SmPC, labelling and package leaflet for the existing film-coated tablets (10 mg, 25 mg and 50 mg) for children of 6 years and older and weighing at least 15 kg, based on pharmacokinetic (PK), safety, and efficacy data from study P1093: a phase 1/2, multicentre, open-label pharmacokinetic, safety, tolerability and antiviral activity of dolutegravir, a novel integrase inhibitor, in combination regimens in HIV-1 infected infants, children and adolescents and PK

and safety data from relevant sub-studies nested within study ODYSSEY (PENTA 20): a phase 2/3 randomised trial of dolutegravir (DTG)-based antiretroviral therapy vs. standard of care (SOC) in children with HIV infection starting first-line or switching to second-line antiretroviral therapy (ART). In addition, the MAH took the opportunity to amend section 4.1 of SmPC to clarify that children should be 'aged at least 6 years' as the current approved indication is inclusive of those aged 6 years. The RMP (version 16) is updated in accordance

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

5.3.17. [Durvalumab - IMFINZI \(CAP\) - EMEA/H/C/004771/II/0023](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to introduce a new posology regimen of 1,500 mg every 4 weeks (Q4W) for the approved indication of the treatment of patients with locally advanced, unresectable non-small cell lung cancer (NSCLC) whose tumours express programmed death-ligand 1 (PD-L1) on $\geq 1\%$ of tumour cells and whose disease has not progressed following platinum based chemoradiation therapy. The RMP (version 4.1) is updated accordingly

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

5.3.18. [Esketamine - SPRAVATO \(CAP\) - EMEA/H/C/004535/II/0001/G](#)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped variations consisting of: 1) extension of indication to include a new indication for the rapid reduction of depressive symptoms in adult patients with a moderate to severe depressive episode of major depressive disorder (MMD) who have current suicidal ideation with intent. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 the SmPC are updated. The package leaflet and the RMP (version 2.1) are updated accordingly; 2) addition of a new pack size (multipack) of 24 nasal spray devices (multipack of 8 packs of 3 nasal spray devices) corresponding to 4 weeks of treatment in the new indication. The package leaflet and labelling are updated in accordance. In addition, the MAH took the opportunity to clarify the wording in Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product'

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

5.3.19. [Human normal immunoglobulin - PRIVIGEN \(CAP\) - EMEA/H/C/000831/II/0161/G](#)

Applicant: CSL Behring GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of: 1) update of sections 4.4, 4.8 and 5.1 of the SmPC in order to amend an existing warning on haemolytic anaemia and to update safety information based on final results from study IgPro10_5003 (listed as a category 3 study in the RMP): an observational hospital-based cohort study in the US to evaluate Privigen (human normal immunoglobulin) use and haemolytic anaemia in adults and children and the Privigen (human normal immunoglobulin) safety profile in children with chronic inflammatory demyelinating

polyneuropathy (CIDP). The package leaflet is updated accordingly; 2) update of sections 4.8 and 5.1 of the SmPC in order to update the list of adverse drug reactions based on final results from study IgPro10_3004: a prospective open-label single-arm study of the pharmacokinetics and safety of intravenous Privigen (human normal immunoglobulin) (IgPro10) in Japanese subjects with primary immunodeficiency. The RMP (version 8.0) is updated accordingly. In addition, the MAH took the opportunity to align the SmPC with the EU core SmPC for human normal immunoglobulin for intravenous administration (IVIg) (EMA/CHMP/BPWP/94038/2007 Rev. 5), to update the local representative for Bulgaria in the package leaflet and to bring the product information 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

5.3.20. Imipenem, cilastatin, relebactam - RECARBRIO (CAP) - EMEA/H/C/004808/II/0001

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of hospital-acquired pneumonia (HAP) including ventilator-associated pneumonia (VAP), with or without concurrent bacteraemia in adults. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 1.1) are updated in accordance. Furthermore, the MAH introduced editorial corrections in the product information and brought it 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

5.3.21. Lacosamide - LACOSAMIDE UCB (CAP) - EMEA/H/C/005243/WS1782/0006; VIMPAT (CAP) - EMEA/H/C/000863/WS1782/0088

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the treatment as adjunctive therapy of primary generalised tonic-clonic seizures in adults, adolescents and children from 4 years of age with idiopathic generalised epilepsy. 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 15.1) are updated in accordance. Furthermore, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1), to align the product information of Lacosamide UCB (lacosamide) with the product information of Vimpat (lacosamide) and to implement some minor corrections in the Bulgarian, Czech, Danish, French, German, Hungarian, Polish and Spanish versions of the product information

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

5.3.22. Liraglutide - SAXENDA (CAP) - EMEA/H/C/003780/II/0026

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include treatment as an adjunct to a healthy nutrition and physical activity counselling for weight management in adolescent patients from the age of 12

years and above with body weight above 60 kg and obesity (body mass index (BMI) corresponding to ≥ 30 kg/m² for adults) based on study NN8022-4180: effect of liraglutide for weight management in pubertal adolescent subjects with obesity, 56-week, double-blind, randomised, parallel-group, placebo-controlled multi-national trial followed by a 26-week period off study-drug. 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 32.0) are updated in accordance. The application relates to paediatric studies submitted according to Article 46 of the paediatric regulation

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

5.3.23. [Metreleptin - MYALEPTA \(CAP\) - EMEA/H/C/004218/II/0012, Orphan](#)

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of section 4.4 of the SmPC in order to add a new warning on the risk of autoimmune disease following exposure to metreleptin. The package leaflet and the key elements to be included in the guide/training material for healthcare professionals are updated accordingly. The RMP (version 2.0) is also updated in accordance

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

5.3.24. [Nintedanib - OFEV \(CAP\) - EMEA/H/C/003821/II/0038](#)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of sections 4.5, 4.6 and 5.2 of the SmPC in order to add drug-drug interaction information with ethinylestradiol/levonorgestrel as a combined oral contraceptive based on final results from clinical study 1199-0340: a phase 1, open-label, 2-period cross-over, fixed-sequence design trial investigating the effect of multiple oral doses of nintedanib on the single dose kinetics of a combination of ethinylestradiol/levonorgestrel in female patients with systemic sclerosis associated interstitial lung disease (SSc-ILD). The package leaflet and the RMP (version 10) are updated accordingly

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

5.3.25. [Nivolumab - OPDIVO \(CAP\) - EMEA/H/C/003985/II/0080](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC) after prior fluoropyrimidine- and platinum-based chemotherapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 16.0) are updated in accordance

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

5.3.26. [Ocrelizumab - OCREVUS \(CAP\) - EMEA/H/C/004043/II/0020](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report for study 17-1133 (listed as a category 3 study in the RMP): a study assessing the effects of ocrelizumab on embryo-foetal and pre- and postnatal development when administered once weekly for up to 23-weeks intravenously to pregnant cynomolgus monkeys (in fulfilment of MEA 006). The RMP (version 5.0) is updated accordingly

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

5.3.27. [Pegaspargase - ONCASPAR \(CAP\) - EMEA/H/C/003789/II/0036/G](#)

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Annika Folin

Scope: Grouped variations consisting of: 1) submission of the results for study 12-266 A(12): an open label single arm phase2 trial evaluating the efficacy and toxicity of treatment regimens including Oncaspar (pegaspargase) in adults aged 18-60 with newly diagnosed Philadelphia chromosome-negative acute lymphoblastic leukaemia ; 2) submission of the results for study CAALL-F01: a prospective multicentre cohort study evaluating Oncaspar (pegaspargase) used in the first-line treatment of children and adolescents with acute lymphoblastic leukaemia (ALL) along with multi-agent chemotherapy. As a consequence, Annex II is updated to remove both studies (i.e. post-authorisation safety studies (PAES)). Additionally, the product information is updated to remove the need for additional monitoring and to implement editorial changes. The RMP (version 4.1) is updated accordingly

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

5.3.28. [Pembrolizumab - KEYTRUDA \(CAP\) - EMEA/H/C/003820/II/0091](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include first-line treatment of unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer in adults based on the results from study KEYNOTE-177: an international, randomised, open-label phase 3 trial of pembrolizumab versus chemotherapy in MSI-H or dMMR stage IV colorectal carcinoma. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 29.1) are updated in accordance. The MAH took the opportunity to introduce minor correction in section 4.4 of the SmPC on immune related endocrinopathies

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

5.3.29. [Tofacitinib - XELJANZ \(CAP\) - EMEA/H/C/004214/X/0024/G](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Grouped application consisting of: 1) extension application to introduce a new

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

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

5.3.30. 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

5.3.31. 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. Belimumab - BENLYSTA (CAP) - PSUSA/00009075/202003

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Betaine anhydrous⁶ - CYSTADANE (CAP) - PSUSA/00000390/202002

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Bevacizumab - AVASTIN (CAP); MVASI (CAP); ZIRABEV (CAP) - PSUSA/00000403/202002

Applicant(s): Amgen Technology (Ireland) Unlimited Company (Mvasi), Pfizer Europe MA EEIG (Zirabev), Roche Registration GmbH (Avastin)

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Bosutinib - BOSULIF (CAP) - PSUSA/00010073/202003

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Brentuximab vedotin - ADCETRIS (CAP) - PSUSA/00010039/202002

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Brimonidine⁷ - MIRVASO (CAP) - PSUSA/00010093/202002

Applicant: Galderma International

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Burosumab - CRYSVITA (CAP) - PSUSA/00010669/202002

Applicant: Kyowa Kirin Holdings B.V.

⁶ Centrally authorised product(s) only

⁷ Centrally authorised product(s) only

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Caplacizumab - CABLIVI (CAP) - PSUSA/00010713/202002

Applicant: Ablynx NV

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Carglumic acid - CARBAGLU (CAP) - PSUSA/00000564/202001

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Ceftazidime, avibactam - ZAVICEFTA (CAP) - PSUSA/00010513/202002

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Ceftolozane, tazobactam - ZERBAXA (CAP) - PSUSA/00010411/202003

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Chlormethine - LEDAGA (CAP) - PSUSA/00010587/202002

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Cholic acid⁸ - KOLBAM (CAP) - PSUSA/00010182/202003

Applicant: Retrophin Europe Ltd

PRAC Rapporteur: Agni Kapou

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Ciclosporin⁹ - IKERVIS (CAP); VERKAZIA (CAP) - PSUSA/00010362/202003

Applicant(s): Santen Oy

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Dabigatran - PRADAXA (CAP) - PSUSA/00000918/202003

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Damoctocog alfa pegol - JIVI (CAP) - PSUSA/00010732/202002

Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated), haemophilus type b conjugate vaccine (adsorbed) - VAXELIS (CAP) - PSUSA/00010469/202002

Applicant: MCM Vaccine B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Doravirine - PIFELTRO (CAP) - PSUSA/00010729/202002

Applicant: Merck Sharp & Dohme B.V.

⁸ Indicated in the treatment of inborn errors in primary bile acid synthesis due to sterol 27-hydroxylase (presenting as cerebrotendinous xanthomatosis, CTX) deficiency, 2- (or α -) methylacyl-CoA racemase (AMACR) deficiency or cholesterol 7 α -hydroxylase (CYP7A1) deficiency

⁹ Topical use only

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. [Doravirine, lamivudine, tenofovir disoproxil - DELSTRIGO \(CAP\) - PSUSA/00010731/202002](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. [Eftrenonacog alfa - ALPROLIX \(CAP\) - PSUSA/00010499/202003](#)

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. [Eluxadoline - TRUBERZI \(CAP\) - PSUSA/00010528/202003](#)

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. [Emtricitabine, rilpivirine, tenofovir alafenamide - ODEFSEY \(CAP\) - PSUSA/00010514/202002](#)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. [Epoetin beta - NEORECORMON \(CAP\) - PSUSA/00001239/202002](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Eravacycline - XERAVA (CAP) - PSUSA/00010718/202002

Applicant: Tetrphase Pharmaceuticals Ireland Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Esketamine¹⁰ - SPRAVATO (CAP) - PSUSA/00010825/202003

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - PSUSA/00010352/202002

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

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.27. Ferric maltol - FERACCRU (CAP) - PSUSA/00010476/202002

Applicant: Norgine B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Fingolimod - GILENYA (CAP) - PSUSA/00001393/202002

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Florbetaben (¹⁸F) - NEURACEQ (CAP) - PSUSA/00010094/202002

Applicant: Life Radiopharma Berlin GmbH

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

¹⁰ Centrally authorised product(s) only

¹¹ Advanced therapy medicinal product

Action: For adoption of recommendation to CHMP

6.1.30. [Fluticasone furoate, umeclidinium, vilanterol - ELEBRATO ELLIPTA \(CAP\); TEMYBRIC ELLIPTA \(CAP\); TRELEGY ELLIPTA \(CAP\) - PSUSA/00010653/202003](#)

Applicant(s): GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. [Fremanezumab - AJOVY \(CAP\) - PSUSA/00010758/202003](#)

Applicant: Teva GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. [Guanfacine - INTUNIV \(CAP\) - PSUSA/00010413/202003](#)

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. [Hepatitis B \(rDNA¹²\) vaccine \(adjuvanted, adsorbed\) - FENDRIX \(CAP\) - PSUSA/00001598/202002](#)

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. [Human coagulation factor X - COAGADEX \(CAP\) - PSUSA/00010481/202003](#)

Applicant: BPL Bioproducts Laboratory GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. [Ibalizumab - TROGARZO \(CAP\) - PSUSA/00010797/202003](#)

Applicant: Theratechnologies Europe Limited

¹² Ribosomal deoxyribonucleic acid

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. [Ibritumomab tiuxetan - ZEVALIN \(CAP\) - PSUSA/00001704/202002](#)

Applicant: Ceft Biopharma s.r.o.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. [Influenza vaccine \(surface antigen, inactivated, prepared in cell cultures\) - FLUCELVAX TETRA \(CAP\) - PSUSA/00010737/202003](#)

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. [Lanadelumab - TAKHZYRO \(CAP\) - PSUSA/00010743/202002](#)

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. [Meropenem, vaborbactam - VABOREM \(CAP\) - PSUSA/00010727/202002](#)

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. [Nitisinone - ORFADIN \(CAP\) - PSUSA/00002169/202002](#)

Applicant: Swedish Orphan Biovitrum International AB

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. [Oritavancin - ORBACTIV \(CAP\) - PSUSA/00010368/202003](#)

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Adam Przybylkowski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.42. [Ospemifene - SENSHIO \(CAP\) - PSUSA/00010340/202002](#)

Applicant: Shionogi B.V.
PRAC Rapporteur: Kirsti Villikka
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.43. [Pirfenidone - ESBRIET \(CAP\) - PSUSA/00002435/202002](#)

Applicant: Roche Registration GmbH
PRAC Rapporteur: Rhea Fitzgerald
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.44. [Plasmodium falciparum and hepatitis B vaccine \(recombinant, adjuvanted\) - MOSQUIRIX \(Art 58¹³\) - EMEA/H/W/002300/PSUV/0045](#)

Applicant: GlaxoSmithkline Biologicals SA
PRAC Rapporteur: Jean-Michel Dogné
Scope: Evaluation of a PSUR procedure
Action: For adoption of recommendation to CHMP

6.1.45. [Rasburicase - FASTURTEC \(CAP\) - PSUSA/00002613/202002](#)

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

6.1.46. [Reslizumab - CINQAERO \(CAP\) - PSUSA/00010523/202002](#)

Applicant: Teva B.V.
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

¹³ Article 58 of Regulation (EC) No 726/2004 allows the Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO) on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)

6.1.47. Ribociclib - KISQALI (CAP) - PSUSA/00010633/202003

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Ropeginterferon alfa-2b - BESREMI (CAP) - PSUSA/00010756/202002

Applicant: AOP Orphan Pharmaceuticals AG

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Rotigotine - LEGANTO (CAP); NEUPRO (CAP) - PSUSA/00002667/202002

Applicant(s): UCB Pharma S.A.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Ruxolitinib - JAKAVI (CAP) - PSUSA/00010015/202002

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Safinamide - XADAGO (CAP) - PSUSA/00010356/202002

Applicant: Zambon S.p.A.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Solriamfetol - SUNOSI (CAP) - PSUSA/00010831/202003

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Telotristat - XERMELO (CAP) - PSUSA/00010639/202002

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Tildrakizumab - ILUMETRI (CAP) - PSUSA/00010720/202003

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.55. Tivozanib - FOTIVDA (CAP) - PSUSA/00010636/202002

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.56. Trastuzumab emtansine - KADCYLA (CAP) - PSUSA/00010136/202002

Applicant: Roche Registration GmbH

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.57. Ulipristal acetate¹⁴ - ESMYA (CAP); ULIPRISTAL ACETATE GEDEON RICHTER (CAP) - PSUSA/00009325/202002

Applicant(s): Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.58. Upadacitinib - RINVOQ (CAP) - PSUSA/00010823/202002

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

¹⁴ Indicated for the treatment of moderate to severe symptoms of uterine fibroids only

Action: For adoption of recommendation to CHMP

6.1.59. Velaglucerase alpha - VPRIV (CAP) - PSUSA/00003103/202002

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Martin Huber

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. Dexmedetomidine - DEXDOR (CAP); NAP - PSUSA/00000998/202003

Applicants: Orion Corporation (Dexdor), various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Dexrazoxane - SAVENE (CAP); NAP - PSUSA/00001001/202002

Applicants: Clinigen Healthcare B.V. (Savene), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Glycopyrronium ¹⁵ - SIALANAR (CAP); NAP - PSUSA/00010529/202003

Applicants: Proveca Pharma Limited (Sialanar), various

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Hepatitis B vaccine (rDNA¹⁶) - HBVAXPRO (CAP); NAP - PSUSA/00001597/202002

Applicants: MSD Vaccins (HBVaxPro), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁵ Indicated for the treatment of severe sialorrhea (chronic pathological drooling)

¹⁶ Ribosomal deoxyribonucleic acid

6.2.5. Imiquimod - ALDARA (CAP), ZYCLARA (CAP); NAP - PSUSA/00001729/202001

Applicants: Meda AB (Aldara, Zyclara), various

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.6. Timolol, travoprost - DUOTRAV (CAP); NAP - PSUSA/00002962/202002

Applicants: Novartis Europharm Limited (DuoTrav), various

PRAC Rapporteur: Eva Segovia

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. Acetylsalicylic acid, atorvastatin, ramipril (NAP) - PSUSA/00010280/202002

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Amitriptyline hydrochloride, chlordiazepoxide (NAP) - PSUSA/00000171/202002

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Aprotinin (NAP) - PSUSA/00000230/202002

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Bicalutamide (NAP) - PSUSA/00000407/202002

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. [Cilostazol \(NAP\) - PSUSA/00010209/202002](#)

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. [Clobazam \(NAP\) - PSUSA/00000798/202002](#)

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. [Clobetasol \(NAP\) - PSUSA/00000799/202002](#)

Applicant(s): various

PRAC Lead: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. [Etoposide \(NAP\) - PSUSA/00001333/202002](#)

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. [Gaxilose \(NAP\) - PSUSA/00010283/202001](#)

Applicant(s): various

PRAC Lead: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. [Haemophilus type b and meningococcal group C conjugate vaccine \(NAP\) - PSUSA/00001583/202002](#)

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. [Haemophilus type b conjugate vaccine \(NAP\) - PSUSA/00001584/202002](#)

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. [Human coagulation factor VIII inhibitor bypassing fraction \(NAP\) - PSUSA/00009174/202002](#)

Applicant(s): various

PRAC Lead: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. [Human plasma¹⁷ \(NAP\) - PSUSA/00001635/202002](#)

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. [Hydroxyethyl starch \(HES\) \(NAP\) - PSUSA/00001694/202003](#)

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. [Ibuprofen \(NAP\); ibuprofen lysine¹⁸ \(NAP\); ibuprofen, caffeine \(NAP\) - PSUSA/00010649/202002](#)

Applicant(s): various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

¹⁷ Pooled and treated for virus inactivation only

¹⁸ All indication(s) except for ductus arteriosus

6.3.16. Influenza vaccine (split virion, inactivated)¹⁹ (NAP) - PSUSA/00010298/202003

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Influenza vaccine (split virion, inactivated, prepared in cell cultures) (NAP) - PSUSA/00010299/202003

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Influenza vaccine (surface antigen, inactivated) (NAP) - PSUSA/00001744/202003

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Influenza vaccine (surface antigen, inactivated, adjuvanted) (NAP) - PSUSA/00010300/202003

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Ipratropium (NAP) - PSUSA/00001780/202001

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Ipratropium, salbutamol (NAP) - PSUSA/00001781/202001

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

¹⁹ All except centrally authorised product(s)

Action: For adoption of recommendation to CMDh

6.3.22. Labetalol (NAP) - PSUSA/00001814/202002

Applicant(s): various

PRAC Lead: Pernille Harg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Levosalbutamol (NAP), salbutamol (NAP) - PSUSA/00010330/202001

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Lisdexamfetamine (NAP) - PSUSA/00010289/202002

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Lorazepam (NAP) - PSUSA/00001909/202001

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Mannitol²⁰ (NAP) - PSUSA/00010005/202002

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.27. Mefloquine (NAP) - PSUSA/00001955/202002

Applicant(s): various

PRAC Lead: Pernille Harg

Scope: Evaluation of a PSUSA procedure

²⁰ All indication(s) except for cystic fibrosis

Action: For adoption of recommendation to CMDh

6.3.28. Mequitazine (NAP) - PSUSA/00001986/202001

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.29. Mesalazine (NAP) - PSUSA/00001990/202002

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.30. Phenobarbital (NAP) - PSUSA/00002370/202001

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.31. Potassium para-aminobenzoate (NAP) - PSUSA/00010130/202002

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.32. Saccharomyces boulardii (NAP) - PSUSA/00009284/202002

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.33. Sevoflurane (NAP) - PSUSA/00002698/202001

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.34. Tick-borne encephalitis vaccine (inactivated) (NAP) - PSUSA/00002951/202001

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.35. Vancomycin (NAP) - PSUSA/00003097/202001

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.36. Verapamil (NAP) - PSUSA/00003105/202001

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Dexmedetomidine - DEXDOR (CAP) - EMEA/H/C/002268/LEG 016.1

Applicant: Orion Corporation

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to LEG 016 [analysis of available mortality data from controlled clinical trials in the dexmedetomidine development programme as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00000998/201903) adopted in November 2019] as per the request for supplementary information (RSI) adopted in May 2020

Action: For adoption of advice to CHMP

6.4.2. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/REC 004.1

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to REC 004 [detailed review of type and frequencies of occurrence of injection site reactions in post-marketing settings as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010668/201905) adopted in December 2019] as per the request for supplementary information (RSI) adopted at CHMP in April 2020

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0044/G

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of section 4.5 of the SmPC to add a warning concerning the interaction between naltrexone/bupropion and digoxin as requested in the conclusions of the latest periodic safety update report single assessment (PSUSA) procedure (PSUSA/00010366/201909) adopted in April 2020. The package leaflet is updated accordingly; 2) update of section 4.8 of the SmPC to include drug-induced lupus erythematosus with naltrexone/bupropion and its individual substances. The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

6.5.2. Pirfenidone - ESBRIET (CAP) - EMEA/H/C/002154/II/0066/G, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Grouped variations consisting of: 1) update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning on drug-induced liver injury (DILI) as requested in the conclusions of LEG 015 concluded in February 2020, assessing a review of cases of serious hepatic reactions and cases of hyponatremia and adequacy of the risk minimisation measures (RMM) of the product information requested in the conclusions of periodic safety update single assessment (PSUSA) procedure (PSUSA/00002435/201902) adopted in September 2019. The package leaflet and the RMP (version 10.0) are updated accordingly. In addition, the MAH took the opportunity to amend the package leaflet to reflect 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' as well as minor changes; 2) update of sections 4.4 and 4.8 of the SmPC in order to add a warning on hyponatraemia and to add hyponatraemia to the list undesirable effects as requested in the conclusions of LEG 015 assessing a review of cases of hyponatremia requested in the conclusions of PSUSA procedure (PSUSA/00002435/201902)

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews²¹

6.6.1. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/MEA 017.2

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Fourth expedited monthly summary safety report for remdesivir for September 2020 including spontaneously reported data and data from compassionate use and expanded access

²¹ Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC

programmes for the duration of the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)²²

7.1.1. Alemtuzumab – LEMTRADA (CAP) - EMEA/H/C/PSP/S/0087

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Protocol for a non-interventional PASS to investigate the risk of mortality in patients prescribed Lemtrada (alemtuzumab) relative to comparable patients using other disease modifying therapies: a cohort study

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

7.1.2. Alemtuzumab – LEMTRADA (CAP) - EMEA/H/C/PSP/S/0088

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Protocol for a non-interventional PASS to investigate drug utilisation and safety monitoring patterns for Lemtrada (alemtuzumab)

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

7.1.3. Asfotase alfa– STRENSIQ (CAP) - EMEA/H/C/PSA/S/0050.1

Applicant: Alexion Europe SAS

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to PSA/S/0050 [substantial amendment to a protocol previously agreed in May 2016 (PSP/0032.1) for study ALX-HPP-501: an observational, longitudinal, prospective, long-term registry of patients with hypophosphatasia to collect information on the epidemiology of the disease, including clinical outcomes and quality of life, and to evaluate safety and effectiveness data in patients treated with Strensiq (asfotase alfa)] as per the request for supplementary information (RSI) adopted in April 2020

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

7.1.4. Buprenorphine – SIXMO (CAP) - EMEA/H/C/PSP/S/0086.2

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

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to PSP/S/0086.1 [protocol for study MOLTeNI-2019-01: a prospective, observational (non-interventional), post-authorisation safety cohort study to evaluate the incidence of breakages and insertion/removal complications of buprenorphine implants

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

(Sixmo) in routine clinical care] as per the request for supplementary information (RSI) adopted in June 2020

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

7.1.5. Cidofovir (NAP) - EMEA/H/N/PSA/S/0058

Applicant: Tillomed Laboratories Ltd. (Cidofovir Emcure Pharma)

PRAC Rapporteur: Rugile Pilviniene

Scope: Substantial amendment to a protocol previously agreed November 2018 (PSP/S/0052.3) for cidofovir exposure registry study: a non-interventional, prospective, exposure (safety outcome) registry study of cidofovir to further elucidate the characteristics of the different patient populations for cidofovir use, to evaluate patterns and compare rates of adverse events occurring in the on-label group with events occurring in the off-label group; and to assess patient outcome following treatment in specified indication

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

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

7.2.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 006.3

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's request to discontinue pregnancy registry study OBS13436: an international Lemtrada pregnancy exposure cohort in multiple sclerosis [final clinical study report (CSR) initially expected in december 2021]

Action: For adoption of advice to CHMP

7.2.2. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/MEA 007.1

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Amendment to a protocol previously agreed in November 2017 for study 109MS401 (ESTEEM): a multicentre, global, observational study to collect information on safety and to document the drug utilisation of Tecfidera (dimethyl fumarate) when used in routine medical practice in the treatment of relapsing multiple sclerosis [final clinical study report (CSR) expected due date: Q4/2024] together with the fifth annual progress report of the study

Action: For adoption of advice to CHMP

7.2.3. Esketamine - SPRAVATO (CAP) - EMEA/H/C/004535/MEA 002

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Protocol for a pregnancy registry study (listed as a category 3 study in the RMP) using

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

the National Pregnancy Registry for Psychiatric Medications (NPRPM) in order to further characterise the impact of the missing information of use during pregnancy on the safety profile of esketamine nasal spray and obtain information on the frequency of major malformations (from initial opinion/marketing authorisation) [final report expected in 4Q 2024]

Action: For adoption of advice to CHMP

7.2.4. Esketamine - SPRAVATO (CAP) - EMEA/H/C/004535/MEA 003

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Protocol for a survey to assess the effectiveness of Spravato (esketamine) educational materials (i.e. healthcare professional (HCP) guide, patient guide, checklist) for additional risk minimisation measures in the European Union related to understanding and management of the important identified risks with esketamine treatment (from initial opinion/marketing authorisation) [final clinical study report (CSR) expected in 4Q/2022]

Action: For adoption of advice to CHMP

7.2.5. Flutemetamol (¹⁸F) - VIZAMYL (CAP) - EMEA/H/C/002557/MEA 002.4

Applicant: GE Healthcare AS

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 002.3 [amendment to a previously agreed protocol in December 2015 for study GE067-027 CPR in order to evaluate the effectiveness of Vizamyl (flutemetamol (¹⁸F)) educational training programme/reader training in Europe and to assess the frequency of image classification errors in clinical practice [final study report expected in Q1 2021]] as per the request for supplementary information (RSI) adopted in April 2020, together with the first recruitment report

Action: For adoption of advice to CHMP

7.2.6. Gilteritinib - XOSPATA (CAP) - EMEA/H/C/004752/MEA 004

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Protocol for study 2215-PV-0001: a cross-sectional survey study among healthcare professionals (HCPs) to assess awareness and knowledge, an evaluation of the effectiveness of a Xospata (gilteritinib) routine risk minimisation measures (RMM) and an additional risk minimisation measure (aRMM)

Action: For adoption of advice to CHMP

7.2.7. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/MEA 021

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Protocol for study CT-P13 4.9: an observational, prospective cohort study to evaluate

safety of Remsima (infliximab) subcutaneous in patients with ankylosing spondylitis, psoriatic arthritis, and psoriasis

Action: For adoption of advice to CHMP

7.2.8. [Inotersen - TEGSEDI \(CAP\) - EMEA/H/C/004782/MEA 007](#)

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Protocol for study TEG4005: a pregnancy surveillance programme of infants and women exposed to Tegsedi (inotersen) during pregnancy

Action: For adoption of advice to CHMP

7.2.9. [Micafungin - MYCAMINE \(CAP\) - EMEA/H/C/000734/MEA 015.12](#)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 015.11 [protocol for study 9463-PV-0002 (listed as a category 3 study in the RMP): a non-interventional PASS/survey on the effectiveness of the updated prescriber checklist for Mycamine (micafungin)] as per the request for supplementary information (RSI) adopted in May 2020

Action: For adoption of advice to CHMP

7.2.10. [Patisiran - ONPATTRO \(CAP\) - EMEA/H/C/004699/MEA 002.5](#)

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 002.4 [protocol for study ALN-TTR02-0009: a prospective observational study on the safety of Onpattro (patisiran) in a real-world cohort of hereditary transthyretin amyloidosis (hATTR) patients] as per the request for supplementary information (RSI) adopted in July 2020

Action: For adoption of advice to CHMP

7.2.11. [Sotagliflozin - ZYNQUISTA \(CAP\) - EMEA/H/C/004889/MEA 004.2](#)

Applicant: Navigant Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 004.1 [protocol for a nested, case-control study to evaluate the risk of malignancies (bladder, renal, breast, Leydig cell, pancreatic, thyroid and prostate cancers) in adult patients with type 1 diabetes mellitus (T1DM) using sotagliflozin in existing healthcare databases in Europe and in the United States [final clinical study report (CSR) expected in April 2030]] as per the request for supplementary information (RSI) adopted in April 2020

Action: For adoption of advice to CHMP

7.2.12. Tafamidis - VYNDAQEL (CAP) - EMEA/H/C/002294/MEA 016.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to MEA 016 [amendment to a protocol previously agreed by CHMP for study B3461001: a sub-analysis of 'transthyretin amyloidosis outcomes survey (THAOS)': a global, multicentre, longitudinal, observational survey of patients with documented transthyretin (TTR) gene mutations or wild-type ATTR amyloidosis, in order to evaluate the effects of tafamidis in non-V30M patients] as per the request for supplementary information (RSI) adopted in June 2020

Action: For adoption of advice to CHMP

7.2.13. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 013.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 013 [protocol for study A3921344 (listed as a category 3 study in the RMP): an active surveillance, post-authorisation study to characterise the safety of tofacitinib in patients with moderately to severely active ulcerative colitis (UC) in the real-world setting using data from the Swedish Quality Register for Inflammatory Bowel Disease (SWIBREG) registry as requested in the conclusions of procedure X/0005/G finalised in May 2018 and in the conclusions of the referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMEA/H/A-20/1485) finalised in November 2019] as per the request for supplementary information (RSI) adopted in May 2020

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)²⁴

7.3.1. Iron^{25 26} (NAP) - EMEA/H/N/PSR/J/0026

Applicant(s): Mesama Consulting (on behalf of a consortium) (Cosmofer, Ferinject, Monofer, Venofer)

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to PSR/J/0026 [results for a joint study on intravenous iron: evaluation of the risk of severe hypersensitivity reactions, as imposed in the conclusions of the referral under Article 31 of Directive 2001/83/EC (EMEA/H/A-31/1322) for intravenous (IV) iron-containing medicines in 2013]] as per the request for supplementary information (RSI) adopted in July 2020

Action: For adoption of recommendation to CMDh

7.3.2. Teicoplanin (NAP) - EMEA/H/N/PSR/S/0025

Applicant(s): Sanofi (Targocid)

²⁴ In accordance with Article 107p-q of Directive 2001/83/EC

²⁵ Intravenous (IV)

²⁶ Iron(III)-hydroxide dextran complex, iron sucrose complex/iron(III)-hydroxide sucrose complex, ferric carboxymaltose complex, iron(III) isomalto-side complex, sodium ferric gluconate complex

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSR/S/0025 [results for a PASS study: a prospective, observational cohort, evaluating the incidence of nephrotoxicity and other adverse events of interest in patients treated with the higher recommended teicoplanin loading dose (12mg/kg twice a day), and comparison with external historical comparator data] as per the request for supplementary information (RSI) adopted in May 2020

Action: For adoption of recommendation to CMDh

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

7.4.1. 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'. 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 is introduced

Action: For adoption of PRAC Assessment Report

7.4.2. Levetiracetam - KEPRA (CAP) - EMEA/H/C/000277/II/0189

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Laurence de Fays

Scope: Submission of the final clinical study report (CSR) for PASS EUPAS26595: a retrospective cohort study comparing the incidence of acute renal failure in patients with epilepsy exposed to levetiracetam versus other antiepileptic drugs using real world data from a claim database in the US

Action: For adoption of PRAC Assessment Report

7.4.3. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/II/0080

Applicant: Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from a survey on physicians' awareness and understanding of the educational materials on the prescriber guide (listed as a category 3 study in the RMP)

Action: For adoption of PRAC Assessment Report

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

7.4.4. Safinamide - XADAGO (CAP) - EMEA/H/C/002396/II/0035

Applicant: Zambon S.p.A.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final clinical study report (CSR) for study Z7219N02 (listed as a category 3 study in the RMP): a European multicentre retrospective-prospective cohort study to observe safinamide safety profile and pattern of use in clinical practice during the first post-commercialisation phase (SYNAPSES). The RMP (version 6.2) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.5. Turoctocog alfa - NOVOEIGHT (CAP) - EMEA/H/C/002719/II/0035

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 5.1 of the SmPC to include the results of completed study NN7008-3553 (GUARDIAN 5) (listed as a category 3 study in the RMP): a multi-centre non-interventional study of safety and efficacy of turoctocog alfa (recombinant factor VIII (rFVIII)) during long-term treatment of severe and moderately severe haemophilia A (FVIII =<2%). The RMP (version 7) 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. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 024.13

Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: MAH's response to MEA 024.12 [annual report 2019 on adverse events and/or lack of efficacy, immunological data, follow-up growth disturbances in children and data on urinary hexose tetrasaccharide (Hex4) from the Pompe registry: a global, multicentre, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease irrespective of treatment status. The registry aims at detecting adverse events and/or lack of efficacy in patients, and at collecting immunological data, and follow-up growth disturbances in children] as per the request for supplementary information (RSI) adopted in March 2020

Action: For adoption of advice to CHMP

7.5.2. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 025.13

Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: MAH's response to MEA 025.12 [annual report 2019 on data on patients with renal or hepatic insufficiency from the Pompe registry: a global, multicentre, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the

onset, progression, and treated course of patients with Pompe disease irrespective of treatment status. The registry aims at detecting adverse events and/or lack of efficacy in patients, and at collecting immunological data, and follow-up growth disturbances in children] as per the request for supplementary information (RSI) adopted in March 2020

Action: For adoption of advice to CHMP

7.5.3. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/MEA 012.9

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

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

Action: For adoption of advice to CHMP

7.5.4. Guanfacine - INTUNIV (CAP) - EMEA/H/C/003759/MEA 005.4

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Second annual progress report for a drug utilisation study (DUS) of Intuniv (guanfacine extended release) in European countries: a non-imposed, non-interventional, multi-country DUS using retrospective database analysis (DUS-database: EUPAS18735) and a prescriber survey (DUS-survey: EUPAS18739) [final report expected in June 2022]

Action: For adoption of advice to CHMP

7.5.5. Sapropterin - KUVAN (CAP) - EMEA/H/C/000943/MEA 003.10

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Tenth annual interim report for the Kuvan Adult Maternal Paediatric European registry (KAMPER), study EMR700773-001: a non-imposed, non-interventional exploring the long-term safety of Kuvan (sapropterin) use in patients with hyperphenylalaninaemia (HPA) as well as information on Kuvan use during pregnancy in women with HPA and data regarding childhood growth and neurocognitive outcomes

Action: For adoption of advice to CHMP

7.5.6. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 026.2

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Annual update for an observational study using EU registries with biomarker data, as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in May 2018 (EMA/H/A-20/1460)] as per the request for supplementary information (RSI) adopted in January 2019

Action: For adoption of advice to CHMP

7.5.7. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 027.2

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Annual update for a genetic analysis (human leukocyte antigen (HLA)) study using data from EU registries with biomarker data in patients with severe drug-induced liver injury (DILI), as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in May 2018 (EMEA/H/A-20/1460)

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 009.2

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Martin Huber

Scope: Third feasibility assessment for a drug utilisation study (DUS) to evaluate the drug utilisation patterns of canagliflozin-containing medicines including off-label usage in type 1 diabetes mellitus (T1DM) and the risk of diabetic ketoacidosis (DKA) using EU databases on market uptake and exposure within the European Union

Action: For adoption of advice to CHMP

7.6.2. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 008.2

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Third feasibility assessment for a drug utilisation study (DUS) to evaluate the drug utilisation patterns of canagliflozin-containing medicines including off-label usage in type 1 diabetes mellitus (T1DM) and the risk of diabetic ketoacidosis (DKA) using EU databases on market uptake and exposure within the European Union

Action: For adoption of advice to CHMP

7.6.3. Insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/LEG 034

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Annika Folin

Scope: First report of the batch-specific adverse drug event review and analysis as requested in the conclusions of procedure X/0169 finalised in November 2019

Action: For adoption of advice to CHMP

7.6.4. Insulin lispro - LIPROLOG (CAP) - EMEA/H/C/000393/LEG 027

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Annika Folin

Scope: First report of the batch-specific adverse drug event review and analysis as requested in the conclusions of procedure X/0130 finalised in November 2019

Action: For adoption of advice to CHMP

7.6.5. [Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA \(CAP\) - EMEA/H/C/003687/MEA 003.8](#)

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Second feasibility assessment report for study NB-451: an observational retrospective study based on secondary data analysis using existing databases, in order to evaluate the potential population of patients or prescriptions in each database and confirm the ability to use each database for the drug utilisation study (DUS) of Mysimba (naltrexone hydrochloride/bupropion hydrochloride) in selected European countries to describe the demographic and baseline characteristics of users of Mysimba (naltrexone hydrochloride/bupropion hydrochloride)

Action: For adoption of advice to CHMP

7.6.6. [Ulipristal acetate - ESMYA \(CAP\) - EMEA/H/C/002041/MEA 024.2](#)

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Feasibility report for study PGL18-002: a retrospective, multi-national, comparative, non-interventional cohort study to investigate the risk of liver injury possibly associated with Esmya (ulipristal acetate) use based on data from various national electronic health record based databases in Europe [final study report expected by Q4 2019] as requested in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in May 2018 (EMEA/H/A-20/1460)

Action: For adoption of advice to CHMP

7.7. **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. Dinutuximab beta - QARZIBA (CAP) - EMEA/H/C/003918/S/0022 (without RMP)

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

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. Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/R/0019 (without RMP)

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - EMEA/H/C/002450/R/0032 (with RMP)

Applicant: Holostem Therapie Avanzate s.r.l., ATMP²⁸

PRAC Rapporteur: Rhea Fitzgerald

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.2.3. Polatuzumab vedotin - POLIVY (CAP) - EMEA/H/C/004870/R/0003 (with RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.4. Vandetanib - CAPRELSA (CAP) - EMEA/H/C/002315/R/0046 (without RMP)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Tiphaine Vaillant

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

²⁸ Advanced therapy medicinal product

8.3. Renewals of the marketing authorisation

8.3.1. Cabazitaxel - JEVTANA (CAP) - EMEA/H/C/002018/R/0042 (with RMP)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Dexamethasone - NEOFORDEX (CAP) - EMEA/H/C/004071/R/0016 (without RMP)

Applicant: Laboratoires CTRS

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Eftrenonacog alfa - ALPROLIX (CAP) - EMEA/H/C/004142/R/0032 (without RMP)

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Elotuzumab - EMPLICITI (CAP) - EMEA/H/C/003967/R/0024 (without RMP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Emtricitabine, tenofovir alafenamide - DESCOVY (CAP) - EMEA/H/C/004094/R/0051 (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

8.3.6. 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

8.3.7. Ixekizumab - TALTZ (CAP) - EMEA/H/C/003943/R/0039 (with RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/R/0024 (without RMP)

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/R/0030 (with RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Adrien Inoubli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Trifluridine, tipiracil - LONSURF (CAP) - EMEA/H/C/003897/R/0020 (without RMP)

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Annika Folin

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

None

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

10.1.1. Andexanet alfa – ONDEXXYA (CAP) – EMEA/H/C/004108/II/0011

Applicant: Portola Netherlands B.V.

PRAC Rapporteur: Menno van der Elst; PRAC Co-Rapporteur: Brigitte Keller-Stanislawsk

Scope: PRAC consultation on an update of sections 4.4 and 4.5 of the SmPC in order to add a new warning on use of heparin after administration of andexanet based on spontaneous reports, medical literature reports, clinical trials and in vitro data. The package leaflet is updated accordingly. The MAH took the opportunity to introduce some additional editorial changes throughout the product information

Action: For adoption of advice to CHMP

10.1.2. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0063

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: PRAC consultation on an update of sections 4.4 and 4.8 of the SmPC to reflect progressive multifocal leukoencephalopathy (PML) in the setting of mild lymphopenia based on data submitted in the ongoing PSUSA/00010143/201903 due for recommendation at the November 2019 PRAC meeting. The package leaflet is updated accordingly. Additionally, the Product Information has been updated in line with the quality review of documents (QRD) template (version 10.1)

Action: For adoption of advice to CHMP

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Gadobenic acid (NAP), gadoteridol (NAP) - DK/H/xxxx/96, DK/H/xxxx/118

Applicant(s): Bracco (Multihance (gadobenic acid), Prohance (gadoteridol))

PRAC Lead: Anette Kirstine Stark

Scope: PRAC consultation on national worksharing variations to update the RMPs to include study to evaluate the effect of gadolinium containing agents (GdCAs) exposure during pregnancy and pregnancy outcomes, as required in the conclusions of the referral procedure under Article 31 of Directive 2001/83/EC on gadolinium containing agents (GdCAs) concluded in 2017 (EMA/H/A-31/1437)

Action: For adoption of advice to Member States

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC meeting dates 2022-2024

Action: For discussion

12.1.2. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals –Q3 2020

Action: For discussion

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

- 12.4.2. PRAC strategic review and learning meeting (SRLM) under the German presidency of the European Union (EU) Council - Langen, Germany, 22 October 2020 – Agenda (virtual meeting)
-

PRAC lead: Brigitte Keller-Stanislawski, Martin Huber

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

- 12.8.1. Marketing authorisation applications (MAA) forecast for 2020 – planning update dated Q3 2020
-

Action: For discussion

- 12.8.2. PRAC workload statistics – Q3 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

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

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

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. Article 58²⁹ (EU-M4all) and centralised procedures - parallel application submissions

Action: For discussion

²⁹ 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)

12.20.2. Collection of data on adverse events related to medicinal products through registries
– survey results

PRAC Lead: Sabine Straus, Martin Huber, Menno van der Elst, Ulla Wändel Liminga

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/