14 April 2020
EMA/PRAC/132684/2020
Human Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 14-17 April 2020

Chair: Sabine Straus – Vice-Chair: Martin Huber

14 April 2020, 10:30 – 19:30, via teleconference

15 April 2020, 08:30 – 19:30, via teleconference

16 April 2020, 08:30 – 19:30, via teleconference

17 April 2020, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

30 April 2020, 09:00-12:00, via teleconference

Health and safety information

In accordance with the Agency's health and safety policy, delegates are to be briefed on health, safety and emergency information and procedures prior to the start of the meeting.

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 14-17 April 2020. See April 2020 PRAC minutes (to be published post May 2020 PRAC meeting).

1.2. Agenda of the meeting on 14-17 April 2020

Action: For adoption

1.3. Minutes of the previous meeting on 09-12 March 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

3.3.1. Ingenol mebutate - PICATO[1] - EMEA/H/A-20/1489

Applicant: LEO Laboratories Ltd

PRAC Rapporteur: Adam Przybylkowski; PRAC Co-rapporteur: Adrien Inoubli

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

Action: For adoption of a recommendation to CHMP

3.4. Re-examination procedures[2]

None

3.5. Others

None

4. Signals assessment and prioritisation[3]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Abiraterone – ZYTIGA (CAP)

Applicant(s): Janssen-Cilag International NV

PRAC Rapporteur: Eva Segovia

Scope: Signal of anaphylactic reaction

Action: For adoption of PRAC recommendation

EPITT 19535 – New signal

Lead Member State(s): ES

4.1.2. Bisoprolol (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

[1] European Commission (EC) decision on marketing authorisation (MA) withdrawal dated 11 February 2020, at the request of the MAH
[2] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC
[3] 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

Scope: Signal of angioedema

Action: For adoption of PRAC recommendation

EPITT 19542 – New signal

Lead Member State(s): FI

4.1.3. Paclitaxel – ABRAXANE (CAP), APEALEA (CAP), PAZENIR (CAP); NAP

Applicant(s): Celgene Europe BV (Abraxane), Oasmia Pharmaceutical AB (Apealea), ratiopharm GmbH (Pazenir), various

PRAC Rapporteur: Menno van der Elst

Scope: Signal of progressive multifocal leukoencephalopathy (PML)

Action: For adoption of PRAC recommendation

EPITT 19553 – New signal

Lead Member State(s): NL, PT

4.1.4. Pomalidomide – IMNOVID (CAP)

Applicant(s): Celgene Europe BV

PRAC Rapporteur: Eva Segovia

Scope: Signal of progressive multifocal leukoencephalopathy (PML)

Action: For adoption of PRAC recommendation

EPITT 19546 – New signal

Lead Member State(s): ES

4.2. New signals detected from other sources

4.2.1. Vedolizumab – ENTYVIO (CAP)

Applicant(s): Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Signal of Evans' syndrome, autoimmune haemolytic anaemia, immune thrombocytopenic purpura

Action: For adoption of PRAC recommendation

EPITT 19547 – New signal

Lead Member State(s): PL

4.3. Signals follow-up and prioritisation

4.3.1. Adalimumab – AMGEVITA (CAP), AMSPARITY (CAP), HALIMATOZ (CAP), HEFIYA (CAP), HULIO (CAP), HUMIRA (CAP) - EMEA/H/C/000481/SDA/116, HYRIMOZ (CAP), IDACIO (CAP), IMRALDI (CAP)

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

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of autoimmune encephalitis

Action: For adoption of PRAC recommendation

EPITT 19483 – Follow-up to November 2019

4.3.2. 5 alfa-reductase inhibitors (5ARIs): finasteride (NAP); dutasteride (NAP)

Applicant(s): various

PRAC Rapporteur: Annika Folin

Scope: Signal of type 2 diabetes mellitus (T2DM)

Action: For adoption of PRAC recommendation

EPITT 19424 – Follow-up to November 2019

4.3.3. Andexanet alfa – ONDEXXYA (CAP) - EMEA/H/C/004108/SDA/010

Applicant(s): Portola Netherlands B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Signal of erroneous assay results for levels of anti-factor Xa activity with use of andexanet alfa

Action: For adoption of PRAC recommendation

EPITT 19493 – Follow-up to December 2019

4.3.4. Ceftriaxone (NAP)

Applicant(s): various

PRAC Rapporteur: Zane Neikena

Scope: Signal of encephalopathy

Action: For adoption of PRAC recommendation

EPITT 19492 – Follow-up to November 2019

4.3.5. Ibuprofen – PEDEA (CAP); NAP; ketoprofen (NAP) and fixed-dose combinations: chlorphenamine, ibuprofen, phenylephrine (NAP); dimenhydrinate, ibuprofen, caffeine (NAP); ibuprofen, ascorbic acid (NAP); ibuprofen, caffeine (NAP); ibuprofen, codeine (NAP); ibuprofen, hydrocodone (NAP); ibuprofen, paracetamol (NAP); ibuprofen, phenylephrine (NAP); ibuprofen, pseudoephedrine (NAP); ketoprofen, omeprazole (NAP), ketoprofen, sucralfate (NAP)

Applicant(s): Recordati Rare Diseases (Pedea), various

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of serious exacerbation of infections

Action: For adoption of PRAC recommendation

EPITT 19415 – Follow-up to November 2019

4.3.6. Idelalisib – ZYDELIG (CAP) - EMEA/H/C/003843/SDA/018

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Martin Huber

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

Action: For adoption of PRAC recommendation

EPITT 19500 – Follow-up to December 2019

4.3.7. Insulin: insulin aspart – FIASP (CAP) - EMEA/H/C/004046/SDA/004, NOVOMIX (CAP) - EMEA/H/C/000308/SDA/055, NOVORAPID (CAP) - EMEA/H/C/000258/SDA/050; insulin aspart, insulin degludec – RYZODEG (CAP) - EMEA/H/C/002499/SDA/007; insulin bovine (NAP); insulin degludec – TRESIBA (CAP) - EMEA/H/C/002498/SDA/014; insulin degludec, liraglutide – XULTOPHY (CAP) - EMEA/H/C/002647/SDA/004; insulin determir – LEVEMIR (CAP) - EMEA/H/C/000528/SDA/053; insulin glargine, lixisenatide - SULIQUA (CAP) - EMEA/H/C/004243/SDA/007; insulin glulisine – APIDRA (CAP) - EMEA/H/C/000557/SDA/042; insulin human – ACTRAPHANE (CAP) - EMEA/H/C/000427/SDA/025, ACTRAPID (CAP) - EMEA/H/C/000424/SDA/026, INSULATARD (CAP) - EMEA/H/C/000441/SDA/029, INSUMAN (CAP) - EMEA/H/C/000201/SDA/050, MIXTARD (CAP) - EMEA/H/C/000428/SDA/027, PROTAPHANE (CAP) - EMEA/H/C/000442/SDA/029, NAP; insulin lispro – HUMALOG (CAP) - EMEA/H/C/000088/SDA/033, INSULIN LISPRO SANOFI (CAP) - EMEA/H/C/004303/SDA/002, LIPROLOG (CAP) - EMEA/H/C/000393/SDA/026; insulin porcine (NAP)

Applicant(s): Eli Lilly Nederland B.V. (Humalog, Liprolog), Novo Nordisk A/S (Actraphane, Actrapid, Fiasp, Insulatard, Levemir, Mixtard, NovoMix, NovoRapid, Protaphane, Ryzodeg, Tresiba, Xultophy), Sanofi-Aventis Deutschland GmbH (Apidra, Insuman), Sanofi-aventis groupe (Insulin Lispro Sanofi, Suliqua), various

PRAC Rapporteur: Hans Christian Siersted

Scope: Signal of cutaneous amyloidosis

Action: For adoption of PRAC recommendation

EPITT 19499 – Follow-up to December 2019

4.3.8. Tumour necrosis factor (TNF) inhibitors: adalimumab - AMGEVITA (CAP), AMSPARITY (CAP), HALIMATOZ (CAP), HEFIYA (CAP), HULIO (CAP), HUMIRA (CAP), HYRIMOZ (CAP), IDACIO (CAP), IMRALDI (CAP); certolizumab pegol - CIMZIA (CAP); etanercept - BENEPALI (CAP), ENBREL (CAP), ERELZI (CAP); golimumab - SIMPONI (CAP); infliximab - FLIXABI (CAP), INFLECTRA (CAP), REMICADE (CAP), REMSIMA (CAP), ZESSLY (CAP)

Applicant(s): AbbVie Deutschland GmbH Co. KG (Humira), Amgen Europe B.V. (Amgevita), Celltrion Healthcare Hungary Kft. (Remsima), Fresenius Kabi Deutschland GmbH (Idacio), Mylan S.A.S. (Hulio), Janssen Biologics B.V. (Simponi, Remicade), Pfizer Europe MA EEIG (Amsparity, Enbrel, Inflectra), Samsung Bioepis NL B.V. (Benepali, Flixabi, Imraldi), Sandoz GmbH (Erelzi, Halimatoz, Hefiya, Hyrimoz, Zessly), UCB Pharma S.A. (Cimzia)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of Kaposi's sarcoma

Action: For adoption of PRAC recommendation

EPITT 19480 – Follow-up to November 2019

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Amikacin - EMEA/H/C/005264, Orphan

Applicant: Insmed Netherlands B.V.

Scope: Treatment of lung infection as part of combination antibacterial drug regiment in adults

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

5.1.2. Avapritinib - EMEA/H/C/005208, Orphan

Applicant: Blueprint Medicines (Netherlands) B.V.

Scope: Treatment of gastrointestinal stromal tumours

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

5.1.3. Belantamab mafodotin - EMEA/H/C/004935, Orphan

Applicant: GlaxoSmithKline (Ireland) Limited

Scope (accelerated assessment): Treatment of patients with relapsed or refractory multiple myeloma

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

5.1.4. Cabazitaxel - EMEA/H/C/005178

Scope: Treatment of adult patients with metastatic castration resistant prostate cancer previously treated with a docetaxel-containing regimen

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

5.1.5. Crizanlizumab - EMEA/H/C/004874, Orphan

Applicant: Novartis Europharm Limited

Scope: Treatment of sickle cell disease

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

5.1.6. Fostemsavir - EMEA/H/C/005011

Scope (accelerated assessment): 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

5.1.7. Idebenone - EMEA/H/C/005123, Orphan

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

Scope: Treatment of respiratory dysfunction in patients with Duchenne muscular dystrophy (DMD) not using glucocorticoids

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

5.1.8. Luspatercept - EMEA/H/C/004444, Orphan

Applicant: Celgene Europe BV

Scope: Treatment of adult patients with very low- to intermediate-risk myelodysplastic syndromes (MDS)-associated anaemia and treatment of adult patients with beta-thalassaemia (β-thalassaemia)-associated anaemia who require red blood cell (RBC) transfusions

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

5.1.9. Paliperidone - EMEA/H/C/005486

Scope: Treatment of schizophrenia

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

5.1.10. Sodium oxybate – HOPVEUS (CAP MAA) - EMEA/H/C/004962

Applicant: D&A Pharma

Scope (re-examination): Medium to long-term maintenance of alcohol abstinence and treatment of mild to moderate alcohol withdrawal syndrome

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

5.1.11. Teriparatide - EMEA/H/C/005233

Scope: Treatment of osteoporosis

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

5.1.12. Valoctocogene roxaparvovec - EMEA/H/C/004749, Orphan, ATMP

Applicant: BioMarin International Limited, ATMP[4]

Scope (accelerated assessment): Treatment of haemophilia A

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

5.2. Medicines in the post-authorisation phase – PRAC-led procedures

5.2.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/II/0031

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated RMP (version 7.0) in order to reflect all amendments and additional activities as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in November 2019 (EMEA/H/A-20/1483)

Action: For adoption of PRAC Assessment Report

5.2.2. Asparaginase - SPECTRILA (CAP) - EMEA/H/C/002661/II/0017

Applicant: medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Jan Neuhauser

Scope: Submission of an updated RMP (version 12) in line with revision 2 of GVP module V on 'Risk management systems' and in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template). The milestones and timelines for study MC-Spectrila.1/ALL: a clinical phase 2 trial to describe pharmacokinetics, pharmacodynamics, safety and immunogenicity of Spectrila (asparaginase) with the pharmaceutical active ingredient recombinant L asparaginase in adult subjects with newly diagnosed acute B-Cell lymphoblastic leukaemia are updated in accordance with the newly applied data lock point (DLP) for the RMP

Action: For adoption of PRAC Assessment Report

[4] Advanced therapy medicinal product

5.2.3. Dexamethasone - OZURDEX (CAP) - EMEA/H/C/001140/II/0037

Applicant: Allergan Pharmaceuticals Ireland

PRAC Rapporteur: Eva Segovia

Scope: Submission of an updated RMP (version 9.0) in order to reflect increased knowledge of the medicinal product and bring it in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.4. Docetaxel - DOCETAXEL ZENTIVA (CAP) - EMEA/H/C/000808/II/0061

Applicant: Zentiva, k.s.

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of an updated RMP (version 1.1) in order to revise the list of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' and to complete Part II modules

Action: For adoption of PRAC Assessment Report

5.2.5. Docetaxel - TAXOTERE (CAP) - EMEA/H/C/000073/II/0134

Applicant: Sanofi Mature IP

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of an updated RMP (version 1.1) in order to revise the list of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' and to complete Part II modules

Action: For adoption of PRAC Assessment Report

5.2.6. Histamine dihydrochloride - CEPLENE (CAP) - EMEA/H/C/000796/II/0040

Applicant: Noventia Pharma Srl

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of an updated RMP (version 8.1) in order to include information about the termination/finalisation of: 1) non-interventional study Ceplene-3290 (listed as a category 3 study in the RMP): an open study designed to gain further knowledge on Ceplene (histamine dihydrochloride) under day to day conditions with special emphasis on tolerability, practicability, usage, and measurable minimal residual disease and course of blast cells and; 2) post-authorisation efficacy study (PAES) Ceplene cohort study 3306: an international, multicentre, observational, non-interventional, registry-based cohort study aiming to describe and evaluate minimal residual disease (MRD) at baseline and follow-up for the assessment of the anti-leukaemic activity of Ceplene (histamine dihydrochloride)/interleukin-2 (IL-2) as remission maintenance therapy in adult patients with acute myeloid leukaemia (AML) in first complete remission (CR1) compared to matched control patients who did not receive Ceplene (histamine dihydrochloride)/IL-2. In addition, the RMP is brought in line with revision 2.0.1 of the guidance on the format of RMP in the

EU (template). As a consequence, the list of safety concerns is amended in particular 'drug effect decreased as a consequence of drug interaction' is added as a new important potential risk

Action: For adoption of PRAC Assessment Report

5.2.7. Nonacog alfa - BENEFIX (CAP) - EMEA/H/C/000139/II/0163

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 10.0) to remove 'less than therapeutic effect (LETE)' as an important identified risk. In addition, specific patient populations previously identified as missing information are removed from the RMP in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

5.2.8. Rivastigmine - EXELON (CAP) - EMEA/H/C/000169/WS1773/0128; PROMETAX (CAP) - EMEA/H/C/000255/WS1773/0128

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of an updated RMP (version 10.0) to reflect the results of study CENA713D2409: a drug utilisation study (DUS) aimed to assess the extent of inappropriate use of Exelon/Prometax (rivastigmine) as per the conclusions of variation WS1557 adopted in July 2019. In addition, the list of safety concerns of the RMP is updated in line with revision 2 of GVP module V on 'Risk management systems' and in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002654/201901) finalised in September 2019

Action: For adoption of PRAC Assessment Report

5.2.9. Sevelamer - RENAGEL (CAP) - EMEA/H/C/000254/WS1775/0114; Sevelamer carbonate - RENVELA (CAP) - EMEA/H/C/000993/WS1775/0051;SEVELAMER CARBONATE WINTHROP (CAP) - EMEA/H/C/003971/WS1775/0024

Applicant: Genzyme Europe BV

PRAC Rapporteur: Laurence de Fays

Scope: Submission of an updated RMP (version 10) in order to remove from the list of safety concerns 'sevelamer crystals associated with serious gastrointestinal disorders' as an important potential risk as per the conclusions of the renewal procedure for Sevelamer Carbonate Winthrop (R/0022) finalised in September 2019

Action: For adoption of PRAC Assessment Report

5.2.10. Tegafur, gimeracil, oteracil - TEYSUNO (CAP) - EMEA/H/C/001242/II/0042

Applicant: Nordic Group B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 9.0) in order to revise the list of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' as requested in the conclusions of the periodic safety update report single assessment (PSUSA) procedure PSUSA/00002875/201801 adopted in September 2018

Action: For adoption of PRAC Assessment Report

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

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

Applicant: Portola Netherlands B.V.

PRAC Rapporteur: Menno van der Elst

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

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

5.3.2. Anidulafungin - ECALTA (CAP) - EMEA/H/C/000788/II/0040

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Extension of the approved indication 'treatment of invasive candidiasis (ICC)' to include paediatric patients aged from 1 month to less than 18 years of age. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 13.0) are updated accordingly. The RMP is also updated in line with revision 2 of GVP module V on 'Risk management systems'. In addition, the MAH took the opportunity to update the information in the product information on fructose in line 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

5.3.3. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/II/0015

Applicant: Merck Europe B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to change posology recommendations, to amend an existing warning and to add myasthenia gravis and

myasthenic syndrome as new adverse drug reactions (ADRs) with a frequency uncommon. The update results from an update of the company core data sheet (CCDS) based on the review of cases of myasthenia gravis/myasthenic syndrome. The package leaflet is updated accordingly. The RMP (version 2.2) is updated with a proposal to reclassify 'other immune-related events (myasthenic syndrome)' from an important potential risk to an important identified risk of 'other immune-related events (myasthenia gravis/myasthenic syndrome)'

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

5.3.4. Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/X/0036/G, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped application consisting of: 1) extension application to add a new strength (20 mg tablets); 2) extension of the existing indication on pulmonary multidrug-resistant tuberculosis (MDR-TB) to include paediatric patients aged from 5 years to less than 18 years of age and weighing more than 15 kg based on the results of the week 24 analysis of cohort 2 (paediatric subjects aged ≥5 to <12 years) of study TMC207-C211: a phase 2, open-label, multicentre, single-arm study to evaluate the pharmacokinetics, safety, tolerability and antimycobacterial activity of TMC207 (bedaquiline) in combination with a background regimen (BR) of MDR-TB Medications for the treatment of children and adolescents 0 months to <18 years of age who have confirmed or probable pulmonary MDR-TB. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 are updated. The package leaflet and the RMP (version 4.4) are updated in accordance

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

5.3.5. Encorafenib - BRAFTOVI (CAP) - EMEA/H/C/004580/WS1695/0008; Binimetinib - MEKTOVI (CAP) - EMEA/H/C/004579/WS1695/0007

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include encorafenib in combination with binimetinib and cetuximab, for the treatment of adult patients with metastatic colorectal cancer (CRC) with a BRAF V600E mutation, who have received prior systemic therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 5.3 of the SmPC are updated. The package leaflet and the RMP (version 1.1) are updated accordingly. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.6. Brodalumab - KYNTHEUM (CAP) - EMEA/H/C/003959/II/0014

Applicant: LEO Pharma A/S

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.4 and 4.8 of the SmPC to reflect a signal of anaphylactic reaction detected in post marketing setting. The package leaflet and the RMP (version 1.2) are updated accordingly. The MAH took the opportunity to introduce minor updates

throughout the product information

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

5.3.7. Buprenorphine, naloxone - SUBOXONE (CAP) - EMEA/H/C/000697/X/0042

Applicant: Indivior Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Extension application to introduce a new pharmaceutical form (sublingual film) associated with four new strengths (2/0.5 mg, 4/1 mg, 8/2 mg and 16/4 mg) and a new route of administration (either sublingual or buccal administration). The RMP (version 14.0) is updated accordingly

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

5.3.8. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/II/0046

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to add the treatment of stage 2 or 3 chronic kidney disease (CKD) and albuminuria, as an adjunct to standard of care, in adults with type 2 diabetes mellitus (T2DM), based on new clinical efficacy and safety data from study DNE3001 (CREDENCE): a randomised, double-blind, event-driven, placebo-controlled, multicentre phase 3 study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with T2DM and diabetic nephropathy. 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 8.1) are 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

5.3.9. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/II/0051

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to add the treatment of stage 2 or 3 chronic kidney disease (CKD) and albuminuria, as an adjunct to standard of care, in adults with type 2 diabetes mellitus (T2DM), based on new clinical efficacy and safety data from study DNE3001 (CREDENCE): a randomised, double-blind, event-driven, placebo-controlled, multicentre phase 3 study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with T2DM and diabetic nephropathy. 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 8.1) are 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

5.3.10. Carfilzomib - KYPROLIS (CAP) - EMEA/H/C/003790/II/0043, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of section 4.8 of the SmPC in order to include cardiomyopathy as a new adverse drug reaction (ADR) with a frequency uncommon. The RMP (version 11.0) is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information

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

5.3.11. Catridecacog - NOVOTHIRTEEN (CAP) - EMEA/H/C/002284/II/0026/G

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Ghania Chamouni

Scope: Grouped variations consisting of an extension of indication to include treatment of bleeding episodes in patients with congenital factor XIII A-subunit deficiency as well as minor surgery based on the results of: 1) study NN1841-3868: Use of recombinant factor XIII (rFXIII) in treatment of congenital FXIII deficiency, a prospective multi-centre observational study; 2) registry PRO-RBDD: a prospective rare bleeding disorders database registry. As a consequence, sections 4.1, 4.2, 4.4, 4.6, 5.1 and 5.2 of the SmPC are updated. The package leaflet, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' and the RMP (version 15) are updated accordingly. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1). Finally, the MAH took the opportunity to introduce minor editorial changes to the product information

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

5.3.12. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0084/G

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information following the final results from three studies (listed as category 3 studies in the RMP) namely: 1) study PS0002 (CIMPASI-2): a phase 3, multicentre, randomized, double-blind, parallel-group, study followed by a dose-blind period and open-label follow-up to evaluate the efficacy and safety of certolizumab pegol in subjects with moderate to severe chronic plaque psoriasis; 2) study PS0003 (CIMPACT): a phase 3, multicentre, randomized, double-blind, parallel-group, placebo- and active-controlled study followed by a placebo-controlled maintenance period and open-label follow-up to evaluate the efficacy and safety of certolizumab pegol in subjects with moderate to severe chronic plaque psoriasis; 3) study PS0005 (CIMPASI-1): a phase 3, multicentre, randomized, double-blind, parallel-group, study followed by a dose-blind period and open-label follow-up to evaluate the efficacy and safety of certolizumab pegol in subjects with moderate to severe chronic plaque psoriasis. The RMP (version 16.0) is updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.13. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0087

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to introduce a change in posology for axial spondyloarthritis (aSpA) and to update the safety and efficacy information based on the results of study AS0005 (C-OPTIMISE) (listed as a category 3 study in the RMP): a multicentre, open-label (part A) followed by a randomised, double-blind, parallel-group, placebo-controlled study (part B) to evaluate maintenance of remission in subjects with active axSpA receiving either certolizumab pegol 200mg once every 2 weeks (q2w) or 200mg once every 4 weeks (q4w) as compared to placebo. The package leaflet and the RMP (version 17.0) are updated accordingly. In addition, the interim study reports for studies AS0006 and AS0007 are submitted to include additional pooled safety data in the SmPC. Study AS0006 is a phase 3, multicentre, randomised, placebo-controlled, double-blind study to evaluate efficacy and safety of certolizumab pegol in subjects with active aSpA without x-ray evidence of ankylosing spondylitis and objective signs of inflammation. Study AS0007 is a multicentre, open-label study to assess the effects of certolizumab pegol on the reduction of anterior uveitis flares in aSpA subjects with a history of anterior uveitis (C-VIEW)

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

5.3.14. Clopidogrel - ISCOVER (CAP) - EMEA/H/C/000175/WS1769/0140; PLAVIX (CAP) - EMEA/H/C/000174/WS1769/0138

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include adult patients with high risk transient ischemic attack (TIA) ($ABCD^2$ score ≥4) or minor ischemic stroke (IS) (National Institutes of Health Stroke Scale (NIHSS) ≤3) within 24 hours of either the TIA or IS event. The new indication is based on the results of 1) study POINT: a double-blind, randomised, placebo-controlled phase 3 study on platelet-oriented inhibition in new TIA and minor IS; 2) study CHANCE: a double-blind, randomised, placebo-controlled phase 3 study comparing the effects of a 3-month clopidogrel regimen, combined with acetylsalicylic acid (ASA) during the first 21days, versus ASA alone for the acute treatment of TIA or minor stroke. As a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 1.0) are updated accordingly

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

5.3.15. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/II/0040, Orphan

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Laurence de Fays

Scope: Extension of indication to include adolescents and children above 6 years with a body weight of at least 30 kg. 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 3.2) are updated accordingly. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.16. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/II/0027

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include atopic dermatitis patients from 6 years to 11 years. 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 5.0) are updated accordingly

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

5.3.17. 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

5.3.18. Granisetron - SANCUSO (CAP) - EMEA/H/C/002296/II/0056/G

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: Grouped variations consisting of: 1) update of section 5.2 of the SmPC to add pharmacokinetic (PK) information following the completion of paediatric PK study 392MD/44/C: an open-label, cross-over, pharmacokinetic study to assess the safety and pharmacokinetics of transdermal granisetron (Sancuso patch) and intravenous (IV) granisetron in a paediatric oncology population (aged 13 to 17 years). The RMP (version 4.0) is updated accordingly; 2) update of the RMP in line with revision 2 of the guidance on the format of RMP in the EU (template). The MAH took the opportunity to update the pregnancy information in section 4.6 to align with the quality review document (QRD) template

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

5.3.19. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - EMEA/H/C/004336/II/0022

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Extension of indication to include adults of 18 years of age or older at increased risk of herpes zoster, supported by clinical studies: 1) study ZOSTER-002: a phase 3, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the prophylactic efficacy, safety, and immunogenicity of Shingrix (herpes zoster vaccine) when administered intramuscularly on a two-dose schedule to adult autologous haematopoietic stem cell transplant (HCT) recipients (MEA 001); 2) study ZOSTER-039: a phase 3, randomised, observer-blind, placebo-controlled, multicentre study to assess the safety and immunogenicity of Shingrix (herpes zoster vaccine) when administered intramuscularly on a two-dose schedule to adults aged 18 years and older with haematologic malignancies (MEA 002); 3) study ZOSTER-041: a phase 3, randomised, observer-blind, placebo-controlled, multicentre clinical study to assess the immunogenicity and safety of Shingrix (herpes zoster vaccine) when administered intramuscularly on a 0- and 1- to 2-months schedule to adults ⩾ 18 years of age with renal transplant (MEA 003); 4) study ZOSTER-028: a phase 2/3, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of Shingrix (herpes zoster vaccine) when administered intramuscularly on a 0 and 1 to 2 months schedule to adults of 18 years of age with solid tumours receiving chemotherapy (MEA 004); 5) study ZOSTER-001: a phase 1/2a, randomised, observer-blind, placebo-controlled, multicentre study to evaluate the safety and immunogenicity of Shingrix (herpes zoster vaccine) and to saline (placebo) when administered as 2 doses or 3 doses to autologous HCT recipients ; 6) study ZOSTER-015: a phase 1/2a, randomised, observer-blind, placebo-controlled, multicentre study to evaluate the safety and immunogenicity of Shingrix (herpes zoster vaccine) in comparison to placebo when administered as 3 doses to adult human immunodeficiency virus (HIV)-infected subjects.. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated in order to add the indication, delete a warning and add new safety and efficacy information. The package leaflet and the RMP (version 2.1) are updated in accordance

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

5.3.20. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0059, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to add the combination with rituximab or obinutuzumab for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL), based on results from study E1912 (PCYC-1126e-CA): a randomized phase 3 study of ibrutinib-based therapy vs standard fludarabine, cyclophosphamide, and rituximab (FCR) chemoimmunotherapy in untreated younger patients with CLL. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated to include information related to the new indication. The package leaflet and the RMP (version 16.1) are updated accordingly. The MAH took the opportunity to introduce minor editorial changes in Annex II and the labelling (Annex III-A)

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

5.3.21. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/II/0082

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to add Crohn's disease, ulcerative colitis, ankylosing spondylitis, psoriatic arthritis and psoriasis to subcutaneous (SC) route of administration presentations in order to bring them in line with the intravenous (IV) route of administration presentations. The RMP (version 12.1) is updated accordingly

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

5.3.22. Insulin glargine - ABASAGLAR (CAP) - EMEA/H/C/002835/WS1587/0028/G; insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/WS1587/0178/G

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Annika Folin

Scope: Grouped variations consisting of: 1) introduction of an additional prefilled pen presentation for Abasaglar (insulin glargine), solution for injection, Humalog (insulin lispro) solution for injection, Humalog (insulin lispro) Kwikpen solution for injection and Humalog (insulin lispro) Junior Kwikpen solution for injection. Each pack contains 5 pre-filled pens.; 2) extension to two x5 multipacks. As a consequence, sections 1, 4.2, 4.4, 6.2, 6.4, 6.5, 6.6 and 8 of the SmPC are updated. The package leaflet and labelling are updated accordingly. In addition, the MAH took the opportunity to introduce an editorial change in the Slovakian address of the package leaflet

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

5.3.23. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/II/0082, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to include a new population for Kalydeco (ivacaftor) 150 mg tablets to extend the use to patients with cystic fibrosis (CF) aged 6 years and older and weighing 25 kg or more who have an R117H mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene and for Kalydeco (ivacaftor) granules 75 mg and 50 mg, to add patients with CF aged 12 months and older and weighing 7 kg to less than 25 kg who have an R117H mutation in the CFTR gene. This is based on a clinical trial and literature data, and post-marketing experience with Kalydeco (ivacaftor). As a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 8.5) are updated accordingly

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

5.3.24. Ixekizumab - TALTZ (CAP) - EMEA/H/C/003943/II/0031

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment of moderate to severe plaque psoriasis in children from the age of 6 years and adolescents who are candidates for systemic therapy for Taltz (ixekizumab). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated with new safety and efficacy information. The package leaflet and the RMP (version 7.1) are 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

5.3.25. 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 15.0) 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

5.3.26. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/II/0112/G

Applicant: Celgene Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Grouped variations consisting of: 1) update of sections 4.2, 4.4 and 4.8 of the SmPC with anaphylaxis following a safety review. The package leaflet is updated accordingly; 2) update of section 6.6 of the SmPC in order to include recommendations to minimise the risk of unintended occupational exposures in healthcare professionals. The MAH took the opportunity to include minor updates to section 4.4 of the SmPC and to introduce more clarity in Annex II-D on 'Specific obligation to complete post-authorisation measures for the conditional marketing authorisation' regarding the educational materials, prescribing and dispensing restrictions. Finally, the MAH introduced some editorial changes throughout the product information

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

5.3.27. Levetiracetam - KEPPRA (CAP) - EMEA/H/C/000277/WS1664/0187

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Laurence de Fays

Scope: Update of section 4.2 of the SmPC to recommend the same dosing for monotherapy and adjunctive therapy based on data from modelling and simulation project. The package

leaflet and the RMP (version 9.0) are updated accordingly. The MAH took the opportunity the opportunity to move Braille to another box section and to review and adapt the German 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

5.3.28. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/II/0055

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of section 4.8 of the SmPC following results from study VX16-809-116 (study 106, safety study in children): a phase 3, open-label, rollover extension study evaluating the long-term safety of lumacaftor/ivacaftor in patients with cystic fibrosis aged 2 and older, homozygous for the deletion of phenylalanine in position 508 of the cystic fibrosis transmembrane conductance regulator (F508del-CFTR) mutation, who initiated treatment in parent study 115. The package leaflet and the RMP (version 7.1) are updated accordingly. The MAH took the opportunity 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

5.3.29. Methotrexate - NORDIMET (CAP) - EMEA/H/C/003983/II/0016

Applicant: Nordic Group B.V.

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include the treatment of mild to moderate Crohn's disease either alone or in combination with corticosteroids in patients refractory or intolerant to thiopurines. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 5.0) are updated in accordance. Furthermore, the MAH took the opportunity to update the RMP in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template) and the outcome of the referral procedure for methotrexate-containing products under Article 31 of Directive 2001/83/EC (EMEA/H/A-31/1463) finalised in July 2019

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

5.3.30. 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

5.3.31. Obinutuzumab - GAZYVARO (CAP) - EMEA/H/C/002799/II/0038, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Submission of final clinical study report (CSR) for study MO28543/GREEN: a multicentre, open-label, single-arm, phase 3b, international study evaluating the safety of obinutuzumab alone or in combination with chemotherapy in patients with previously untreated or relapsed/refractory chronic lymphocytic leukaemia (in fulfilment of the post authorisation commitment MEA 005). The RMP (version 6.1) is updated accordingly

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

5.3.32. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/II/0017

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to add the option of a shorter infusion for second and subsequent doses of Ocrevus (ocrelizumab): from the approved 3.5 hours infusion to 2 hours, based on the primary analysis of a therapeutic use substudy MA30143 (shorter infusion substudy (Ensemble Plus)): an open-label, single-arm study to evaluate the effectiveness and safety of ocrelizumab in patients with early stage relapsing remitting multiple sclerosis. The Package Leaflet is updated accordingly. The RMP (version 4.0) is updated accordingly

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

5.3.33. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0033

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to support the use of Lynparza (olaparib) tablets (100 mg and 150 mg) for the maintenance treatment of germline breast cancer gene (BRCA) mutation (gBRCAm) metastatic pancreatic cancer based on the results from the pivotal phase 3 study POLO: a phase 3, randomised, double blind, placebo controlled, multicentre study of maintenance olaparib monotherapy in patients with gBRCA mutated metastatic pancreatic cancer whose disease has not progressed on first line platinum based chemotherapy. As a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated. The package leaflet and the RMP (version 18) are updated in accordance. In addition, the MAH took the opportunity to update section 4.8 for Lynparza (olaparib) hard capsules (50 mg) to revise the list of adverse drug reactions (ADR) based on a pooled safety data analysis. Furthermore, the product information is brought in line with the latest Annex to the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use' on sodium content. The MAH also took the opportunity to include some minor editorial changes in the product information

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

5.3.34. Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/II/0007/G, Orphan

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Grouped variations consisting of an update of sections 4.4, 4.8 and 5.1 of the SmPC based on final results from: 1) study 1655-003 (listed as a category 3 study in the RMP): a long-term extension of a phase 2, open-label, dose-finding study; 2) study 165-302 (listed as a category 3 study in the RMP): a phase 3, randomised, double-blind, placebo-controlled, four-arm, discontinuation study to evaluate executive function in adults with phenylketonuria. The RMP (version 2.0) is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes in the product information

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

5.3.35. Perampanel - FYCOMPA (CAP) - EMEA/H/C/002434/II/0047

Applicant: Eisai GmbH

PRAC Rapporteur: Ghania Chamouni

Scope: Extension of indication to include adjunctive treatment in paediatric patients from 2 to 11 years of age in partial-onset (focal) seizures with or without secondary generalisation and primary generalised tonic-clonic seizures with idiopathic generalised epilepsy. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 4.3) are updated accordingly

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

5.3.36. Pomalidomide - IMNOVID (CAP) - EMEA/H/C/002682/II/0036/G, Orphan

Applicant: Celgene Europe BV

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations consisting of: 1) update of sections 4.2, 4.4 and 4.8 of the SmPC with information on anaphylaxis and section 4.8 of SmPC with hypothyroidism as an adverse drug reaction (ADR) following a safety review. The package leaflet is updated accordingly; 2) update of section 6.6 of the SmPC in order to include recommendations to minimise the risk of unintended occupational exposures in healthcare professionals. The MAH took the opportunity to include minor updates to section 4.4 of the SmPC and to introduce more clarity in Annex II-D on 'Specific obligation to complete post-authorisation measures for the conditional marketing authorisation' regarding the educational materials, prescribing and dispensing restrictions

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

5.3.37. Ravulizumab - ULTOMIRIS (CAP) - EMEA/H/C/004954/II/0002

Applicant: Alexion Europe SAS

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include the treatment of patients with atypical haemolytic

uremic syndrome (aHUS). 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 1.6) are updated accordingly. In addition, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated to include in the educational materials the risk of thrombotic microangiopathy (TMA) with the new indication

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

5.3.38. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/X/0074/G

Applicant: Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped applications consisting of: 1) extension application to introduce a new pharmaceutical form, granules for oral suspension, 1 mg/mL; 2) extension of indication to include treatment of venous thromboembolism (VTE) and prevention of VTE recurrence in term neonates, infants and toddlers, children and adolescents aged less than 18 years following initiation of standard anticoagulation treatment for Xarelto (rivaroxaban) 15 mg and 20 mg tablets. As a consequence, sections 4.2, 4.4, 4.5, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 12.1) are updated accordingly. In addition, sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated for all other dose strengths (2.5/10 mg and 15/20 mg initiation packs). Furthermore, the MAH took the opportunity to update the product information with regards to sodium content in line with the Annex to the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'

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

5.3.39. Thalidomide - THALIDOMIDE CELGENE (CAP) - EMEA/H/C/000823/II/0061/G

Applicant: Celgene Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Grouped variations consisting of: 1) update of sections 4.2, 4.4 and 4.8 of the SmPC with information on anaphylaxis following a safety review. The package leaflet is updated accordingly; 2) update of section 6.6 of the SmPC in order to include recommendations to minimise the risk of unintended occupational exposures in healthcare professionals. The MAH took the opportunity to include minor updates to section 4.4 of the SmPC and to introduce more clarity in Annex II-D on 'Specific obligation to complete post-authorisation measures for the conditional marketing authorisation' regarding the educational materials, prescribing and dispensing restrictions

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

5.3.40. Zoledronic acid - ZOMETA (CAP) - EMEA/H/C/000336/II/0091

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of sections 4.4 and 5.1 of the SmPC in order to update the safety information on osteonecrosis of the jaw (ONJ) based on final results from study

CZOL446EUS122 (listed as a category 3 study in the RMP): a non-interventional, prospective, observational, multicentre cohort study to assess the incidence of ONJ in cancer patients with bone metastases starting zoledronic acid treatment. The RMP (version 12) is updated accordingly

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Abemaciclib - VERZENIOS (CAP) - PSUSA/00010724/201909

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Alemtuzumab - LEMTRADA (CAP) - PSUSA/00010055/201909

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Avelumab - BAVENCIO (CAP) - PSUSA/00010635/201909

Applicant: Merck Europe B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Bedaquiline - SIRTURO (CAP) - PSUSA/00010074/201909

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Cariprazine - REAGILA (CAP) - PSUSA/00010623/201910

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Cemiplimab - LIBTAYO (CAP) - PSUSA/00010780/201909

Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Chenodeoxycholic acid[5] - CHENODEOXYCHOLIC ACID LEADIANT (CAP) - PSUSA/00010590/201910

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Cholic acid[6] - ORPHACOL (CAP) - PSUSA/00010208/201909

Applicant: Laboratoires CTRS

PRAC Rapporteur: Sofia Trantza

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Choriogonadotropin alfa - OVITRELLE (CAP) - PSUSA/00000736/201909

Applicant: Merck Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[5] Indicated for the treatment of inborn errors of primary bile acid synthesis due to sterol 27 hydroxylase deficiency (presenting as cerebrotendinous xanthomatosis (CTX)) in infants, children and adolescents aged 1 month to 18 years and adults – centrally authorised product(s) only

[6] Treatment of inborn errors in primary bile acid synthesis due to 3β-hydroxy-Δ5-C27-steroid oxidoreductase deficiency or Δ4-3-oxosteroid-5β-reductase indication(s) only

6.1.10. Ciclosporin[7] - IKERVIS (CAP); VERKAZIA (CAP) - PSUSA/00010362/201909

Applicant: Santen Oy

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Crizotinib - XALKORI (CAP) - PSUSA/00010042/201908

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Dacomitinib - VIZIMPRO (CAP) - PSUSA/00010757/201909

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Dapagliflozin - EDISTRIDE (CAP); FORXIGA (CAP) - PSUSA/00010029/201910

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Darunavir, cobicistat, emtricitabine, tenofovir alafenamide - SYMTUZA (CAP) - PSUSA/00010646/201909

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Darvadstrocel - ALOFISEL (CAP) - PSUSA/00010676/201909

Applicant: Takeda Pharma A/S, ATMP[8]

[7] Topical use only
[8] Advanced therapy medicinal product

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.16. Denosumab[9] - PROLIA (CAP) - PSUSA/00000954/201909

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Dexamethasone[10] - NEOFORDEX (CAP) - PSUSA/00010480/201909

Applicant: Laboratoires CTRS

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Dulaglutide - TRULICITY (CAP) - PSUSA/00010311/201909

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Dupilumab - DUPIXENT (CAP) - PSUSA/00010645/201909

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Eluxadoline - TRUBERZI (CAP) - PSUSA/00010528/201909

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[9] Indicated for osteoporosis and for bone loss associated with hormone ablation in prostate cancer only
[10] Indicated in symptomatic multiple myeloma only, centrally authorised product(s) only

6.1.21. Etravirine - INTELENCE (CAP) - PSUSA/00001335/201909

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Fremanezumab - AJOVY (CAP) - PSUSA/00010758/201909

Applicant: Teva GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Galcanezumab - EMGALITY (CAP) - PSUSA/00010733/201909

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Glycopyrronium[11] - SIALANAR (CAP) - PSUSA/00010529/201909

Applicant: Proveca Pharma Limited

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Idebenone[12] - RAXONE (CAP) - PSUSA/00010412/201909

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Infliximab - FLIXABI (CAP); INFLECTRA (CAP); REMICADE (CAP); REMSIMA (CAP); ZESSLY (CAP) - PSUSA/00010759/201908

Applicant(s): Celltrion Healthcare Hungary Kft. (Remsima), Janssen Biologics B.V. (Remicade), Pfizer Europe MA EEIG (Inflectra), Sandoz GmbH (Zessly), Samsung Bioepis NL

[11] Indicated for the treatment of severe sialorrhea (chronic pathological drooling), centrally authorised product(s) only
[12] Centrally authorised product(s) only

B.V. (Flixabi)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Insulin aspart - FIASP (CAP); NOVOMIX (CAP); NOVORAPID (CAP) - PSUSA/00001749/201909

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Insulin degludec, liraglutide - XULTOPHY (CAP) - PSUSA/00010272/201909

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Isavuconazole - CRESEMBA (CAP) - PSUSA/00010426/201909

Applicant: Basilea Pharmaceutica Deutschland GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Lorlatinib - LORVIQUA (CAP) - PSUSA/00010760/201909

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Lusutrombopag - MULPLEO (CAP) - PSUSA/00010755/201909

Applicant: Shionogi B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Mepolizumab - NUCALA (CAP) - PSUSA/00010456/201909

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Mogamulizumab - POTELIGEO (CAP) - PSUSA/00010741/201909

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Naldemedine - RIZMOIC (CAP) - PSUSA/00010753/201909

Applicant: Shionogi B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Naloxegol - MOVENTIG (CAP) - PSUSA/00010317/201909

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Naltrexone, bupropion - MYSIMBA (CAP) - PSUSA/00010366/201909

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Netupitant, palonosetron - AKYNZEO (CAP) - PSUSA/00010393/201910

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Niraparib - ZEJULA (CAP) - PSUSA/00010655/201909

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Ocrelizumab - OCREVUS (CAP) - PSUSA/00010662/201909

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Panitumumab - VECTIBIX (CAP) - PSUSA/00002283/201909

Applicant: Amgen Europe B.V.

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Pitolisant - WAKIX (CAP) - PSUSA/00010490/201909

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Raltegravir - ISENTRESS (CAP) - PSUSA/00010373/201909

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Ribociclib - KISQALI (CAP) - PSUSA/00010633/201909

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Risankizumab - SKYRIZI (CAP) - PSUSA/00010765/201909

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Ritonavir - NORVIR (CAP) - PSUSA/00002651/201908

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Rivaroxaban - XARELTO (CAP) - PSUSA/00002653/201909

Applicant: Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Sodium zirconium cyclosilicate - LOKELMA (CAP) - PSUSA/00010675/201909

Applicant: AstraZeneca AB

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Sofosbuvir, ledipasvir - HARVONI (CAP) - PSUSA/00010306/201910

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Telbivudine - SEBIVO (CAP) - PSUSA/00002880/201908

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Tenecteplase - METALYSE (CAP) - PSUSA/00002888/201908

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Tildrakizumab - ILUMETRI (CAP) - PSUSA/00010720/201909

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Tobramycin[13] - VANTOBRA (CAP) - PSUSA/00010370/201909

Applicant: PARI Pharma GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Trabectedin - YONDELIS (CAP) - PSUSA/00003001/201909

Applicant: Pharma Mar, S.A.

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Velmanase alfa - LAMZEDE (CAP) - PSUSA/00010677/201909

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[13] Nebuliser solution, centrally authorised product(s) only

6.1.55. Vernakalant hydrochloride - BRINAVESS (CAP) - PSUSA/00003109/201908

Applicant: Correvio

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.56. Vortioxetine - BRINTELLIX (CAP) - PSUSA/00010052/201909

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2. PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) and nationally authorised products (NAPs)

6.2.1. Anagrelide - ANAGRELIDE MYLAN (CAP); XAGRID (CAP); NAP - PSUSA/00000208/201909

Applicants: Mylan S.A.S (Anagrelide Mylan), Shire Pharmaceuticals Ireland Limited (Xagrid), various

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Budesonide, formoterol - BIRESP SPIROMAX (CAP); DUORESP SPIROMAX (CAP); NAP - PSUSA/00010585/201908

Applicants: Teva Pharma B.V. (BiResp Spiromax, DuoResp Spiromax), various

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Octocog alfa - ADVATE (CAP); HELIXATE NEXGEN[14]; KOGENATE BAYER (CAP); KOVALTRY (CAP); NAP - PSUSA/00002200/201908

Applicants: Baxter AG (Advate), Bayer AG (Helixate NexGen, Kogenate Bayer, Kovaltry), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

[14] European Commission (EC) decision on the marketing authorisation withdrawal granted on 19 December 2019

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Thalidomide - THALIDOMIDE CELGENE (CAP); NAP - PSUSA/00002919/201910

Applicants: Celgene Europe BV (Thalidomide Celgene), various

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Trientine - CUFENCE (CAP); CUPRIOR (CAP); NAP - PSUSA/00010637/201909

Applicants: GMP-Orphan SA (Cuprior), Univar Solutions BV (Cufence), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.6. Zoledronic acid[15] - ZOLEDRONIC ACID HOSPIRA (CAP); ZOLEDRONIC ACID MEDAC (CAP); ZOMETA (CAP); NAP - PSUSA/00003149/201908

Applicants: Medac Gesellschaft fur klinische Spezialpraparate mbH (Zoledronic acid medac), Novartis Europharm Limited (Zometa), Pfizer Europe MA EEIG (Zoledronic acid Hospira), various

PRAC Rapporteur: Anette Kirstine Stark

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. Biperiden (NAP) – PSUSA/00000415/201908

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Conjugated estrogens (CE), medroxyprogesterone acetate (MPA) (NAP) – PSUSA/00000582/201908

Applicant(s): various

[15] Indicated for the treatment of cancer and fractures only

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Dermatophagoides pteronyssinus, dermatophagoides farina[16] [17] [18] (NAP) – PSUSA/00010582/201909

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Dexamfetamine (NAP) – PSUSA/00000986/201909

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Finasteride (NAP) – PSUSA/00001392/201908

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Fluocinolone acetonide[19] (NAP) – PSUSA/00010224/201908

Applicant(s): various

PRAC Lead: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Human plasma protease C1 inhibitor[20] (NAP) – PSUSA/00010163/201908

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

[16] Allergen for therapy
[17] For oromucosal use only
[18] Medicinal product(s) authorised via mutually recognition procedure and decentralised procedure only
[19] Intravitreal implant(s) in applicator only
[20] Nationally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Hydrocortisone[21] (NAP) – PSUSA/00010328/201908

Applicant(s): various

PRAC Lead: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Lercanidipine (NAP) – PSUSA/00001841/201908

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Modafinil (NAP) – PSUSA/00010242/201908

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Nifuroxazide (NAP) – PSUSA/00002160/201908

Applicant(s): various

PRAC Lead: Jana Lukačišinová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Oxcarbazepine (NAP) – PSUSA/00002235/201908

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[21] Except medicinal product(s) indicated in adrenal insufficiency in a modified release tablet formulation

6.3.13. Paricalcitol (NAP) – PSUSA/00002316/201908

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Sotalol (NAP) – PSUSA/00002774/201908

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/LEG 036

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Cumulative review of cases of angioedema as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00000226/201905) adopted in December 2019

Action: For adoption of advice to CHMP

6.4.2. Brodalumab - KYNTHEUM (CAP) - EMEA/H/C/003959/LEG 005.1

Applicant: LEO Pharma A/S

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to LEG 005 [review of all available data from clinical trials, spontaneous reports and published literature relating to the risk of inflammatory bowel disease (IBD) and potential mechanism/biological plausibility of the occurrence of IBD as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010341/201812) for secukinumab adopted in July 2019] as per the request for supplementary information (RSI) adopted in December 2019

Action: For adoption of advice to CHMP

6.4.3. Ixekizumab - TALTZ (CAP) - EMEA/H/C/003943/LEG 004.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to LEG 004 [review of all available data from clinical trials,

spontaneous reports and published literature relating to the risk of inflammatory bowel disease (IBD) and potential mechanism/biological plausibility of the occurrence of IBD as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010341/201812) for secukinumab adopted in July 2019] as per the request for supplementary information (RSI) adopted in December 2019

Action: For adoption of advice to CHMP

6.4.4. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/LEG 070

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Analyses of cumulative data on pregnancy including foetal outcomes as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002127/201908) adopted in February 2020

Action: For adoption of advice to CHMP

6.4.5. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/LEG 007.1

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to LEG 007 [review of all available data from clinical trials, spontaneous reports and published literature relating to the risk of inflammatory bowel disease (IBD) and potential mechanism/biological plausibility of the occurrence of IBD as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010341/201812) adopted in July 2019] as per the request for supplementary information (RSI) adopted in December 2019

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Docetaxel - TAXOTERE (CAP) - EMEA/H/C/000073/II/0136/G

Applicant: Sanofi Mature IP

PRAC Rapporteur: Ghania Chamouni

Scope: Grouped variations consisting of: 1) update of sections 4.4 and 4.8 of the SmPC to add a warning and safety information about tumour lysis syndrome (TLS) based on a cumulative safety review requested in the conclusions of the latest periodic safety update report single assessment (PSUSA) procedure (PSUSA/00001152/201611) concluded in September 2017. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor corrections to the SmPC and update the list of local representatives in the package leaflet; 2) update of section 4.8 of the SmPC to add safety information about myositis based on cumulative safety review requested in the conclusions of the latest PSUSA procedure (PSUSA/00001152/201611) concluded in September 2017. The package leaflet is updated accordingly

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. Asfotase alfa – STRENSIQ (CAP) – EMEA/H/C/PSA/S/0050

Applicant: Alexion Europe SAS

PRAC Rapporteur: Rhea Fitzgerald

Scope: 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)

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

7.1.2. Rurioctocog alfa pegol – ADYNOVI (CAP) - EMEA/H/C/PSA/S/0045.1

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to PSA/S/0045.1 [substantial amendment to a protocol previously agreed in July 2019 (PSP/S/0077.1) for a study evaluating the long-term safety of Adynovi/Adynovate (rurioctocog alfa pegol) in adults and adolescents ≥12 years of age with haemophilia A] as per the request for supplementary information (RSI) adopted in December 2019

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

7.1.3. Turoctocog alfa pegol – ESPEROCT (CAP) - EMEA/H/C/PSP/S/0085.1

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller Stanislawski

Scope: MAH's response to PSP/S/0085 [protocol for a multinational, prospective, open labelled, non-controlled, non-interventional post-authorisation study of turoctocog alfa pegol (N8-GP) including the polyethylene glycol (PEG) moiety during long-term routine prophylaxis and treatment of bleeding episodes in patients with haemophilia A] as per the request for supplementary information (RSI) adopted in January 2020

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

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

7.1.4. Volanesorsen – WAYLIVRA (CAP) - EMEA/H/C/PSP/S/0080.2

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSP/S/0080.1 [protocol for a multinational observational registry (WAY4001) of patients treated with volanesorsen to evaluate the safety on severe thrombocytopenia and bleeding in patients with familial chylomicronemia syndrome (FCS)] as per the request for supplementary information (RSI) adopted in January 2020

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. Cangrelor - KENGREXAL (CAP) - EMEA/H/C/003773/MEA 002.2

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Ilaria Baldelli

Scope: MAH's response to MEA 002.1 [protocol for study DFIDM-1801 (ARCANGELO (itAlian pRospective study on CANGrELOr)): a multicentre prospective observational study of acute coronary syndrome patients undergoing percutaneous coronary intervention (PCI) who receive cangrelor and transition to either clopidogrel, prasugrel or ticagrelor] as per the request for supplementary information (RSI) adopted in December 2019

Action: For adoption of advice to CHMP

7.2.2. Dibotermin alfa - INDUCTOS (CAP) - EMEA/H/C/000408/LEG 074.2

Applicant: Medtronic BioPharma B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to LEG 074.1 [MAH's response to LEG 074.1 [detailed evaluation of the effectiveness of the current educational materials as requested in the conclusions of the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001034/201709) adopted in April 2018, including the submission of a protocol for a survey amongst physicians to assess their knowledge and understanding of selected risks of Inductos (dibotermin alfa) in Europe] as per the request for supplementary information (RSI) adopted in November 2019

Action: For adoption of advice to CHMP

7.2.3. Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/MEA 047.4

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

[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

Scope: MAH's response to MEA 047.3 [protocol for study No GS EU 276 4487: a prospective, longitudinal, observational registry of emtricitabine/tenofovir disoproxil fumarate for human immunodeficiency virus 1 (HIV-1) pre-exposure prophylaxis (PrEP) of adults and adolescents in Europe] as per the request for supplementary information (RSI) adopted in December 2019

Action: For adoption of advice to CHMP

7.2.4. Flutemetamol (^{18}F) - VIZAMYL (CAP) - EMEA/H/C/002557/MEA 002.3

Applicant: GE Healthcare AS

PRAC Rapporteur: Martin Huber

Scope: Amendment to a previously agreed protocol in December 2015 for study GE067-027 CPR in order to evaluate the effectiveness of Vizamyl (flutemetamol (^{18}F)) reader training in Europe and to assess the frequency of image classification errors in clinical practice

Action: For adoption of advice to CHMP

7.2.5. Hydrocortisone - PLENADREN (CAP) - EMEA/H/C/002185/MEA 009.2

Applicant: Shire Services BVBA

PRAC Rapporteur: Annika Folin

Scope: MAH's response to MEA 009.1 [amended protocol for study SHP617-400 (EU AIR) (0918-400): a non-interventional (PASS) registry study: A European multicentre, multi-country, post-authorisation observational study (registry) to monitor the safety of long-term treatment with Plenadren (hydrocortisone) and other glucocorticoid replacement therapies in patients with chronic adrenal insufficiency with a focus on intercurrent illness, adrenal crisis and serious adverse events] as per the request for supplementary information (RSI) adopted in November 2019

Action: For adoption of advice to CHMP

7.2.6. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 001.3

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 001.2 [protocol for a long-term observational study to evaluate and further characterize the events of thrombocytopenia, glomerulonephritis and retinal toxicity/eye disease related to vitamin A deficiency when Tegsedi (inotersen) is prescribed in normal clinical practice, consisting of a protocol for a cohort of inotersen-exposed patients (TEG4001) and a protocol for an external comparator cohort (TEG4003)] as per the request for supplementary information (RSI) adopted in November 2019

Action: For adoption of advice to CHMP

7.2.7. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 002.3

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 002.2 [protocol for study TEG4002: a retrospective chart review for evaluating adherence to and effectiveness of the proposed platelet monitoring schedule, proposed cut-off points, dose adaptation, and initiation of corticosteroids on thrombocyte recovery] as per the request for supplementary information (RSI) adopted in November 2019

Action: For adoption of advice to CHMP

7.2.8. Interferon beta-1a - AVONEX (CAP) - EMEA/H/C/000102/MEA 088

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Protocol for a joint PASS for study 2600153 (INFORM): an observational study regarding interferon beta exposure in the second and third trimesters of pregnancy - a register-based drug utilisation study (DUS) in Finland and Sweden

Action: For adoption of advice to CHMP

7.2.9. Interferon beta-1a - REBIF (CAP) - EMEA/H/C/000136/MEA 045

Applicant: Merck Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Protocol for a joint PASS for study 2600153 (INFORM): an observational study regarding interferon beta exposure in the second and third trimesters of pregnancy - a register-based drug utilisation study (DUS) in Finland and Sweden

Action: For adoption of advice to CHMP

7.2.10. Interferon beta-1b - BETAFERON (CAP) - EMEA/H/C/000081/MEA 025

Applicant: Bayer AG

PRAC Rapporteur: Martin Huber

Scope: Protocol for a joint PASS for study 2600153 (INFORM): an observational study regarding interferon beta exposure in the second and third trimesters of pregnancy - a register-based drug utilisation study (DUS) in Finland and Sweden

Action: For adoption of advice to CHMP

7.2.11. Interferon beta-1b - EXTAVIA (CAP) - EMEA/H/C/000933/MEA 023

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Martin Huber

Scope: Protocol for a joint PASS for study 2600153 (INFORM): an observational study regarding interferon beta exposure in the second and third trimesters of pregnancy - a register-based drug utilisation study (DUS) in Finland and Sweden

Action: For adoption of advice to CHMP

7.2.12. Patisiran - ONPATTRO (CAP) - EMEA/H/C/004699/MEA 002.3

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 002.2 [protocol for study ALN-TTR02-0009: a prospective observational study to monitor and assess 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 December 2019

Action: For adoption of advice to CHMP

7.2.13. Peginterferon beta-1a - PLEGRIDY (CAP) - EMEA/H/C/002827/MEA 010

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Protocol for a joint PASS for study 2600153 (INFORM): an observational study regarding interferon beta exposure in the second and third trimesters of pregnancy - a register-based drug utilisation study (DUS) in Finland and Sweden

Action: For adoption of advice to CHMP

7.2.14. Romosozumab - EVENITY (CAP) - EMEA/H/C/004465/MEA 001

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adrien Inoubli

Scope: Protocol for study OP0005: a European non-interventional PASS to study the adherence to the risk minimisation measures (RMMs) in the product information by estimating the compliance with contraindications and target indication(s) amongst incident romosozumab users, and analysing the utilisation pattern using the EU-adverse drug reactions (EU-ADR) Alliance [final study results expected in March 2026] (from initial opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.2.15. Romosozumab - EVENITY (CAP) - EMEA/H/C/004465/MEA 002

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adrien Inoubli

Scope: Protocol for study OP0004: a European non-interventional PASS to evaluate potential differences in terms of serious cardiovascular adverse events between romosozumab and currently available therapies used in comparable patients in real-world conditions using the EU-adverse drug reactions (EU-ADR) Alliance [final study results expected in December 2026] (from initial opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.2.16. Romosozumab - EVENITY (CAP) - EMEA/H/C/004465/MEA 003

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adrien Inoubli

Scope: Protocol for study OP0006: a European non-interventional PASS to evaluate potential differences in terms of serious infection between romosozumab and currently available therapies used in comparable patients in real-world conditions using the EU-adverse drug reactions (EU-ADR) Alliance [final study results expected in December 2024] (from initial opinion/marketing authorisation)

Action: For adoption of advice to CHMP

7.2.17. Ropeginterferon alfa-2b - BESREMI (CAP) - EMEA/H/C/004128/MEA 001.2

Applicant: AOP Orphan Pharmaceuticals AG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to MEA 001.1 [protocol for EUPAS29462 study: a prospective, multicentre, non-interventional observational PASS to further investigate the safety and tolerability of ropeginterferon alfa-2b in polycythaemia vera patients with a special focus on hepatotoxicity to evaluate the effectiveness of risk minimisation measures and to evaluate cardiovascular safety during titration phase [final study report expected in Q3 2023]] as per the request for supplementary information (RSI) adopted December 2019

Action: For adoption of advice to CHMP

7.2.18. Sotagliflozin - ZYNQUISTA (CAP) - EMEA/H/C/004889/MEA 004.1

Applicant: Navigant Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 004 [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 November 2019

Action: For adoption of advice to CHMP

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

None

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

7.4. Results of PASS non-imposed in the marketing authorisation(s)[25]

7.4.1. Agalsidase beta - FABRAZYME (CAP) - EMEA/H/C/000370/II/0113

Applicant: Genzyme Europe BV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of the final report from study AGALSC08994 (listed as a category 3 study in the RMP): a post-authorisation study on Fabrazyme (agalsidase beta) home infusion educational materials effectiveness evaluation: a survey of healthcare providers and patients/caregivers. The RMP (version 2.0) is updated accordingly. The RMP is also updated in line with revision 2 of the guidance on the format of RMP in the EU (template) and with information on study AGAL02603: a multicentre, multinational study of the effects of Fabrazyme (agalsidase beta) treatment on lactation and infants and study AGAL19211: the Fabry registry/pregnancy sub-registry

Action: For adoption of PRAC Assessment Report

7.4.2. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0034/G, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Submission of the final reports from studies 20150163 and 20150228 (listed as category 3 studies in the RMP) assessing the effectiveness of the additional risk minimisation measures (aRMM) for healthcare professionals (study 20150163) and patients/caregivers (study 20150228)

Action: For adoption of PRAC Assessment Report

7.4.3. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/II/0068

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of the final report related to the physician survey (NO6987) conducted for Exjade (deferasirox) to assess the impact of educational materials on the prescribers' awareness of doses and biological monitoring recommendations and to assess the awareness and appropriate use of both formulations (dispersible tablets and film-coated tablets). The RMP (version 17.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.4. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/WS1653/0230; LIFMIOR (CAP) - EMEA/H/C/004167/WS1653/0024

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Eva Segovia

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

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

Action: For adoption of PRAC Assessment Report

7.4.5. Hydroxycarbamide - SIKLOS (CAP) - EMEA/H/C/000689/II/0045

Applicant: Addmedica S.A.S.

PRAC Rapporteur: Laurence de Fays

Scope: Update of sections 4.2, 4.3, 4.4, 4.5, 4.6, 4.8 and 4.9 of the SmPC in order to reflect the final study results of non-interventional cohort study ESCORT-HU (European Sickle Cell Disease Cohort-Hydroxyurea): an observational prospective cohort study to measure the occurrence of adverse events and serious adverse events and to harmonise the product information with other hydroxyurea (HU)-containing products. In addition, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is amended to delete the reference to the treatment guide for physicians. The package leaflet and the RMP (version 20) are updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.6. Infliximab - INFLECTRA (CAP) - EMEA/H/C/002778/II/0079

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of the final clinical study report (CSR) for study C1231002 (PERSIST): an observational cohort study designed to evaluate real life drug persistence in biologic naive rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis patients receiving CT-P13 (infliximab biosimilar) or those switched to CT-P13 from stable treatment with the reference medicinal product containing infliximab

Action: For adoption of PRAC Assessment Report

7.4.7. Infliximab - INFLECTRA (CAP) - EMEA/H/C/002778/II/0080

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of the final clinical study report (CSR) for study C1231001 (CONNECT-IBD): a non-interventional study designated as a PASS conducted voluntarily to capture data from real-world clinical practice to characterise the population and document drug utilisation patterns. In addition, available safety data and data on the effectiveness of CT-P13 (infliximab biosimilar) was collected in patients with Crohn's disease or ulcerative colitis in the context of standard of care utilisation of the reference medicinal product containing infliximab

Action: For adoption of PRAC Assessment Report

7.4.8. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/II/0073

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of the final clinical study report (CSR) for study C1231001 (CONNECT-IBD): a non-interventional study designated as a PASS conducted voluntarily to capture data from real-world clinical practice to characterise the population and document drug utilisation patterns. In addition, available safety data and data on the effectiveness of CT-P13 (infliximab biosimilar) was collected in patients with Crohn's disease or ulcerative colitis in the context of standard of care utilisation of the reference medicinal product containing infliximab

Action: For adoption of PRAC Assessment Report

7.4.9. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/II/0074

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of the final clinical study report (CSR) for study C1231002 (PERSIST): an observational cohort study designed to evaluate real life drug persistence in biologic naive rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis patients receiving CT-P13 (infliximab biosimilar) or those switched to CT-P13 from stable treatment with the reference medicinal product containing infliximab

Action: For adoption of PRAC Assessment Report

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

7.5.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.9

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

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

Action: For adoption of advice to CHMP

7.5.2. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 002.3

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Eva Segovia

Scope: Fourth annual interim report from an established nationwide register (British Society for Rheumatology Rheumatoid Arthritis Register (BSRBR-RA)) for patients with

rheumatological disorders treated with biologic agents, designed as a national prospective study whose primary purpose is to assess long-term toxicity from the use of these agents in routine practice [final report expected in 2027]

Action: For adoption of advice to CHMP

7.5.3. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 003.3

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Eva Segovia

Scope: Fourth annual interim report from an established nationwide register (Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT)) for patients with rheumatological disorders treated with biologic agents, designed as a national prospective study whose primary purpose is to assess long-term toxicity from the use of these agents in routine practice [final report expected in 2027]

Action: For adoption of advice to CHMP

7.5.4. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 004.3

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Eva Segovia

Scope: Fourth annual interim report for study from ARTIS (Anti-Rheumatic Treatment in Sweden) register: a national prospective, observational, uncontrolled cohort study evaluating the risk of selected adverse events (AEs) in rheumatoid arthritis (RA), juvenile idiopathic arthritis, and other rheumatic disease patients treated with etanercept [final report expected in 2027]

Action: For adoption of advice to CHMP

7.5.5. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 005.3

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Eva Segovia

Scope: Fourth annual interim report for study from BADBIR (British Association of Dermatologists Biologic Interventions Register) register: a national prospective, observational, uncontrolled cohort study evaluating the risk of selected adverse events (AEs) in rheumatoid arthritis (RA), juvenile idiopathic arthritis, and other rheumatic disease patients treated with etanercept [final report expected in 2027]

Action: For adoption of advice to CHMP

7.5.6. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 033.3

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Second annual interim report for study MK-8259-050 (listed as a category 3 study in

the RMP): an observational PASS for golimumab in treatment of poly-articular juvenile idiopathic arthritis (pJIA) using the German Biologics JIA registry (BiKeR)

Action: For adoption of advice to CHMP

7.5.7. Lonoctocog alfa - AFSTYLA (CAP) - EMEA/H/C/004075/MEA 002.1

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Progress report for study CSL627_3001: a multicentre, open-label, phase 3 extension study which will investigate the safety and efficacy of recombinant factor VIII (rVIII)-single chain (CSL627) for prophylaxis and on-demand treatment of bleeding episodes in a total of at least 250 previously treated patients (PTP) with severe congenital haemophilia A

Action: For adoption of advice to CHMP

7.5.8. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/MEA 008.7

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 008.6 [third annual interim report for study CA209234 (listed as a category 3 study in the RMP): a PASS exploring the pattern of use, safety, and effectiveness of nivolumab in routine oncology practice [final clinical study report (CSR) expected in December 2024] as per the request for supplementary information (RSI) adopted in December 2019

Action: For adoption of advice to CHMP

7.5.9. Rivastigmine - EXELON (CAP) - EMEA/H/C/000169/MEA 036.5

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Annual report (covering the period from 01 February 2018 to 31 January 2019) of the drug utilisation study (DUS) on the effectiveness of risk minimisation measures (RMM) for multiple patch use

Action: For adoption of advice to CHMP

7.5.10. Rivastigmine - PROMETAX (CAP) - EMEA/H/C/000255/MEA 037.5

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Annual report (covering the period from 01 February 2018 to 31 January 2019) of the drug utilisation study (DUS) on the effectiveness of risk minimisation measures (RMM) for multiple patch use

Action: For adoption of advice to CHMP

7.5.11. Sirolimus - RAPAMUNE (CAP) - EMEA/H/C/000273/MEA 054.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim analysis study report for study B1741224: a non-interventional observational population-based cohort study to monitor the safety and effectiveness of sirolimus in patients with sporadic lymphangioleiomyomatosis (S-LAM)

Action: For adoption of advice to CHMP

7.5.12. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 022.19

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Ninth annual report for study C0168Z03 (PSOLAR: PSOriasis Longitudinal Assessment and Registry): an international prospective cohort study/registry programme designed to collect data on psoriasis (PSO) patients that are eligible to receive systemic therapies, including generalised phototherapy and biologics, together with MAH's response to MEA 022.18 [eighth annual report for study C0168Z03] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/MEA 075.1

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: MAH's response to MEA 075 [interim study results for study CICL670F2202 (CALYPSO): a randomized, open-label, multicentre, two arm, phase 2 study allowing to evaluate the safety of deferasirox granules in paediatric patients with iron overload [final clinical study report (CSR) expected in June 2021] (from X/54)] as per the request for supplementary information (RSI) adopted in November 2019

Action: For adoption of advice to CHMP

7.6.2. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/MEA 005

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of the MAH's assessment of a letter to the editor in the New England Journal of Medicine (NEJM) entitled 'deaths associated with emicizumab in patients with hemophilia A'[26] published in November 2019

[26] N Engl J Med 2019; 381: 1878-1879: DOI 10.1056/nejmC1909742

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

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

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/S/0032 (without RMP)

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Cholic acid - ORPHACOL (CAP) - EMEA/H/C/001250/S/0033 (without RMP)

Applicant: Laboratoires CTRS

PRAC Rapporteur: Sofia Trantza

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Susoctocog alfa - OBIZUR (CAP) - EMEA/H/C/002792/S/0028 (without RMP)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Tafamidis - VYNDAQEL (CAP) - EMEA/H/C/002294/S/0055 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Ghania Chamouni

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. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/R/0057 (without RMP)

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Aripiprazole - ARIPIPRAZOLE SANDOZ (CAP) - EMEA/H/C/004008/R/0014 (without RMP)

Applicant: Sandoz GmbH

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Carfilzomib - KYPROLIS (CAP) - EMEA/H/C/003790/R/0044 (without RMP)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Cobimetinib - COTELLIC (CAP) - EMEA/H/C/003960/R/0019 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Everolimus - VOTUBIA (CAP) - EMEA/H/C/002311/R/0065 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Glycerol phenylbutyrate - RAVICTI (CAP) - EMEA/H/C/003822/R/0034 (without RMP)

Applicant: Immedica Pharma AB

PRAC Rapporteur: Ilaria Baldelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/R/0031 (with RMP)

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Pemetrexed - PEMETREXED MEDAC (CAP) - EMEA/H/C/003905/R/0008 (with RMP)

Applicant: medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Ghania Chamouni

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Pemetrexed - PEMETREXED SANDOZ (CAP) - EMEA/H/C/004011/R/0008 (without RMP)

Applicant: Sandoz GmbH

PRAC Rapporteur: Ghania Chamouni

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Phenylephrine, ketorolac - OMIDRIA (CAP) - EMEA/H/C/003702/R/0015 (with RMP)

Applicant: Omeros Ireland Limited

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Pregabalin - PREGABALIN ACCORD (CAP) - EMEA/H/C/004024/R/0015 (with RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Pregabalin - PREGABALIN SANDOZ (CAP) - EMEA/H/C/004010/R/0012 (with RMP)

Applicant: Sandoz GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Pregabalin - PREGABALIN SANDOZ GMBH (CAP) - EMEA/H/C/004070/R/0013 (with RMP)

Applicant: Sandoz GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/R/0031 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.14. Tasimelteon - HETLIOZ (CAP) - EMEA/H/C/003870/R/0018 (without RMP)

Applicant: Vanda Pharmaceuticals Germany GmbH

PRAC Rapporteur: Adam Przybylkowski

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

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

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC Rules of Procedure - revision

Action: For adoption

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

Action: For discussion

12.4.2. Heads of Medicines Agencies (HMA)-EMA joint big data taskforce – call for nomination to the steering group

Action: For adoption

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 Q1 2020

Action: For information

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. 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. Strategy on measuring the impact of pharmacovigilance - PRAC interest group (IG) Impact – results and recommendations from case study on stakeholder engagement for valproate

PRAC lead: Antoine Pariente, Daniel Morales

Action: For discussion

12.20.2. Summary of product characteristics (SmPC) Advisory Group (AG) – call for nomination

Action: For adoption

12.20.3. Workshop on the role of registries in the monitoring of cancer therapies based on tumours' genetic and molecular features, 29 November 2019, Amsterdam, the Netherlands – final report: main observation and follow-up actions

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/