29 October 2018
EMA/PRAC/765002/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 29-31 October 2018

Chair: Sabine Straus – Vice-Chair: Martin Huber

29 October 2018, 09:00 – 19:30, room 3/A

30 October 2018, 08:30 – 19:30, room 3/A

31 October 2018, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

15 November 2018, 09:00-12:00, room 9/B, 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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Table of contents

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 29-31 October 2018. See November 2018 PRAC minutes (to be published post December 2018 PRAC meeting).

1.2. Agenda of the meeting on 29-31 October 2018

Action: For adoption

1.3. Minutes of the previous meeting on 01-04 October 2018

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Peramivir – ALPIVAB (CAP)

Applicant(s): Biocryst UK Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of hepatic failure

Action: For adoption of PRAC recommendation

EPITT 19314 – New signal

Lead Member State(s): SE

4.2. New signals detected from other sources

4.2.1. Dabigatran – PRADAXA (CAP)

Applicant(s): Boehringer Ingelheim

PRAC Rapporteur: Anette Kristine Stark

Scope: Signal of hallucinations

Action: For adoption of PRAC recommendation

EPITT 19298 – New signal

Lead Member State(s): DK

4.2.2. Mepolizumab – NUCALA (CAP)

Applicant(s): GlaxoSmithKline Trading

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of hypertensive crisis and hypertension

Action: For adoption of PRAC recommendation

EPITT 19301 – New signal

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

Lead Member State(s): DE

4.2.3. Niraparib – ZEJULA (CAP)

Applicant(s): Tesaro UK Limited

PRAC Rapporteur: Patrick Batty

Scope: Signal of sepsis

Action: For adoption of PRAC recommendation

EPITT 19311 – New signal

Lead Member State(s): UK

4.2.4. Nivolumab – OPDIVO (CAP)

Applicant(s): Bristol-Myers Squibb Pharma

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of hypoparathyroidism

Action: For adoption of PRAC recommendation

EPITT 19310 – New signal

Lead Member State(s): DE

4.2.5. Paracetamol (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of maternal paracetamol use during pregnancy and premature ductus arteriosus closure in offspring

Action: For adoption of PRAC recommendation

EPITT 19297 – New signal

Lead Member State(s): BE, FR

4.2.6. Rivaroxaban – XARELTO (CAP)

Applicant(s): Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of recurrent thrombosis in patients with antiphospholipid syndrome

Action: For adoption of PRAC recommendation

EPITT 19320 – New signal

Lead Member State(s): SE

4.3. Signals follow-up and prioritisation

4.3.1. Clomipramine (NAP); Serotonin and noradrenaline reuptake inhibitors (SNRI)[3]: desvenlafaxine (NAP); duloxetine - CYMBALTA (CAP), DULOXETINE LILLY (CAP), DULOXETINE MYLAN (CAP), DULOXETINE ZENTIVA (CAP), XERISTAR (CAP), YENTREVE (CAP); milnacipran (NAP); venlafaxine (NAP); Selective serotonin reuptake inhibitors (SSRI)[4]: citalopram (NAP); escitalopram (NAP); fluoxetine (NAP); fluvoxamine (NAP); paroxetine (NAP); sertraline (NAP); Vortioxetine – BRINTELLIX (CAP)

Applicant(s): Eli Lilly Nederland B.V. (Cymbalta, Duloxetine Lilly, Xeristar, Yentreve), Generics UK Limited (Duloxetine Mylan), H. Lundbeck A/S (Brintellix), Zentiva k.s. (Duloxetine Zentiva), various

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Signal of persistent sexual dysfunction after drug withdrawal

Action: For adoption of PRAC recommendation

EPITT 19277 – Follow-up to September 2018

4.3.2. Paracetamol (NAP)

Applicant(s): various

PRAC Rapporteur: Laurence de Fays

Scope: Signal of paracetamol use in pregnancy and child neurodevelopment and effects on the urogenital apparatus

Action: For adoption of PRAC recommendation

EPITT 17796 – Follow-up to February 2018

4.3.3. Tacrolimus[5] – ADVAGRAF (CAP), ENVARSUS (CAP), MODIGRAF (CAP), TACFORIUS (CAP), NAP

Applicant(s): Astellas Pharma Europe B.V. (Advagraf, Modigraf), Chiesi Farmaceutici S.p.A. (Envarsus), Teva B.V. (Tacforius); various

PRAC Rapporteur: Rhea Fitzgerald

Scope: Signal of hepatitis E infection

Action: For adoption of PRAC recommendation

EPITT 19246 – Follow-up to June 2018

4.3.4. Xylometazoline (NAP)

Applicant(s): various

PRAC Rapporteur: Zane Neikena

[3] Indicated in the treatment of major depressive disorder (MDD)
[4] Indicated in the treatment of major depressive disorder (MDD)
[5] Systemic formulations only

Scope: Signal of serious ventricular arrhythmia in patients with long QT syndrome

Action: For adoption of PRAC recommendation

EPITT 19242 – Follow-up to June 2018

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Adalimumab - EMEA/H/C/004475

Scope: Treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis

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

5.1.2. Adalimumab - EMEA/H/C/005158

Scope: Treatment of rheumatoid arthritis

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

5.1.3. Atazanavir - EMEA/H/C/004859

Scope: Treatment of human immunodeficiency virus 1 (HIV-1) infection

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

5.1.4. Bevacizumab - EMEA/H/C/004697

Scope: Treatment of adult patients with metastatic carcinoma of the colon or rectum, metastatic breast cancer, unresectable advanced, metastatic or recurrent non-small cell lung cancer, advanced and/or metastatic renal cell cancer, persistent, recurrent, or metastatic carcinoma of the cervix

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

5.1.5. Buprenorphine - EMEA/H/C/004743

Scope: Substitution treatment for opioid drug dependence

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

5.1.6. Canakinumab - EMEA/H/C/004754

Scope: Treatment for the prevention of major cardiovascular events

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

5.1.7. Cannabidiol - EMEA/H/C/004675, Orphan

Applicant: GW Research Ltd

Scope: Adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS)

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

5.1.8. Dacomitinib - EMEA/H/C/004779

Scope: First-line treatment of adults with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR)-activating mutations

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

5.1.9. Fremanezumab - EMEA/H/C/004833

Scope: Prevention of episodic and chronic migraine

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

5.1.10. Hydroxycarbamide - EMEA/H/C/004837

Scope: Prevention of complications of Sickle cell disease

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

5.1.11. Miglustat - EMEA/H/C/004904

Scope: Treatment of adult patients with mild to moderate type 1 Gaucher disease and only in the treatment of patients for whom enzyme replacement therapy is unsuitable

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

5.1.12. Silodosin - EMEA/H/C/004964

Scope: Treatment of prostatic hyperplasia (BPH)

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

5.1.13. Sotagliflozin - EMEA/H/C/004889

Scope: Adjunct treatment to insulin therapy to improve glycaemic control in adults with type 1 diabetes mellitus (T1DM)

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

5.1.14. Turoctocog alfa pegol - EMEA/H/C/004883, Orphan

Applicant: Novo Nordisk A/S

Scope: Treatment and prophylaxis of bleeding in patients with haemophilia A

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

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

5.2.1. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/II/0182

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 14.0) in order to include a review of the currently specified safety concerns and recently assessed safety concerns and to bring it in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

5.2.2. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/II/0023

Applicant: Celgene Europe BV

PRAC Rapporteur: Eva Segovia

Scope: Update of the RMP (version 11.0) in order to reclassify and/or rename the known safety concerns associated with the use of Otezla (apremilast) in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.3. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0072

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 14.0) in order to revise the distribution list of educational materials (addition of dermatologists) and to revise the RMP in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template), including the update of the important identified risks and important potential risks. The PASS protocol for study UP0038 designed to assess the effectiveness of the educational material is updated to add dermatologists to the healthcare professional study population, to remove Italy and Spain from the study participation and to make additional administrative changes. In addition, the MAH took the opportunity to introduce some administrative changes in the RMP

Action: For adoption of PRAC Assessment Report

5.2.4. Fidaxomicin - DIFICLIR (CAP) - EMEA/H/C/002087/II/0033

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 10) in order to reflect the final outcome (Year 5) of study AG2012-3459 (ClosER study: *Clostridium difficile* European Resistance surveillance study) (listed as a category 3 study in the RMP (MEA 002.4)): a prospective, longitudinal, pan-European, in vitro sentinel surveillance study of susceptibility of *Clostridium difficile* to fidaxomicin and other antibiotics

Action: For adoption of PRAC Assessment Report

5.2.5. Micafungin - MYCAMINE (CAP) - EMEA/H/C/000734/II/0038

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of the RMP (version 20.0) in order to streamline and improve the educational programme and communication to prescribing physicians as requested in variation II/0035 concluded in June 2018

Action: For adoption of PRAC Assessment Report

5.2.6. Osimertinib - TAGRISSO (CAP) - EMEA/H/C/004124/II/0026

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP (version 12.0) following the completion of study D6030C00001 (BLOOM study): a phase 1, open-label, multicentre study to assess the safety, tolerability, pharmacokinetics and preliminary anti-tumour activity of osimertinib (AZD9291) in patients with epidermal growth factor receptor (EGFR) mutation positive advanced stage non-small cell lung cancer (NSCLC) in order to remove 'use in patients with Eastern Cooperative Oncology Group (ECOG) performance status ≥2' and 'use in patients with symptomatic brain metastases' as missing information

Action: For adoption of PRAC Assessment Report

5.2.7. Paclitaxel - ABRAXANE (CAP) - EMEA/H/C/000778/II/0092

Applicant: Celgene Europe BV

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP (version 17.0) in order to propose the reclassification and/or renaming of known safety concerns associated with the use of Abraxane (paclitaxel) in line with revision 2 of GVP module V on 'Risk management systems'

Action: For adoption of PRAC Assessment Report

5.2.8. Piperaquine tetraphosphate, artenimol - EURARTESIM (CAP) - EMEA/H/C/001199/II/0032

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Julie Williams

Scope: Update of the RMP (version 15.2) to close the pregnancy registry in line with revision 2 of the guidance on the format of RMP in the EU (template). In addition, the MAH took the opportunity to include the 'distribution of a new version of the educational material', to add 'delayed haemolytic anaemia' and 'severe cutaneous adverse reactions' such as Stevens-Johnson syndrome and toxic epidermal necrolysis as important potential risks, to limit the reproductive risk to the first trimester of pregnancy; to update on several studies, to include Eurartesim (piperaquine tetraphosphate/artenimol) into the WHO[6] list of essential medicines and to update the details of the MAH

Action: For adoption of PRAC Assessment Report

[6] World Health Organization

5.2.9. Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0144

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Update of the RMP (version 16.0) to remove the additional risk minimisation measure of educational outreaches for the important identified risk of 'infusion related reactions' and 'acute infusion related reactions' (IRR)

Action: For adoption of PRAC Assessment Report

5.2.10. Tolcapone - TASMAR (CAP) - EMEA/H/C/000132/II/0061

Applicant: Meda AB

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of the RMP (version 7) in order to reflect currently available data from post-marketing experience and patient exposure data, to align the RMP with revision 2 of GVP module V on 'Risk management systems' as well as to remove 'dopaminergic effects due to increased bioavailability of co-administered levodopa (e.g. dyskinesia)' as an important identified risk and 'drug interactions with significant clinical consequence including sudden sleep onset' as a potential risk

Action: For adoption of PRAC Assessment Report

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

5.3.1. Ambrisentan - VOLIBRIS (CAP) - EMEA/H/C/000839/II/0054

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.2 and 5.2 of the SmPC based on results of GSK1325760 study: a juvenile nonclinical toxicology study to further investigative the respiratory function following oral dosing from postnatal days 7 through 36, including an assessment of recovery. The RMP (version 7.5) is updated accordingly. In addition, the MAH took the opportunity to correct typographical errors including the frequency of the adverse drug reaction 'rash' in section 4.8 of the SmPC as well as the date of renewal. The MAH also proposed to introduce a minor update in the Braille section. Moreover, the MAH took the opportunity to propose a combined version of the SmPCs for the different authorised strengths

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

5.3.2. Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/II/0028, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.4 of the SmPC in order to update the safety information with inclusion of a statement on bedaquiline resistance in line with the outcome of the PSUSA procedure (EMEA/H/C/PSUSA/00010074/201709) finalised in April 2018 (LEG 011). The RMP (version 3.0) is updated based on the data triggering the SmPC update and to reflect

completion of studies which were assessed in previous procedures. 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

5.3.3. Deferiprone - FERRIPROX (CAP) - EMEA/H/C/000236/II/0126/G

Applicant: Apotex Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Grouped variations consisting of an update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update safety information on the use of Ferriprox (deferiprone) in patients with renal or hepatic impairment, based on the final results of two clinical studies (listed as category 3 studies in the RMP): 1) study LA39-0412: an open-label study to compare the pharmacokinetic profiles of a single dose of Ferriprox (deferiprone) in subjects with impaired renal function and healthy volunteers); 2) study LA40-0412: an open-label study to compare the pharmacokinetic profiles of a single dose of Ferriprox in subjects with impaired hepatic function and healthy volunteers. The package leaflet and labelling are updated accordingly. The RMP (version 13.1) is updated accordingly and in line with revision 2 of the guidance on the format of RMP in the EU (template). In addition, the MAH took the opportunity to introduce minor edits in the product information

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

5.3.4. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/X/0004/G

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped applications consisting of: 1) extension application to add a new strength of 200 mg solution for injection in pre-filled syringe with safety system (PFS-S) and pre-filled pen (PFP); 2) extensions of indication to add as indications: 'add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older, who are inadequately controlled with medium-to-high dose inhaled corticosteroids (ICS) plus another medicinal product for maintenance treatment, including those with or without an eosinophilic phenotype', 'maintenance therapy to improve lung function' and 'maintenance therapy to reduce oral steroid use and improve lung function in steroid-dependent asthma patients' based on pivotal studies, namely: study DRI12544: a randomized, double-blind, placebo-controlled, dose-ranging study to evaluate dupilumab in patients with moderate to severe uncontrolled asthma; study LIBERTY ASTHMA QUEST: a randomized, double blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of dupilumab in patients with persistent asthma; and study VENTURE: a randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of dupilumab in patients with severe steroid dependent asthma. As a consequence, SmPC sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 are updated. The package leaflet and the RMP (version 2.0) are updated accordingly. In addition, the MAH proposed to merge the SmPCs for the 200 mg and 300 mg strengths

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

5.3.5. Eltrombopag, eltrombopag olamine - REVOLADE (CAP) - EMEA/H/C/001110/II/0049

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include first line treatment of adult and paediatric patients aged 2 years and older with severe aplastic anaemia. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 50.0) are updated accordingly

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

5.3.6. Erlotinib - TARCEVA (CAP) - EMEA/H/C/000618/II/0058

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Update of sections 4.2, and 5.1 of the SmPC based on phase 3 clinical study MO22162 (CURRENTS) comparing a higher dose of Tarceva (erlotinib) (300 mg) over the recommended daily dose (150 mg) in current smokers with locally advanced or metastatic non-small cell lung cancer (NSCLC) in the second-line setting after failure of chemotherapy. The package leaflet and the RMP (version 7.0) are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes in sections 4.4, 4.5, 4.6, 4.7, 4.8 and 5.2 of the SmPC

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

5.3.7. Insulin aspart - NOVOMIX (CAP) - EMEA/H/C/000308/II/0095

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.2, 4.5 and 5.1 of the SmPC to include data on the use of NovoMix 30 combination use with glucagon-like peptide 1 (GLP-1) receptor agonists. The package leaflet and the RMP (version 3) are updated accordingly

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

5.3.8. Insulin glargine - TOUJEO (CAP) - EMEA/H/C/000309/II/0106

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study EFC13799: a randomised phase 3b study, open-label, 2-arm, parallel-group, multicentre, 26-week study assessing the safety and efficacy of Toujeo (insulin glargine, HOE901-U300) versus Lantus (insulin glargine 100 U/mL) in patients ≥ 65 years with treatment of type 2 diabetes mellitus (T2DM) inadequately controlled on antidiabetic regimens either including no insulin, or with basal insulin as their only insulin. The RMP is updated accordingly (version 5)

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

5.3.9. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/II/0102/G, Orphan

Applicant: Celgene Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Grouped applications consisting of: 1) extension of indication to include the treatment in combination with bortezomib and dexamethasone of adult patients with previously untreated multiple myeloma; 2) addition of 7-capsule pack sizes for the 7.5 mg, 20 mg and 25 mg strengths of Revlimid (lenalidomide) to support the proposed posology and lenalidomide dose modification. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 6.5 and 8 of the SmPC are updated. The package leaflet and the RMP (version 36.1) are updated accordingly. Additionally, minor editorial changes are introduced throughout the product information and Annex II-D 'conditions or restrictions with regard to the safe and effective use of the medicinal product' on key elements of the risk minimisation measures (RMM) to include information on timing of blood and semen donation in line with SmPC section 4.4

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

5.3.10. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/X/0034/G

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Grouped variations consisting of: 1) extension application to introduce a new pharmaceutical form (granules) in 2 strengths (100/125 mg and 150/188 mg) for paediatric use from 2 to 5 years. The RMP (version 4.0) is updated accordingly; 2) update of sections 4.1, 4.2, 4.5, 4.8 and 5.3 of the SmPC of the tablet formulations to bring it in line with the proposed paediatric 2-5 year old extension application

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

5.3.11. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0029/G

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of section 4.8 to adjust the list of adverse drug reactions and their corresponding frequencies in line with the outcome of the PSUSA procedure (PSUSA/00010366/201709) finalised in April 2018 ; 2) update of sections 4.2, 4.4 and 5.2 of the SmPC to add results from a phase 1 open label parallel study to evaluate the pharmacokinetics of a single oral dose of extended-release combination of naltrexone and bupropion in subjects with normal hepatic function or varying degrees of impaired hepatic function and remove the recommendation to not use naltrexone/bupropion in patients with mild hepatic impairment. The existing warning is updated accordingly. The warning related to contraindications is aligned to section 4.3 to add end-stage renal failure patients. As a consequence, the RMP is updated accordingly (version 11). In addition, the MAH took the opportunity to update the warning on lactose in accordance 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

5.3.12. Nintedanib - OFEV (CAP) - EMEA/H/C/003821/II/0021, Orphan

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of section 4.8 of the SmPC in order to include 'myocardial infarction' as a new adverse drug reaction with a frequency 'uncommon' in order to fulfil LEG 004.1 in line with the outcome of the PSUSA procedure (PSUSA/00010319/201704) finalised at the November 2017 PRAC meeting. The package leaflet and the RMP (version 6.0) are updated accordingly and in line with revision 2 of the guidance on the format of RMP in the EU (template)

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

5.3.13. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS1278/0042; Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS1278/0053

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope (re-examination procedure): Extension of indication to include the combination treatment with nivolumab and ipilimumab of adult patients with intermediate/poor-risk advanced renal cell carcinoma. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of Opdivo and Yervoy SmPCs are updated. The package leaflet and the RMP (version 19.0 for Yervoy and version 13.0 for Opdivo) are updated accordingly. In addition, the MAH took the opportunity to introduce some editorial changes throughout the Yervoy (ipilimumab) and Opdivo (nivolumab) product information

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

5.3.14. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/II/0002

Applicant: Roche Registration GmbH

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.4 and 4.5 of the SmPC in order to include information on vaccination based on interim results from study BN29739 (listed as a category 3 study in the RMP): a phase 3b, multicentre, randomised, parallel-group, open-label study to evaluate the effects of ocrelizumab on immune response in patients with relapsing forms of multiple sclerosis (MS). The package leaflet and the RMP (version 2.0) are updated accordingly

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

5.3.15. Oseltamivir - TAMIFLU (CAP) - EMEA/H/C/000402/II/0136

Applicant: Roche Registration GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 to guide prescribers on the use of Tamiflu (oseltamivir) for treatment in immunocompromised (IC) patients based on results from study NV20234: a phase 3, double-blind, randomized, stratified, multicentre study of conventional and double dose oseltamivir for the treatment of influenza in IC patients. The package leaflet and RMP (version 18) are updated accordingly. In addition, the MAH took the opportunity to correct some minor errors

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

5.3.16. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0060

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include, in combination with carboplatin and either paclitaxel or nab-paclitaxel, for the first-line treatment of metastatic squamous non-small cell lung cancer (NSCLC) in adults. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 20.1) are updated accordingly. Additionally, the MAH took the opportunity to introduce some editorial corrections to section 5.1 of the SmPC in line with the outcome of variation EMEA/H/C/003820/II/0052 finalised in May 2018

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

5.3.17. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[7]) - EMEA/H/W/002300/II/0036

Applicant: GlaxoSmithKline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of section 4.4 of the SmPC in order to modify the warning on 'protection against *Plasmodium falciparum* malaria' over time. This update is based on the final results from study MALARIA-076 (listed as a category 3 study in the RMP): an open extension to phase 3, multicentre study MALARIA-055 PRI (110021) to evaluate long-term efficacy, safety and immunogenicity of Mosquirix (plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted)) malaria vaccine in infants and children. The RMP (version 4.1) is updated accordingly

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

5.3.18. Ramucirumab - CYRAMZA (CAP) - EMEA/H/C/002829/II/0027

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include Cyramza (ramucirumab) as monotherapy for the treatment of adult patients with hepatocellular carcinoma who have an alpha fetoprotein (AFP) of ≥ 400 ng/mL, after prior sorafenib therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in accordance. The package leaflet and the RMP (version 8.1) are updated accordingly

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

5.3.19. Ribociclib - KISQALI (CAP) - EMEA/H/C/004213/II/0004

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Doris Stenver

Scope: Extension of indication to include treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or

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

metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant. In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist for Kisqali (ribociclib). This is based on data from: 1) study CLEE011E2301: a phase 3 randomized, double-blind, placebo-controlled study of ribociclib (LEE011) or placebo in combination with tamoxifen and goserelin or a non-steroidal aromatase inhibitor (NSAI) and goserelin for the treatment of premenopausal women with hormone receptor positive, HER2- negative, advanced breast cancer; 2) study CLEE011F2301: a randomized double-blind, placebo-controlled study of ribociclib in combination with fulvestrant for the treatment of men and postmenopausal women with hormone receptor positive, HER2 negative, advanced breast cancer who have received no or only one line of prior endocrine treatment. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 2.0) are updated accordingly. In addition, the MAH took the opportunity to introduce some editorial changes in the SmPC and to make an administrative update to the Estonian and Latvian local representatives addresses in the package leaflet

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

5.3.20. Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0149

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Extension of indication to include the maintenance of remission of granulomatosis with polyangiitis (GPA) (Wegener's) and microscopic polyangiitis (MPA). 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 17.0) are updated accordingly. In addition, the MAH took the opportunity to implement a terminology change in Annex II

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

5.3.21. Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0150

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Extension of indication to include the treatment of patients with moderate to severe pemphigus vulgaris (PV). As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 17.0) are updated accordingly

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

5.3.22. Rolapitant - VARUBY (CAP) - EMEA/H/C/004196/II/0007/G

Applicant: Tesaro UK Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Grouped variations consisting of: 1) update of section 4.5 of the SmPC regarding interaction with organic cation transporter 1 (OCT1) substrates to reflect the results from non-clinical study 17TESAP2R1: an in vitro evaluation of the substrate and inhibitor potential of rolapitant for efflux and update of transporters; 2) update of section 4.5 of the SmPC regarding interaction with UDP-glucuronosyltransferase (UGT) substrates following the

submission of the results from non-clinical studies, namely: study 170594: evaluation of potential UGT inhibition by rolapitant in cryopreserved human hepatocytes; and study TSRP/REP/07CRD75486/2017: evaluation of potential rolapitant metabolism by recombinantly expressed human UGT enzymes; 3) update of section 4.5 of the SmPC following the submission of the results from study 1000-01-001: an open-label, single-dose study to assess the effects of rolapitant (oral) on the pharmacokinetics of caffeine (CYP1A2[8]) in healthy subjects. The RMP is updated accordingly (version 1.2)

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

5.3.23. Sodium oxybate - XYREM (CAP) - EMEA/H/C/000593/II/0076

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication to include adolescents and children older than 7 years to the existing indication of treatment of narcolepsy with cataplexy in adults. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 9.0) are updated accordingly

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

5.3.24. Ticagrelor - BRILIQUE (CAP) - EMEA/H/C/001241/II/0042

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2, 4.9 and 5.2 of the SmPC in order to update the safety information in relation to renal impairment based on the final results from study D5130L00067: a single dose, randomized, open label, parallel group study conducted to compare the pharmacokinetics (PK), pharmacodynamics (PD), safety and tolerability of ticagrelor in haemodialysis patients to subjects with normal renal function. The RMP is updated accordingly (version 11)

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. Alogliptin - VIPIDIA (CAP); alogliptin, metformin - VIPDOMET (CAP); alogliptin, pioglitazone - INCRESYNC (CAP) - PSUSA/00010061/201804

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[8] Cytochrome P450 1A2

6.1.2. Bezlotoxumab - ZINPLAVA (CAP) - PSUSA/00010576/201804

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Cariprazine - REAGILA (CAP) - PSUSA/00010623/201804

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Chenodeoxycholic acid - CHENODEOXYCHOLIC ACID LEADIANT (CAP) - PSUSA/00010590/201804

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Colesevelam - CHOLESTAGEL (CAP) - PSUSA/00000864/201803

Applicant: Genzyme Europe BV

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Defibrotide - DEFITELIO (CAP) - PSUSA/00010086/201804

Applicant: Gentium S.r.l.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Diphtheria, tetanus, pertussis antigens (pertussis toxoid, filamentous haemagglutinin) (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated), haemophilus type b conjugate vaccines (adsorbed) - HEXACIMA (CAP); HEXAXIM (Art 58[9]); HEXYON (CAP) - PSUSA/00010091/201804

Applicants: Sanofi Pasteur (Hexacima, Hexaxim), Sanofi Pasteur Europe (Hexyon)

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

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Edoxaban - LIXIANA (CAP); ROTEAS (CAP) - PSUSA/00010387/201804 (with RMP)

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Empagliflozin - JARDIANCE (CAP); empagliflozin, metformin - SYNJARDY (CAP) - PSUSA/00010388/201804

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Emtricitabine - EMTRIVA (CAP) - PSUSA/00001209/201804

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Emtricitabine, tenofovir alafenamide - DESCOVY (CAP) - PSUSA/00010515/201804

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - PSUSA/00001210/201804

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Everolimus[10] - VOTUBIA (CAP) - PSUSA/00001343/201803

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Exenatide - BYDUREON (CAP); BYETTA (CAP) - PSUSA/00009147/201803

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Febuxostat - ADENURIC (CAP) - PSUSA/00001353/201804

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Fenofibrate, pravastatin - PRAVAFENIX (CAP) - PSUSA/00001363/201804

Applicant: Laboratoires SMB s.a.

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Florbetapir (^{18}F) - AMYVID (CAP) - PSUSA/00010032/201804

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - PSUSA/00010678/201804

Applicant: GlaxoSmithKline Biologicals SA

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

[10] Indicated in the treatment of astrocytoma

Action: For adoption of recommendation to CHMP

6.1.19. Histamine[11] - CEPLENE (CAP) - PSUSA/00001610/201804

Applicant: Noventia Pharma Srl

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Idarucizumab - PRAXBIND (CAP) - PSUSA/00010435/201804

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Insulin glargine - ABASAGLAR (CAP); LANTUS (CAP); LUSDUNA (CAP); SEMGLEE (CAP); TOUJEO (CAP) - PSUSA/00001751/201804

Applicants: Eli Lilly Nederland B.V. (Abasaglar), Sanofi-Aventis Deutschland GmbH (Lantus, Toujeo), Merck Sharp & Dohme B.V. (Lusduna), Mylan S.A.S (Semglee)

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Insulin glulisine - APIDRA (CAP) - PSUSA/00001752/201804

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Irinotecan[12] - ONIVYDE (CAP) - PSUSA/00010534/201804

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[11] Indicated in the treatment of acute myeloid leukaemia
[12] Liposomal formulations only

6.1.24. Japanese encephalitis vaccine (inactivated) - IXIARO (CAP) - PSUSA/00001801/201803

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Mannitol[13] - BRONCHITOL (CAP) - PSUSA/00009226/201804

Applicant: Pharmaxis Pharmaceuticals Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Meningococcal group A, C, W-135, Y conjugate vaccines (conjugated to tetanus toxoid carrier protein) - NIMENRIX (CAP) - PSUSA/00010044/201804

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Netupitant, palonosetron - AKYNZEO (CAP) - PSUSA/00010393/201804

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Oestrogens conjugated, bazedoxifene - DUAVIVE (CAP) - PSUSA/00010321/201804

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Olaratumab - LARTRUVO (CAP) - PSUSA/00010541/201804

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

[13] Indicated in the treatment of cystic fibrosis

Action: For adoption of recommendation to CHMP

6.1.30. Parathyroid hormone - NATPAR (CAP) - PSUSA/00010591/201804

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Patiromer - VELTASSA (CAP) - PSUSA/00010618/201804

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Pitolisant - WAKIX (CAP) - PSUSA/00010490/201803

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Propranolol[14] - HEMANGIOL (CAP) - PSUSA/00010250/201804

Applicant: Pierre Fabre Dermatologie

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Ramucirumab - CYRAMZA (CAP) - PSUSA/00010323/201804 (with RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Regadenoson - RAPISCAN (CAP) - PSUSA/00002616/201804

Applicant: GE Healthcare AS

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

[14] Centrally authorised product(s) only

Action: For adoption of recommendation to CHMP

6.1.36. Siltuximab - SYLVANT (CAP) - PSUSA/00010254/201804

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Temsirolimus - TORISEL (CAP) - PSUSA/00002887/201803

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Thiotepa[15] - TEPADINA (CAP) - PSUSA/00002932/201803

Applicant: Adienne S.r.l.

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Tocilizumab - ROACTEMRA (CAP) - PSUSA/00002980/201804

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. Vandetanib - CAPRELSA (CAP) - PSUSA/00009327/201804

Applicant: Genzyme Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[15] Centrally authorised product(s) only

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

6.2.1. Bimatoprost - LUMIGAN (CAP); NAP - PSUSA/00000413/201803

Applicants: Allergan Pharmaceuticals Ireland (Lumigan), various

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Cladribine[16] - LITAK (CAP); NAP - PSUSA/00000787/201802

Applicants: Lipomed GmbH (Litak), various

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Dexmedetomidine - DEXDOR (CAP); NAP - PSUSA/00000998/201803

Applicants: Orion Corporation (Dexdor), various

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Hepatitis B vaccine (rDNA) - HBVAXPRO (CAP); NAP - PSUSA/00001597/201802

Applicants: MSD Vaccins (HBVAXPRO), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Tenofovir disoproxil - TENOFOVIR DISOPROXIL MYLAN (CAP); TENOFOVIR DISOPROXIL ZENTIVA (CAP); VIREAD (CAP); NAP - PSUSA/00002892/201803

Applicants: Mylan S.A.S (Tenofovir Disoproxil Mylan), Zentiva k.s. (Tenofovir Disoproxil Zentiva), Gilead Sciences Ireland UC (Viread), various

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[16] All indications except multiple sclerosis

6.2.6. Zonisamide - ZONEGRAN (CAP); NAP - PSUSA/00003152/201803

Applicants: Eisai GmbH (Zonegran), various

PRAC Rapporteur: Rhea Fitzgerald

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. Allergen for therapy: dermatophagoides pteronyssinus, dermatophagoides farina[17] [18] (NAP) - PSUSA/00010582/201803

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Ampicillin, sulbactam (NAP) - PSUSA/00000197/201802

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Aprotinin (NAP) - PSUSA/00000230/201802

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Bacillus Calmette-Guerin[19] (BCG) (NAP) - PSUSA/00000303/201803

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[17] Oromucosal use only
[18] Products authorised via mutually recognition procedure (MRP) and decentralised procedure (CP) only
[19] For immunotherapy only

6.3.5. Bacillus Calmette-Guerin (BCG) vaccine[20] (NAP) - PSUSA/00000304/201803

Applicant(s): various

PRAC Lead: Roxana Stefania Stroe

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Cabergoline (NAP) - PSUSA/00000477/201803

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Citrulline malate (NAP) - PSUSA/00010579/201803

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Dienogest, ethinylestradiol (NAP) - PSUSA/00001057/201803

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Dobutamine (NAP) - PSUSA/00001151/201803

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Enoxaparin[21] (NAP) - PSUSA/00010560/201804

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

[20] Freeze-dried only
[21] All products except biosimilar(s)

Action: For adoption of recommendation to CMDh

6.3.11. Fenspiride (NAP) - PSUSA/00001368/201804

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Fluorodopa (^{18}F) (NAP) - PSUSA/00010002/201803

Applicant(s): various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Germanium (^{68}Ge) chloride, gallium (^{68}Ga) chloride (NAP) - PSUSA/00010364/201803

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Influenza vaccine (split virion, inactivated)[22] (NAP) - PSUSA/00010298/201803

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Influenza vaccine (split virion, inactivated, prepared in cell cultures) (NAP) - PSUSA/00010299/201803

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Influenza vaccine (surface antigen, inactivated) (NAP) - PSUSA/00001744/201803

Applicant(s): various

[22] All products except centrally authorised products

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Influenza vaccine (surface antigen, inactivated, adjuvanted) (NAP) - PSUSA/00010300/201803

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Ioxaglic acid (NAP) - PSUSA/00001777/201802

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Latanoprost[23] (NAP) - PSUSA/00001834/201804

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Meningococcal group A, C, W135, Y polysaccharide vaccine (NAP) - PSUSA/00010602/201803

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Nitrazepam (NAP) - PSUSA/00002170/201803

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[23] Paediatric indication only

6.3.22. Nitrofurantoin, nifurtoinol (NAP) - PSUSA/00002174/201802

Applicant(s): various

PRAC Lead: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Ondansetron (NAP) - PSUSA/00002217/201802

Applicant(s): various

PRAC Lead: Gabriela Jazbec

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Pimecrolimus (NAP) - PSUSA/00002411/201803

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Promestriene[24] (NAP) - PSUSA/00009271/201803

Applicant(s): various

PRAC Lead: Roxana Stefania Stroe

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Spironolactone (NAP) - PSUSA/00002780/201803

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.27. Tenoxicam (NAP) - PSUSA/00002893/201802

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[24] Cream and vaginal capsules only

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/LEG 028.1

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: MAH's responses to LEG 028 [cumulative review of cases of liver injury from all available sources (post marketing cases, clinical trial data and literature) as requested in the conclusions of PSUSA/00000226/201705 adopted at the December 2017 PRAC] as per the request for supplementary information (RSI) adopted in May 2018

Action: For adoption of advice to CHMP

6.4.2. Ledipasvir, sofosbuvir - HARVONI (CAP) - EMEA/H/C/003850/LEG 020

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Justification for not submitting a variation to implement cardiac arrhythmias associated with co-administration of sofosbuvir-containing regimens and amiodarone as a warning and to include Stevens-Johnson syndrome (SJS) as an undesirable effect in the product information as requested in the conclusions of the PSUSA procedure for sofosbuvir (PSUSA/00010134/201712) adopted in June 2018

Action: For adoption of advice to CHMP

6.4.3. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/LEG 011

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Justification for not submitting a variation to implement cardiac arrhythmias associated with co-administration of sofosbuvir-containing regimens and amiodarone as a warning and to include Stevens-Johnson syndrome (SJS) as an undesirable effect in the product information as requested in the conclusions of the PSUSA procedure for sofosbuvir (PSUSA/00010134/201712) adopted in June 2018

Action: For adoption of advice to CHMP

6.4.4. Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/004350/LEG 005

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Justification for not submitting a variation to implement cardiac arrhythmias associated with co-administration of sofosbuvir-containing regimens and amiodarone as a warning and to include Stevens-Johnson syndrome (SJS) as an undesirable effect in the product information as requested in the conclusions of the PSUSA procedure for sofosbuvir (PSUSA/00010134/201712) adopted in June 2018

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[25]

7.1.1. Cerliponase alfa – BRINEURA (CAP) - EMEA/H/C/PSP/S/0063.1

Applicant: BioMarin International Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to PSP/S/0063 [protocol for study 190-504 (replacing study 190-501): a non-interventional PASS (observational drug study) in order to evaluate the long-term safety of cerliponase alfa, including the occurrence of serious hypersensitivity reactions and anaphylaxis in patients with neuronal ceroid lipofuscinosis type 2 (CLN2)] as per the request for supplementary information (RSI) adopted in June 2018

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

7.1.2. Cidofovir (NAP) - EMEA/H/N/PSP/S/0052.3

Applicant: Emcure Pharma UK Ltd (Cidofovir Emcure Pharma)

PRAC Rapporteur: Julie Williams

Scope: MAH's response to PSP/S/0052.2 [protocol for cidofovir exposure registry study: a non-interventional, prospective, exposure (safety outcome) registry study of cidofovir to further elucidate the characteristics of the different patient populations for cidofovir use, gather details of adverse events and patient outcome following treatment in a specified indication] as per the request for supplementary information (RSI) adopted in May 2018

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

7.1.3. Prasterone – INTRAROSA (CAP) - EMEA/H/C/PSP/S/0061.1

Applicant: Endoceutics Limited

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to PSP/S/0061 [protocol for a non-interventional PASS: a drug utilisation study (DUS) to describe the baseline characteristics and utilisation patterns of EU postmenopausal women initiating treatment with Intrarosa (prasterone) and to assess whether EU prescribers abide by the contraindications stated in the EU SmPC] as per the request for supplementary information (RSI) adopted in June 2018

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

7.1.4. Susoctocog alfa – OBIZUR (CAP) - EMEA/H/C/PSA/S/0033

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Protocol for a prospective and retrospective non-interventional study to evaluate the safety, utilisation and effectiveness of Obizur (susoctocog alfa) in the treatment of bleeding

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

episodes in real-life clinical practice in Europe and in the US

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[26]

7.2.1. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/MEA 005.4

Applicant: Celgene Europe BV

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 005.3 [MAH's response to MEA005.2 [PASS protocol in order to collect long-term data using the British Society of Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR) psoriatic arthritis (PsA) registry 'BSRBR PsA registry': a disease registry in the EU for PsA and psoriasis] as per the request for supplementary information (RSI) adopted in June 2018

Action: For adoption of advice to CHMP

7.2.2. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/MEA 010.1

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: MAH's response to MEA 010 [submission of a protocol for study WO40486: an observational study to evaluate the effectiveness of healthcare professional (HCP) educational materials, in particular the HCP brochure aiming at facilitating early recognition and intervention of the following important immune-related risks: pneumonitis, hepatitis, colitis, hypothyroidism, hyperthyroidism, adrenal insufficiency, hypophysitis, type 1 diabetes mellitus (T1DM), neuropathies, meningoencephalitis, pancreatitis, and infusion-related reactions [submission of the final clinical study report (CSR): December 2022]] as per the request for supplementary information (RSI) adopted in May 2018

Action: For adoption of advice to CHMP

7.2.3. Cobimetinib - COTELLIC (CAP) - EMEA/H/C/003960/MEA 003.3

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 003.2 [protocol for study ML39302 (COVENIS) (listed as a category 3 study in the RMP): a non-interventional study to investigate the effectiveness, safety and utilisation of cobimetinib and vemurafenib in patients with and without brain metastases with BRAF V600 mutant melanoma under real world conditions (final clinical study report (CSR) due date: December 2022)] as per the request for supplementary information (RSI) adopted in July 2018

Action: For adoption of advice to CHMP

[26] 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

7.2.4. Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/MEA 047.1

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 047 [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) in the European Union] as per the request for supplementary information (RSI) adopted in June 2018

Action: For adoption of advice to CHMP

7.2.5. Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/MEA 004

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Protocol for study CSIMM000265: a retrospective cohort study using health administrative claims databases to assess adverse pregnancy and infant outcomes in women with psoriasis who were exposed to guselkumab versus other biologic therapies during pregnancy

Action: For adoption of advice to CHMP

7.2.6. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 007.2

Applicant: Samsung Bioepis UK Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 007.1 [protocol for study SB2-G42-CD: a prospective observational cohort study in Crohn's disease (CD) for two years to observe safety, efficacy and immunogenicity of Flixabi (infliximab) with active comparator in CD] as per the request for supplementary information (RSI) adopted in May 2018

Action: For adoption of advice to CHMP

7.2.7. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/MEA 036.1

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 036 [protocol for the extension of the Dutch melanoma treatment registry (DMTR) to include paediatric subjects and collect safety data to obtain additional safety information in paediatric patients [final clinical study report (CSR) expected in December 2028]] as per the request for supplementary information (RSI) adopted in June 2018

Action: For adoption of advice to CHMP

7.2.8. Lipegfilgrastim - LONQUEX (CAP) - EMEA/H/C/002556/MEA 004.6

Applicant: Sicor Biotech UAB

PRAC Rapporteur: Patrick Batty

Scope: Updated protocol for study XM22-ONC-50002: a multi-country, multicentre, retrospective observational drug utilisation study (DUS) to describe the pattern of lipegfilgrastim use and specifically to quantify the extent of lipegfilgrastim off-label use in routine clinical practice in several countries in the European Union (EU) as requested in the outcome of MEA 004.5 adopted in June 2018

Action: For adoption of advice to CHMP

7.2.9. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/MEA 041.5

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Amended protocol for study WA29358 (paediatric registry) previously agreed in September 2015: an observational safety and effectiveness study of patients with polyarticular juvenile idiopathic arthritis treated with tocilizumab

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[27]

7.3.1. Valproate (NAP) - EMEA/H/N/PSI/J/0003

Applicant: Sanofi-aventis Recherche & Development (on behalf of a consortium)

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Third interim result report for a joint drug utilisation study (DUS) of valproate and related substances conducted in Europe aiming at describing the prescribing practices before and after the dissemination of risk minimisation measures (RMM) (i.e. educational materials and direct healthcare professional communication (DHPC)) and assessing the effectiveness of these measures using databases, as requested in the outcome of the referral procedure on valproate and related substances (EMEA/H/A-31/1387) concluded in 2014

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

7.4. Results of PASS non-imposed in the marketing authorisation(s)[28]

7.4.1. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/II/0173

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study BSRBR-RA (British Society for Rheumatology Biologics Registers Rheumatoid Arthritis): a registry in the UK, evaluating the influence of tumour necrosis factor (TNF) inhibitor treatment on cancer incidence in rheumatoid arthritis (RA) patients with a history of malignancy. No changes to the product information are proposed

Action: For adoption of PRAC Assessment Report

[27] In accordance with Article 107p-q of Directive 2001/83/EC
[28] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

7.4.2. Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/II/0050/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from studies (listed as category 3 studies in the RMP), namely: 1) study IM103074: an observational study designed to assess the pattern of use of belatacept in US transplant recipients in routine clinical practice; 2) study IM103077: an observational study designed to assess the patterns of use of belatacept in renal transplantation using the collaborative transplant study. The RMP is updated accordingly (version 16.0). In addition, the MAH took the opportunity to update the RMP in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template) and also to reflect minor editorial changes and the earlier completion dates for two remaining studies (listed as category 3 studies in the RMP): study IM103075: a study to assess the association between the use of belatacept and the risk of post-transplant lymphoproliferative disease (PTLD) in US renal transplant recipients; and study IM103076: evaluation of Nulojix (belatacept) long term safety in transplant (ENLiST) registry in order to estimate the incidence rates (IRs) of confirmed PTLD and central nervous system (CNS) PTLD in adult renal transplant recipients treated with belatacept in the US

Action: For adoption of PRAC Assessment Report

7.4.3. Colistimethate sodium - COLOBREATHE (CAP) - EMEA/H/C/001225/II/0039

Applicant: Teva B.V.

PRAC Rapporteur: Julie Williams

Scope: Submission of the final report from study CLB-MD-08 (listed as a category 3 study in the RMP): a non-interventional PASS cross-sectional survey study to evaluate the effectiveness of Colobreathe (colistimethate sodium) risk minimisation educational programme among healthcare professionals and patients. This submission also fulfils MEA 012.1

Action: For adoption of PRAC Assessment Report

7.4.4. Trastuzumab - HERCEPTIN (CAP) - EMEA/H/C/000278/II/0147

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report from the pregnancy registry H4621g study (MotHER) (listed as a category 3 study in the RMP): an observational study of pregnancy and pregnancy outcome in women with breast cancer treated with trastuzumab, pertuzumab in combination with trastuzumab, or ado-trastuzumab emtansine during pregnancy or within 7 months prior to conception. The RMP is updated accordingly (version 20.0) and in line with the outcome of variation EMEA/H/C/000278/II/140 finalised in March 2018

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. Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/MEA 024.1

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim report for study BMS IM103-075: a retrospective analysis of data from the United Network for Organ Sharing (UNOS) to assess the association between Nulojix (belatacept) use and risk of post-transplant lymphoproliferative disorder (PTLD) in renal transplant recipients in the US

Action: For adoption of advice to CHMP

7.5.2. Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/MEA 025.1

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim study reports / IM103-076 Prospective ENLiST Registry Study

Interim report for study BMS IM103076: a prospective registry study evaluating Nulojix (belatacept) long-term safety in transplant (ENLIST) to describe the pattern of Nulojix (belatacept) use at the time of transplant

Action: For adoption of advice to CHMP

7.5.3. Colistimethate sodium - COLOBREATHE (CAP) - EMEA/H/C/001225/MEA 013.1

Applicant: Teva B.V.

PRAC Rapporteur: Julie Williams

Scope: Seventh interim report for study CLB-MD-05: an open-label observational safety study of Colobreathe (colistimethate sodium dry powder for inhalation) compared with other inhaled antipseudomonal antibiotics in cystic fibrosis patients using cystic fibrosis registries

Action: For adoption of advice to CHMP

7.5.4. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/MEA 025

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Patrick Batty

Scope: Year 4 interim report for study 3038-1: FDA annual post-marketing long-term safety update (from variation II/40/G finalised in March 2018) to characterize the safety of long-term exposure to ibrutinib based on data and pooled analyses from trials of patients with mantle cell lymphoma and chronic lymphocytic leukaemia

Action: For adoption of advice to CHMP

7.5.5. Imiglucerase - CEREZYME (CAP) - EMEA/H/C/000157/MEA 040.10

Applicant: Genzyme Europe BV

PRAC Rapporteur: Menno van der Elst

Scope: Eighth report from the Gaucher pregnancy and lactation sub-registry to assess the pregnancy outcomes including adverse events in women with Gaucher disease, untreated and treated with Cerezyme during pregnancy. This report covers the period from 02 May 2015 to 04 May 2018

Action: For adoption of advice to CHMP

7.5.6. Mixture of polynuclear iron(III)-oxyhydroxide, sucrose and starches - VELPHORO (CAP) - EMEA/H/C/002705/MEA 002.8

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Julie Williams

Scope: Second interim report (24 months) for study VFMCRP-MEAF-PA21-01-EU (VERIFIE: Velphoro Evaluation of Real-lIfe saFety, effectIveness and adherencE): a non-interventional study to investigate the short- and long-term real-life safety, effectiveness, and adherence of Velphoro (mixture of polynuclear iron(III)-oxyhydroxide, sucrose and starches) in patients with hyperphosphataemia undergoing haemodialysis or peritoneal dialysis (PD)

Action: For adoption of advice to CHMP

7.5.7. Roflumilast - DAXAS (CAP) - EMEA/H/C/001179/ANX 002.7

Applicant: AstraZeneca AB

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to ANX 002.5 and ANX 002.6 [first and second interim results for PASS D7120R00003 (previously RO-2455-403-RD): a long-term post-marketing observational study exploring the safety of roflumilast in the treatment of chronic obstructive pulmonary disease (COPD), combined data results from Sweden, Germany and the US (Annex II-D condition) [final clinical study report (CSR) expected in March 2021]] as per the request for supplementary information (RSI) adopted at the September 2018 PRAC meeting

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 006.10

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Martin Huber

Scope: Bi-annual status report for study DNE3001 (CREDENCE): a randomised, double-blind, event-driven, placebo-controlled, multicentre study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with type 2 diabetes mellitus and diabetic nephropathy) from the Independent Data Monitoring Committee (IDMC) (eighth IDMC report dated July 2018)

Action: For adoption of advice to CHMP

7.6.2. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 005.10

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Bi-annual status report for study DNE3001 (CREDENCE): a randomised, double-blind, event-driven, placebo-controlled, multicentre study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with type 2 diabetes mellitus and diabetic nephropathy) from the Independent Data Monitoring Committee (IDMC) (eighth IDMC report dated July 2018)

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

Disclosure of 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. Cerliponase alfa - BRINEURA (CAP) - EMEA/H/C/004065/S/0009 (without RMP)

Applicant: BioMarin International Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Galsulfase - NAGLAZYME (CAP) - EMEA/H/C/000640/S/0073 (without RMP)

Applicant: BioMarin International Limited

PRAC Rapporteur: Patrick Batty

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/S/0032 (without RMP)

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Modified vaccinia Ankara virus - IMVANEX (CAP) - EMEA/H/C/002596/S/0037 (without RMP)

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Julie Williams

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.5. Nelarabine - ATRIANCE (CAP) - EMEA/H/C/000752/S/0044 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

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. Bedaquiline - SIRTURO (CAP) - EMEA/H/C/002614/R/0031 (without RMP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/R/0002 (without RMP)

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Cabozantinib - COMETRIQ (CAP) - EMEA/H/C/002640/R/0029 (without RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.4. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - EMEA/H/C/002450/R/0021 (with RMP)

Applicant: Chiesi Farmaceutici S.p.A., ATMP[29]

PRAC Rapporteur: Julie Williams

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.2.5. Vandetanib - CAPRELSA (CAP) - EMEA/H/C/002315/R/0032 (without RMP)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Capsaicin - QUTENZA (CAP) - EMEA/H/C/000909/R/0047 (with RMP)

Applicant: Grunenthal 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. Indacaterol, glycopyrronium - ULUNAR BREEZHALER (CAP) - EMEA/H/C/003875/R/0028 (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

8.3.3. Propranolol - HEMANGIOL (CAP) - EMEA/H/C/002621/R/0018 (without RMP)

Applicant: Pierre Fabre Dermatologie

PRAC Rapporteur: Eva Segovia

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Riociguat - ADEMPAS (CAP) - EMEA/H/C/002737/R/0026 (without RMP)

Applicant: Bayer AG

[29] Advanced therapy medicinal product

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Sevelamer carbonate - RENVELA (CAP) - EMEA/H/C/000993/R/0046 (without RMP)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Laurence de Fays

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Umeclidinium, vilanterol - ANORO ELLIPTA (CAP) - EMEA/H/C/002751/R/0022 (without RMP)

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Umeclidinium, vilanterol - LAVENTAIR ELLIPTA (CAP) - EMEA/H/C/003754/R/0025 (without RMP)

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Umeclidinium bromide - INCRUSE ELLIPTA (CAP) - EMEA/H/C/002809/R/0021 (with RMP)

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

Disclosure of information on results of pharmacovigilance inspections could undermine the

protection of the purpose of these inspections, investigations and audits. Therefore such information is not reported in the agenda.

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

11.2.1. Roflumilast - DE/H/5807/001/DC, DE/H/5808/001/DC, DE/H/5811/001/DC, DE/H/5805/001/DC, DE/H/5806/001/DC

PRAC Lead: Martin Huber

Scope: PRAC consultation on the evaluation of initial marketing authorisation application(s) under the decentralised procedure for generic roflumilast-containing medicinal products on request of Germany

Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC working group - Best practice guide – recommendations on efficiency of plenary meetings - implementation

PRAC lead: Martin Huber, Ulla Wändel Liminga, Menno van der Elst, Tatiana Magálová, Ghania Chamouni, Albert van der Zeijden, Jan Neuhauser

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Heads of Medicines Agencies (HMA)-EMA joint big data taskforce

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. PRAC work plan 2019 – preparation

PRAC lead: Sabine Straus, Martin Huber

Action: For discussion

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system – quarterly workload measures and performance indicators – Q3 2018 and predictions

Action: For discussion

12.8.2. PRAC workload statistics – Q3 2018

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits - Working Group of Quality Managers (WGQM) - report to PRAC

PRAC lead: Jan Neuhauser

Action: For discussion

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 monitoring

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 plan (RMP) template for industry - revision

Action: For adoption

12.14.2. Risk management systems

None

12.14.3. 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 work plan status update

Action: For discussion

13. Any other business

Next meeting on: 26-29 November 2018

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/