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Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 13-16 May 2019

Chair: Sabine Straus – Vice-Chair: Martin Huber

13 May 2019, 13:00 – 19:30, room 1/C

14 May 2019, 08:30 – 19:30, room 1/C

15 May 2019, 08:30 – 19:30, room 1/C

16 May 2019, 08:30 – 16:00, room 1/C

Organisational, regulatory and methodological matters (ORGAM)

29 May 2019, 09:00 – 12:00, room 6/D, 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 ongoing 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 13-16 May 2019. See May 2019 PRAC minutes (to be published post June 2019 PRAC meeting).

1.2. Agenda of the meeting on 13-16 May 2019

Action: For adoption

1.3. Minutes of the previous meeting on 08-11 April 2019

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

2.3.1. Fenspiride (NAP) - EMEA/H/A-107i/1480

Applicant(s): various

PRAC Rapporteur: Julia Pallos; PRAC Co-rapporteur: Adrien Inoubli

Scope: Review of the benefit-risk balance following notification by France of a referral under Article 107i of Directive 2001/83/EC, based on pharmacovigilance data

Action: For adoption of a recommendation to CMDh

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

3.2.1. Methotrexate - JYLAMVO (CAP), NORDIMET (CAP); NAP - EMEA/H/A-31/1463

Applicants: Nordic Group B.V. (Nordimet), Therakind Limited (Jylamvo), various

PRAC Rapporteur: Martin Huber; PRAC Co-rapporteur: Željana Margan Koletić

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

Action: For adoption of a list of outstanding issues (LoOI)

3.3. Procedures for finalisation

None

3.4. Re-examination procedures¹

None

3.5. Others

None

4. Signals assessment and prioritisation²

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Direct-acting antivirals (DAAV): daclatasvir – DAKLINZA (CAP); dasabuvir – EXVIERA (CAP); elbasvir, grazoprevir – ZEPATIER (CAP); glecaprevir, pibrentasvir – MAVIRET (CAP); ledipasvir, sofosbuvir – HARVONI (CAP); ombitasvir, paritaprevir, ritonavir – VIEKIRAX (CAP); sofosbuvir – SOVALDI (CAP); sofosbuvir, velpatasvir – EPCLUSA (CAP); sofosbuvir, velpatasvir, voxilaprevir – VOSEVI (CAP)

Applicant(s): AbbVie Deutschland GmbH & Co. KG (Exviera, Maviret, Viekirax); Bristol-Myers Squibb Pharma (Daklinza); Gilead Sciences Ireland UC (Eplusa, Harvoni, Sovaldi, Vosevi); Merck Sharp & Dohme B.V. (Zepatier)

PRAC Rapporteur: To be appointed

Scope: Signal of autoimmune hepatitis

Action: For adoption of PRAC recommendation

EPITT 19395 – New signal

Lead Member State(s): ES, PT, UK

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

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

4.1.2. Febuxostat – ADENURIC (CAP); FEBUXOSTAT MYLAN (CAP); NAP

Applicant(s): Menarini International (Adenuric); Mylan S.A.S. (Febuxostat Mylan), various

PRAC Rapporteur: To be appointed

Scope: Signal of gynaecomastia

Action: For adoption of PRAC recommendation

EPITT 19412 – New signal

Lead Member State(s): AT

4.1.3. Ferric carboxymaltose (NAP); iron (NAP); iron dextran (NAP); iron (III) isomaltoside (NAP); iron sucrose (NAP); sodium ferric gluconate (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of arteriospasm coronary

Action: For adoption of PRAC recommendation

EPITT 19408 – New signal

Lead Member State(s): LV, UK

4.1.4. Ibuprofen (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)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of acute generalised exanthematous pustulosis (AGEP)

Action: For adoption of PRAC recommendation

EPITT 19409 – New signal

Lead Member State(s): DK, FR, PL

4.1.5. Mesalazine (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of nephrolithiasis

Action: For adoption of PRAC recommendation

EPITT 19405 – New signal

Lead Member State(s): DE

4.1.6. Sebelipase alfa – KANUMA (CAP)

Applicant(s): Alexion Europe SAS

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of nephrotic syndrome

Action: For adoption of PRAC recommendation

EPITT 19410 – New signal

Lead Member State(s): SE

4.1.7. Tigecycline – TYGACIL (CAP); NAP

Applicant(s): Pfizer Europe MA EEIG, various

PRAC Rapporteur: To be appointed

Scope: Signal of bradycardia

Action: For adoption of PRAC recommendation

EPITT 19394 – New signal

Lead Member State(s): ES

4.2. New signals detected from other sources

4.2.1. 5 alfa-reductase inhibitors (5ARIs): finasteride (NAP); dutasteride (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of type 2 diabetes mellitus (T2DM)

Action: For adoption of PRAC recommendation

EPITT 19424 – New signal

Lead Member State(s): HU, SE

4.2.2. Amino acid, lipid combinations with vitamins or trace elements^{3 4} (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of adverse outcomes in neonates treated with solutions not protected from light

Action: For adoption of PRAC recommendation

EPITT 19423 – New signal

Lead Member State(s): SE

³ For parenteral nutrition of neonates only

⁴ Including amino acid combinations, glucose, triglyceride combinations (e.g. olive oil, soya bean oil, fish oil), with or without electrolytes, mineral compounds (intravenous (I.V) application)

- 4.2.3. Ibuprofen (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): various

PRAC Rapporteur: To be appointed

Scope: Signal of serious exacerbation of infections

Action: For adoption of PRAC recommendation

EPITT 19415 – New signal

Lead Member State(s): DK, FR, IT, PL, SE

4.2.4. Lithium (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of drug induced lichenoid reaction

Action: For adoption of PRAC recommendation

EPITT 19389 – New signal

Lead Member State(s): DE

4.3. Signals follow-up and prioritisation

- 4.3.1. Clomipramine (NAP); Serotonin and noradrenaline reuptake inhibitors (SNRI)⁵: desvenlafaxine (NAP); duloxetine - CYMBALTA (CAP) - EMEA/H/C/000572/SDA/049, DULOXETINE LILLY (CAP) - EMEA/H/C/004000/SDA/005, DULOXETINE MYLAN (CAP), DULOXETINE ZENTIVA (CAP), XERISTAR (CAP) - EMEA/H/C/000573/SDA/050, YENTREVE (CAP) - EMEA/H/C/000545/SDA/045; milnacipran (NAP); venlafaxine (NAP); Selective serotonin reuptake inhibitors (SSRI)⁶: citalopram (NAP); escitalopram (NAP); fluoxetine (NAP); fluvoxamine (NAP); paroxetine (NAP); sertraline (NAP); Vortioxetine – BRINTELLIX (CAP) - EMEA/H/C/002717/SDA/006
-

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

EPITT 19277 – Follow-up to November 2018

Action: For adoption of PRAC recommendation

⁵ Indicated in the treatment of major depressive disorder (MDD)

⁶ Indicated in the treatment of major depressive disorder (MDD)

- 4.3.2. Clopidogrel – CLOPIDOGREL APOTEX (CAP), CLOPIDOGREL BGR (CAP), CLOPIDOGREL HCS (CAP), CLOPIDOGREL KRKA (CAP), CLOPIDOGREL KRKA D.D. (CAP), CLOPIDOGREL MYLAN (CAP), CLOPIDOGREL RATIOPHARM (CAP), CLOPIDOGREL RATIOPHARM GMBH (CAP), CLOPIDOGREL TAD (CAP), CLOPIDOGREL TEVA (CAP), CLOPIDOGREL ZENTIVA (CAP), GREPID (CAP), ISCOVER (CAP), PLAVIX (CAP) - EMEA/H/C/000174/SDA/034, ZYLLT (CAP); NAP; clopidogrel/acetylsalicylic acid – CLOPIDOGREL/ACETYLSALICYLIC ACID ZENTIVA (CAP), DUOPLAVIN (CAP); NAP
Lopinavir, ritonavir – KALETRA (CAP), LOPINAVIR/RITONAVIR MYLAN (CAP), NAP; ritonavir – NORVIR (CAP), RITONAVIR (CAP); NAP
-

Applicant(s): AbbVie Deutschland GmbH & Co. KG (Kaletra, Norvir), Apotex Europe BV (Clopidogrel Apotex), Archie Samuel s.r.o. (Clopidogrel Ratiopharm GmbH), HCS bvba (Clopidogrel HCS), Krka, d.d., Novo mesto (Clopidogrel Krka, Clopidogrel Krka d.d., Zyllt), Laboratoires Biogaran (Clopidogrel BGR), Mylan S.A.S (Clopidogrel Mylan, Lopinavir/Ritonavir Mylan, Ritonavir Mylan), Pharmathen S.A. (Grepid), Sanofi-aventis groupe (Clopidogrel/Acetylsalicylic acid Zentiva, Iscover), Sanofi Clir SNC (Duoplavin, Plavix), TAD Pharma GmbH (Clopidogrel TAD), Teva B.V. (Clopidogrel Ratiopharm, Clopidogrel Teva), Zentiva k.s. (Clopidogrel Zentiva), various

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Signal of interaction with ritonavir boosted antiviral human immunodeficiency virus (HIV) therapy leading to insufficient inhibition of platelet aggregation

EPITT 19325 – Follow-up to December 2018

Action: For adoption of PRAC recommendation

- 4.3.3. Pantoprazole – CONTROLOC CONTROL (CAP) - EMEA/H/C/001097/SDA/017, PANTOLOLOC CONTROL (CAP) - EMEA/H/C/001100/SDA/016, PANTOZOL CONTROL (CAP) - EMEA/H/C/001013/SDA/017, SOMAC CONTROL (CAP) - EMEA/H/C/001098/SDA/022; NAP
-

Applicant(s): Takeda GmbH (Controloc Control, Pantoloc Control, Pantozol Control, Somac Control), various

PRAC Rapporteur: Rugile Pilviniene

Scope: Signal of colitis microscopic

EPITT 19342 – Follow-up to January 2019

Action: For adoption of PRAC recommendation

- 4.3.4. Sertraline (NAP)
-

Applicant(s): various

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Signal of maculopathy

EPITT 19341 – Follow-up to January 2019

Action: For adoption of PRAC recommendation

4.3.5. Tocilizumab – ROACTEMRA (CAP) - EMEA/H/C/000955/SDA/054.1

Applicant(s): Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of facial paralysis

EPITT 19295 – Follow-up to February 2019

Action: For adoption of PRAC recommendation

4.3.6. Tofacitinib - XELJANZ (CAP)

Applicant(s): Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Signal of increased risk of pulmonary embolism and overall mortality arising from a post-authorisation safety study in patients with cardiovascular risk factors treated for rheumatoid arthritis with tofacitinib 10 mg twice daily

EPITT 19382 – Follow-up to March 2019

Action: For adoption of PRAC recommendation

4.3.7. Vascular endothelial growth factor (VEGF) inhibitors: afibercept – EYLEA (CAP), ZALTRAP (CAP); axitinib – INLYTA (CAP); bevacizumab – AVASTIN (CAP), MVASI (CAP); cabozantinib – CABOMETYX (CAP), COMETRIQ (CAP); lenvatinib - KISPLYX (CAP), LENVIMA (CAP); nintedanib – OFEV (CAP), VARGATEF (CAP); pazopanib – VOTRIENT (CAP); pegaptanib – MACUGEN (CAP); ponatinib – ICLUSIG (CAP); ramucirumab – CYRAMZA (CAP); ranibizumab – LUCENTIS (CAP); regorafenib – STIVARGA (CAP); sorafenib – NEXAVAR (CAP), NAP; sunitinib – SUTENT (CAP); NAP; tivozanib – FOTIVDA (CAP); vandetanib – CAPRELSA (CAP)

Applicant(s): Amgen Europe B.V. (Mvasi), Bayer AG (Eylea, Nexavar, Stivarga), Boehringer Ingelheim (Ofev, Vargatef), Eisai Europe Ltd. (Kispilyx, Lenvima), Eli Lilly Nederland B.V. (Cyramza), EUSA Pharma (UK) Limited (Fotivda), Genzyme Europe BV (Caprelsa), Incyte Biosciences Distribution (Iclusig), Ipsen Pharma (Cabometyx, Cometriq), Novartis Europharm Limited (Lucentis, Votrient), Pfizer Europe MA EEIG (Inlyta, Sutent), PharmaSwiss Ceska Republika (Macugen), Roche Registration GmbH (Avastin), Sanofi-aventis groupe (Zaltrap), various

PRAC Rapporteur: Annika Folin

Scope: Signal of artery dissections and aneurysms

Action: For adoption of PRAC recommendation

EPITT 19330 – Follow-up to December 2018

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Dapagliflozin, saxagliptin, metformin hydrochloride - EMEA/H/C/004910

Scope: Treatment in adults aged 18 years and older with type 2 diabetes mellitus (T2DM) to improve glycaemic control in patients who require $\geq 1.5\%$ reduction in HbA1c to reach glycaemic target, where metformin with or without sulphonylurea (SU) does not provide adequate glycaemic control, improve glycaemic control when metformin with or without sulphonylurea (SU) and either saxagliptin or dapagliflozin does not provide adequate glycaemic control when already being treated with saxagliptin and dapagliflozin and metformin

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

5.1.2. Deferasirox - EMEA/H/C/005014

Scope: Treatment of chronic iron overload

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

5.1.3. Delafloxacin - EMEA/H/C/004860

Scope: Treatment of acute bacterial skin and skin structure infection (ABSSSI) in adults

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

5.1.4. Erlotinib - EMEA/H/C/005071

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

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

5.1.5. Etanercept - EMEA/H/C/004711

Scope: Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, axial spondyloarthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, plaque psoriasis and paediatric plaque psoriasis

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

5.1.6. Gilteritinib - EMEA/H/C/004752, Orphan

Applicant: Astellas Pharma Europe B.V.

Scope (accelerated assessment): Treatment of patients who have relapsed or refractory acute myeloid leukaemia (AML) with a FMS-like tyrosine kinase 3 (FLT3) mutation

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

5.1.7. Levodopa - EMEA/H/C/004786

Scope: Treatment of symptoms of 'off' periods in Parkinson's disease

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

5.1.8. Romosozumab - EMEA/H/C/004465

Scope: Treatment of osteoporosis

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

5.1.9. Siponimod - EMEA/H/C/004712

Scope: Treatment of secondary progressive multiple sclerosis (SPMS)

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

5.1.10. Tigecycline - EMEA/H/C/005114

Scope: Treatment of complicated skin and soft tissue infections (cSSTI) excluding diabetic foot infections, complicated intra-abdominal infections (cIAI)

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. Aliskiren - RASILEZ (CAP) - EMEA/H/C/000780/WS1581/0123; Aliskiren, hydrochlorothiazide - RASILEZ HCT (CAP) - EMEA/H/C/000964/WS1581/0093

Applicant: Noden Pharma DAC

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of an updated RMP (version 14) in order to reflect changes in the categorisation of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' and in line with revision 2 of the guidance on the format of RMP in the EU (template). The update also includes the addition of the new important potential risk of non-melanoma skin cancer (related to Rasilez HCT (aliskiren/hydrochlorothiazide) only) as per the final recommendation of the signal on hydrochlorothiazide-containing products and skin cancer (EPITT 19138) adopted in September 2018

Action: For adoption of PRAC Assessment Report

5.2.2. Darvadstrocel - ALOFISEL (CAP) - EMEA/H/C/004258/II/0006, Orphan

Applicant: Takeda Pharma A/S, ATMP⁷

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 7) in order to propose the replacement of the existing observational PASS (listed as category 3 study: 'a study to evaluate the long term safety of Alofisel (darvadstrocel (Cx601)) in patients treated and retreated (i.e. repeated dosing and immunogenicity) and to assess the effectiveness of Alofisel (darvadstrocel) in patients treated and retreated (i.e. repeated dosing) in routine clinical practice (for treatment of complex perianal fistulas in adult patients with non-active/mildly active luminal Crohn's disease, when fistulas have shown an inadequate response to at least

⁷ Advanced therapy medicinal product

one conventional or biologic therapy)' with two separate studies: 1) a long-term safety extension of the ADMIRE-CD II study: a phase 3 randomized, double-blind, parallel-group, placebo-controlled, multicentre study to assess efficacy and safety of darvadstrocel (Cx601), allogeneic expanded adipose-derived stem cells for complex perianal fistula(s) in Crohn's disease; and 2) a retreatment PASS. The European multi-database linkage study is added for the assessment of the potential risk of tumourgenicity

Action: For adoption of PRAC Assessment Report

5.2.3. [Filgrastim - FILGRASTIM HEXAL \(CAP\) - EMEA/H/C/000918/WS1608/0049; ZARZIO \(CAP\) - EMEA/H/C/000917/WS1608/0050](#)

Applicant: Sandoz GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 12.0) in order to align the due dates and deliverables for post-authorisation measure MEA 007 relating to study EP06-501: a non-interventional, prospective, long-term safety data collection of Zarzio/Filgrastim Hexal (filgrastim) in healthy unrelated stem cell donors undergoing peripheral blood progenitor cell mobilisation. The due date is extended from December 2019 to March 2020, to combine the annual safety report (ASR) with the 5-year interim clinical study report (CSR) in 2020 and the final CSR in 2024 and for the MEA to cover the entire duration of study EP06-501

Action: For adoption of PRAC Assessment Report

5.2.4. [Human papillomavirus vaccine \[types 6, 11, 16, 18\] \(recombinant, adsorbed\) - GARDASIL \(CAP\) - EMEA/H/C/000703/II/0081](#)

Applicant: MSD Vaccins

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 13.1) in order to update the list of safety concerns by removing all remaining important identified and potential risks and missing information 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

5.2.5. [Icatibant - FIRAZYR \(CAP\) - EMEA/H/C/000899/II/0047, Orphan](#)

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 7.0) to reflect the completion of paediatric study HGT-FIR-086: a multicentre, open-label, non-randomized study to assess the pharmacokinetics, tolerability, and safety of a single subcutaneous administration of icatibant in children and adolescents with hereditary angioedema, to update the list of safety concerns accordingly and to remove the study as an additional pharmacovigilance activity. In addition, the RMP is updated in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.6. Measles, mumps, rubella and varicella vaccine (live) - PROQUAD (CAP) - EMEA/H/C/000622/II/0134

Applicant: MSD Vaccins

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 6.1) in order to reflect changes in the categorisation of safety concerns in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.7. Octocog alfa - KOVALTRY (CAP) - EMEA/H/C/003825/II/0022

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of the RMP (version 2.0) in line with revision 2 of GVP module V on 'Risk management systems' and in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.8. Pazopanib - VOTRIENT (CAP) - EMEA/H/C/001141/II/0054

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated RMP (version 17.0) in order to postpone the submission due date for the clinical study report (CSR) for study VEG108844 (COMPARZ): a study of pazopanib versus sunitinib in the treatment of subjects with locally advanced and/or metastatic renal cell carcinoma, and its sub-studies. In addition, the RMP is updated to reflect PRAC recommendations for additional assessments of some risks and to revise the categorisation of the safety concerns in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.9. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0068

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP (version 23.1) in order to discuss the effectiveness of the educational materials put in place for Keytruda (pembrolizumab) at the time of the initial marketing authorisation, to provide a proposal to update these materials and to revise the safety specification as requested in the outcome of the PSUR single assessment procedure (PSUSA/00010403/201803) finalised in October 2018

Action: For adoption of PRAC Assessment Report

5.2.10. Pregabalin - PREGABALIN MYLAN (CAP) - EMEA/H/C/004078/WS1603/0013;
PREGABALIN MYLAN PHARMA (CAP) - EMEA/H/C/003962/WS1603/0011

Applicant: Mylan S.A.S

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of an updated RMP (version 6) to get adjusted to the RMP of the originator medicinal product containing pregabalin. In addition, the RMP is updated in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.11. Sunitinib - SUTENT (CAP) - EMEA/H/C/000687/II/0073

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Amelia Cupelli

Scope: Update of the RMP (version 17.0) in order to reflect changes in the categorisation of safety concerns in line with revision 2 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.12. Umeclidinium, vilanterol - ANORO ELLIPTA (CAP) -
EMEA/H/C/002751/WS1586/0028; LAVENTAIR ELLIPTA (CAP) -
EMEA/H/C/003754/WS1586/0031

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of an updated RMP (version 8.0) following the completion of the annual renewal procedures (R/0022 and R/0025) in November 2018 concluding on the commitments to remove the important identified risks of 'hypersensitivity' and 'paradoxical bronchospasm' from the list of safety concerns and to update all relevant sections of 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). In addition, the MAH proposed to remove some additional risks ('narrow angle glaucoma', 'bladder outflow obstruction and urinary retention', 'safety in pregnancy and lactation', 'safety in long-term use' and 'safety in severe hepatic impairment')

Action: For adoption of PRAC Assessment Report

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

5.3.1. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0024

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Update of sections 4.2, 4.4, and 4.8 of the SmPC in order to add a warning regarding the risk of immune-related myositis identified during a comprehensive analysis of patients treated with Tecentriq (atezolizumab). Annex 2-D on 'conditions or restrictions with regard to the safe and effective use of the medicinal product' are also updated regarding

additional risk minimisation(s). Furthermore, a direct healthcare professional communication (DHPC) is proposed to inform healthcare professionals (HCPs) about the risk of immune-related myositis. The package leaflet and the RMP (version 11.0) are updated accordingly

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

5.3.2. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/X/0017

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension application to add a new strength of 840 mg (60 mg/mL) for Tecentriq (atezolizumab) concentrate for solution for infusion in a vial and to add a new indication for the treatment of metastatic triple-negative breast cancer (TNBC). The new indication applies only to the 840 mg strength. The RMP (version 7.0) is updated accordingly

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/0009/G, Orphan

Applicant: Merck Europe B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Grouped variations consisting of: 1) extension of indication to include a new indication as the first-line combination treatment with avelumab and axitinib in adult patients with advanced renal cell carcinoma (aRCC). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 1.7) are updated accordingly; 2) change in section 4.2 of the SmPC to support the switch of the avelumab dosing regimen from 10 mg/kg every two weeks (weight-based) to a flat dose of 800 mg every two weeks applicable to the new proposed indication aRCC and the existing one on Merkel cell carcinoma (MCC). The MAH took the opportunity to introduce some editorial changes in the product information

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/II/0033/G, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) extension of indication to include patients 12 years of age and older based on week 24 analysis of cohort 1 (adolescent subjects aged ≥ 12 to < 18 years) for study TMC207-TIDP59-C211: a phase 2, open-label, multicentre, single-arm study to evaluate the pharmacokinetics, safety, tolerability and anti-mycobacterial activity of bedaquiline (TMC207) in combination with a background regimen (BR) of multidrug resistant tuberculosis (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, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 3.2) are updated accordingly; 2) update of section 4.9 of the SmPC to remove reference to the use of activated charcoal as an aid to remove unabsorbed bedaquiline in case of overdose

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

5.3.5. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/II/0065

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add a warning on suicidality and depression based on interim results from study BEL115467 (listed in Annex II): a randomized, double-blind, placebo-controlled 52-week study to assess adverse events of special interest in adults with active, autoantibody-positive systemic lupus erythematosus receiving belimumab. The package leaflet and the RMP (version 30) are updated accordingly

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

5.3.6. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/II/0014/G

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Grouped variations consisting of: 1) addition of an auto-injector delivery device, Fasentra 30 mg solution for injection in pre-filled pen, 2) update of sections 4.2, 6.4, 6.5 and 6.6 of the SmPC in order to update the information for self-administration for Fasentra 30 mg solution for injection in pre-filled syringe. The labelling and the package leaflet are updated accordingly. In addition, the RMP (version 2.0) is updated to reflect the information about the new presentation, to include additional information on completed studies, namely: study ALIZE: 'a multicentre, randomized, double-blind, parallel group, placebo-controlled, phase 3b study to evaluate the potential effect of benralizumab on the humoral immune response to the seasonal influenza vaccination in adolescent and young adult patients with severe asthma'; study GREGALE: 'a multicentre, open-label, functionality, reliability, and performance study of an accessorized pre-filled syringe with home-administered subcutaneous benralizumab in adult patients with severe asthma'; study AMES: 'a multicentre, randomised, open-label, parallel group, phase 1 study designed to compare benralizumab pharmacokinetics exposure in healthy subjects following single subcutaneous administration of a fixed 30 mg dose of benralizumab when using an autoinjector and accessorised pre-filled syringe'; study GRECO: 'a multicentre, open-label, functionality, reliability and performance study of a single-use auto-injector with home-administered subcutaneous benralizumab in adult patients with severe asthma'. The RMP is also updated with exposure data post marketing authorisation (MA) approval, and additional details on the following post-authorisation safety studies: study D3250R00026 (pregnancy registry): benralizumab pregnancy exposure study: a Vaccines and Medications in Pregnancy Surveillance System (VAMPSS) post marketing surveillance study, and study D3250R00042 (malignancy PASS): 'a descriptive study of the incidence of malignancy in patients with severe asthma overall and among those receiving benralizumab and other biologic therapy'. Furthermore, the RMP is brought 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

5.3.7. [Bosutinib - BOSULIF \(CAP\) - EMEA/H/C/002373/II/0037](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.6 and 5.3 of the SmPC based on final results from study 17GR319 (00655202) (listed as a category 3 study in the RMP): an oral (gavage) study of the effects of bosulif (PF-05208763) on pre- and postnatal development, including maternal function in rats. The package leaflet and the RMP (version 4.5) are updated accordingly

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

5.3.8. [Ceftolozane, tazobactam - ZERBAXA \(CAP\) - EMEA/H/C/003772/II/0020](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of nosocomial pneumonia, including ventilator associated pneumonia for Zerbaxa (ceftolozane/tazobactam) based on results from study CXA-NP-11-04 (PN008): a prospective, randomised, double-blind, phase 3 study to assess the safety and efficacy of intravenous ceftolozane/tazobactam compared to meropenem in adult patients with ventilated nosocomial pneumonia. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 2.1) are updated accordingly. The MAH took the opportunity to implement editorial changes in sections 5.2 of the SmPC and to bring section 4.4 of the SmPC and section 2 of the package leaflet in line with the latest Annex to the European Union (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

5.3.9. [Ciclosporin - IKERVIS \(CAP\) - EMEA/H/C/002066/WS1490/0014; VERKAZIA \(CAP\) - EMEA/H/C/004411/WS1490/0001](#)

Applicant: Santen Oy

PRAC Rapporteur: Jan Neuhauser

Scope: Update of the RMP (version 7.0) in order to bring the RMP in line with revision 2 of the guidance on the format of RMP in the EU (template). The milestones for Verkazia (ciclosporin) PASS on 'quantification of the risk of periocular skin cancer, conjunctival or corneal neoplasia in children treated with Verkazia (ciclosporin) for vernal keratoconjunctivitis (VKC)' have also been updated. In addition, the MAH proposed to align Ikervis (ciclosporin) SmPC section 4.4 on concomitant therapy and effects on immune system with Verkazia (ciclosporin) SmPC in order to harmonise the routine risk minimisation measures for both medicinal products. The MAH took this opportunity to implement the latest quality review of documents (QRD) template and the safety features for Ikervis (ciclosporin)

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

5.3.10. Cinacalcet - MIMPARA (CAP) - EMEA/H/C/000570/II/0062/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) update of section 4.4 of the SmPC to provide additional information on switching from etelcalcetide to Mimpara (cinacalcet) as requested by PRAC in the conclusions of the PSUR single assessment procedure for etelcalcetide (PSUSA/00010533/201711) adopted in May 2018; 2) update of section 6.1 of the SmPC to replace the term 'silica, dental type' by 'amorphous silicon dioxide'. The RMP is updated (version 9.0) in order to reflect changes in the categorisation of safety concerns 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

5.3.11. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0027, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Update of sections 4.4 and 4.8 of the SmPC to add new safety information on the recently identified risk of 'hepatitis B reactivation (HBV)'. The package leaflet and the RMP (version 5) are updated accordingly. In addition, the MAH proposes a direct healthcare professional communication (DHPC) to inform prescribers on the newly identified risk

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

5.3.12. Darunavir, cobicistat, emtricitabine, tenofovir alafenamide - SYMTUZA (CAP) - EMEA/H/C/004391/II/0017/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Grouped variations consisting of an update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update the safety information based on week-96 results from two studies (listed as category 3 studies in the RMP): 1) study TMC114FD2HTX3001 (AMBER): a phase 3, randomized, active-controlled, double-blind study to evaluate efficacy and safety of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) once daily fixed-dose combination regimen versus a regimen consisting of darunavir/cobicistat fixed dose combination (DRV/COBI FDC) co-administered with emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) FDC in antiretroviral (ARV) treatment-naive human immunodeficiency virus type 1 (HIV-1) infected subjects, 2) study TMC114IFD3013 (EMERALD): a phase 3, randomized, active-controlled, open-label study to evaluate switching to a D/C/F/TAF once-daily single-tablet regimen versus continuing the current regimen consisting of a boosted protease inhibitor combined with FTC/TDF in virologically-suppressed HIV-1 infected subjects. The package leaflet is updated accordingly. The RMP (version 5.0) is also updated accordingly and brought 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 update section 4.2 of the SmPC and package leaflet to include advice in the event of vomiting in line with the approved SmPC for elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide-containing product. The MAH also introduced some minor editorial changes in the SmPC and updated the list of local representatives in the package leaflet in line with the latest quality review of documents

(QRD) template (version 10.0)

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

5.3.13. [Deferiprone - FERRIPROX \(CAP\) - EMEA/H/C/000236/II/0128](#)

Applicant: Apotex Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Update of section 4.4 of the SmPC and the patient/carer reminder card in order to update and change the recommended frequency of absolute neutrophil count (ANC) monitoring throughout Ferriprox (deferiprone) treatment from a weekly basis to every week for the first six months of therapy, once every two weeks after six months and to monthly after one year of therapy. The package leaflet and the RMP (version 13.2) are updated accordingly. In addition, the MAH took the opportunity to update minor linguistic amendments in the Hungarian and Maltese product information

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

5.3.14. [Fidaxomicin - DIFICLIR \(CAP\) - EMEA/H/C/002087/X/0034/G](#)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped application consisting of: 1) extension application to introduce a new pharmaceutical form associated with new strength (40 mg/mL granules for oral suspension); 2) extension of indication to include paediatric use of Dificlir (fidaxomicin) in children from birth to less than 18 years of age. The RMP (version 11.0) is updated accordingly. The SmPC of Dificlir (fidaxomicin) 200 mg film-coated tablet, labelling and package leaflet are updated accordingly. In addition, the MAH took the opportunity to update the package leaflet with the statement on 'sodium-free' in accordance with the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'. Furthermore, the MAH updated the details of the local representative in Czech Republic

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

5.3.15. [Fingolimod - GILENYA \(CAP\) - EMEA/H/C/002202/II/0053](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Update of sections 4.4, 4.6 and 4.8 of the SmPC to add a warning for women stopping treatment for the purpose of becoming pregnant and for pregnant women and to add information to prescribers on 'severe exacerbation of disease after Gilenya (fingolimod) discontinuation', timing of reported events and further recommendations on monitoring of patients. The package leaflet is updated accordingly

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

5.3.16. [Insulin human \(rDNA⁸\) - ACTRAPHANE \(CAP\) - EMEA/H/C/000427/WS1582/0076; ACTRAPID \(CAP\) - EMEA/H/C/000424/WS1582/0070; INSULATARD \(CAP\) - EMEA/H/C/000441/WS1582/0073; MIXTARD \(CAP\) EMEA/H/C/000428/WS1582/0077; PROTAPHANE \(CAP\) - EMEA/H/C/000442/WS1582/0072](#)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of an updated RMP (version 3.0) for insulin human-containing products to reclassify the risk of 'medication errors' from an important potential risk to an important identified risk as requested in the outcome of the PSUR single assessment procedure (PSUSA/00001753/201710) finalised in June 2018 and in line with the 'Good practice guide on risk minimisation and prevention of medication errors' dated 2015. In addition, the RMP is brought 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). As a consequence, the MAH proposed to remove this risk as it is fully characterised and managed through routine pharmacovigilance. Section 4.4 of the SmPC is updated in order to add a warning on accidental mix-ups/medication. The package leaflet is updated accordingly. Furthermore, the MAH took the opportunity to include minor updates to Annex III-A on 'labelling' and to bring the package leaflet in line with the latest quality review document (QRD) template (version 10.0)

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

5.3.17. [Interferon beta-1a - REBIF \(CAP\) - EMEA/H/C/000136/II/0137/G](#)

Applicant: Merck Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) update of sections 4.3, 4.6 and 5.3 of the SmPC in order to add information about pregnancy and update the statement regarding breast-feeding following the completion of the European interferon beta (IFN- β) pregnancy registry (eighth annual and final report) and the final clinical study report (CSR) of the register-based study in the Nordic countries EUPAS13054: multiple sclerosis pregnancy study - pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon beta - a register-based study in the Nordic countries; 2) update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles (fulfilment of MEA 43.2 and 39). The package leaflet is updated accordingly. The RMP (version 10.0) is updated accordingly, including the deletion of the important potential risk 'pregnancy outcomes'. The RMP is also updated to bring it 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

5.3.18. [Interferon beta-1b - BETAFERON \(CAP\) - EMEA/H/C/000081/II/0124/G](#)

Applicant: Bayer AG

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of sections 4.3 and 4.6 of the SmPC in

⁸ Recombinant deoxyribonucleic acid

order to add information on pregnancy and update the statement regarding breast-feeding following the completion of the European interferon beta (IFN- β) pregnancy registry (eighth annual and final report) and the final clinical study report (CSR) of the register-based study in the Nordic countries EUPAS13054: multiple sclerosis pregnancy study - pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon beta - a register-based study in the Nordic countries; 2) update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles (fulfilment of MEA 024.2 and 21). The package leaflet has been updated accordingly. The RMP (version 4.1) is updated accordingly, including the deletion of the important potential risk 'pregnancy outcomes'. The RMP is also updated to bring it 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

5.3.19. Interferon beta-1b - EXTAVIA (CAP) - EMEA/H/C/000933/II/0096/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of sections 4.3 and 4.6 of the SmPC in order to add information on pregnancy and update the statement regarding breast-feeding following the completion of the European interferon beta (IFN- β) pregnancy registry (eighth annual and final report) and the final clinical study report (CSR) of the register-based study in the Nordic countries EUPAS13054: multiple sclerosis pregnancy study - pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon beta - a register-based study in the Nordic countries; 2) update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles (fulfilment of MEA 022.2 and 019). The package leaflet is updated accordingly. The RMP (version 4.1) is updated accordingly, including the deletion of the important potential risk 'pregnancy outcomes'. The RMP is also updated to bring it 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

5.3.20. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/II/0107, Orphan

Applicant: Celgene Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Extension of indication to include Revlimid (lenalidomide) in combination with rituximab for the treatment of adult patients with previously treated follicular lymphoma or marginal zone lymphoma. 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 36.2) are updated accordingly

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

5.3.21. Letemovir - PREVYMIS (CAP) - EMEA/H/C/004536/II/0011, Orphan

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.4 and 4.5 of the SmPC in order to update the safety

information following the final results of clinical pharmacology trial MK-8228-038 (listed as a category 3 study in the RMP): a study to assess the effect of rifampin on the single-dose and steady-state pharmacokinetics of letermovir (MK-8228) in healthy adult subjects. The package leaflet and the RMP (version 2.1) are updated accordingly

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

5.3.22. Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/II/0021

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information based on the final results from study 200363 part B and two open label extension (OLE) studies namely study 201312 and study MEA115666 (listed as category 3 studies in the RMP). These are interventional PASS conducted to assess the long-term (52 weeks) safety and tolerability of mepolizumab when administered subcutaneously to patients aged 6 to 11 years old with severe eosinophilic asthma (study 200363 part B), to describe the long-term safety profile of mepolizumab (MEA115666), and to provide extended treatment to subjects from study MEA115661 and further describe long-term safety in these subjects (study 201312). The RMP (version 5.0) is updated accordingly and brought 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

5.3.23. Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/X/0018

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension application to introduce a new pharmaceutical form, solution for injection (in pre-filled syringe or in pre-filled pen). The RMP (version 4.0) is updated accordingly

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

5.3.24. Moroctocog alfa - REFACTO AF (CAP) - EMEA/H/C/000232/II/0151

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of sections 4.8 and 5.1 of the SmPC based on the final results from study 3082B2-313 (B1831001) (listed as a category 3 study in the RMP): an open-label study to evaluate prophylaxis treatment, and to characterize the efficacy, safety, and pharmacokinetics of b-domain deleted recombinant factor VIII albumin free (moroctocog alfa [AF_CC]) in children with haemophilia A (MEA 116). The RMP (version 13.0) is updated accordingly. In addition, the SmPC is brought in line with revision 3 of the 'Guideline on core SmPC for human plasma derived and recombinant coagulation factor VIII products' (EMA/CHMP/BPWP/1619/1999 rev. 3)

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

5.3.25. Nalotimagene carmaleucel - ZALMOXIS (CAP) - EMEA/H/C/002801/II/0016, Orphan

Applicant: MolMed S.p.A, ATMP⁹

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Proposal to terminate study TK008 (listed as a category 2 study, specific condition to the conditional marketing authorisation): a phase 3, randomised trial of haploidentical hematopoietic cell transplantation (HCT) with or without an add back strategy of human herpes simplex virus thymidine kinase type 1 gene (HSV-Tk) donor lymphocytes in patients with high risk acute leukaemia, and replace it with study TK013: a two-step study consisting in an initial feasibility study, followed by a single-arm trial with matched-pair controls from the European Society for Blood and Marrow Transplantation (EBMT) registry. The RMP (version 8.1) is updated accordingly

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

5.3.26. 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

5.3.27. Obinutuzumab - GAZYVARO (CAP) - EMEA/H/C/002799/II/0034, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Submission of the final results of the pivotal study BO21005/GOYA: a phase 3, multicentre, open-label randomized trial comparing the efficacy of obinutuzumab (GA101 (RO5072759)) in combination with cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) (G-CHOP) versus rituximab and CHOP (R-CHOP) in previously untreated patients with CD20-positive diffuse large B-cell lymphoma (DLBCL), to address the additional pharmacovigilance activities required in the EU RMP. The RMP (version 5.0) is

⁹ Advanced therapy medicinal product

updated accordingly

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

5.3.28. Panitumumab - VECTIBIX (CAP) - EMEA/H/C/000741/II/0093

Applicant: Amgen Europe B.V.

PRAC Rapporteur: David Olsen

Scope: Submission of an updated RMP (version 23) brought in line with revision 2 of GVP module V on 'Risk management systems'. In addition, the MAH proposed the removal of some additional risk minimisation measures (aRMM). As a result Annex II is updated. The MAH took the opportunity to update sections 4.2 and 4.4 of the SmPC to include the table on dose modification previously located in section 4.4. In addition, section 4.4 is updated to implement the statement on 'sodium' content in accordance with the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'. Furthermore, minor corrections are introduced in section 4.8 of the SmPC and in the list of the local representatives

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

5.3.29. Pegfilgrastim - PELGRAZ (CAP) - EMEA/H/C/003961/II/0005

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Menno van der Elst

Scope: Change in the immediate packaging of Pelgraz (pegfilgrastim) finished product solution for injection 6mg/0.6 mL to add an additional presentation as a solution for injection in pre-filled injector in addition to the existing approved solution for injection in Pre-filled syringe. The RMP (version 1.4) is updated accordingly

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

5.3.30. Peginterferon beta-1a - PLEGRIDY (CAP) - EMEA/H/C/002827/II/0052/G

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) update of sections 4.3 and 4.6 of the SmPC in order to add information on pregnancy and update the statement regarding breast-feeding following the completion of the European interferon beta (IFN- β) pregnancy registry (eighth annual and final report) and the final clinical study report (CSR) of the register-based study in the Nordic countries EUPAS13054: multiple sclerosis pregnancy study - pregnancy outcomes in multiple sclerosis populations exposed and unexposed to interferon beta - a register-based study in the Nordic countries; 2) update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles (fulfilment of MEA 8.2 and 002). The package leaflet has been updated accordingly. The RMP (version 4.1) is updated accordingly, including the deletion of the important potential risk 'pregnancy outcomes'. The RMP is also updated to bring it 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

5.3.31. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0072

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include a new indication for Keytruda (pembrolizumab) as monotherapy for the treatment of recurrent locally advanced or metastatic oesophageal cancer in adults whose tumours express programmed death-ligand 1 (PD-L1) with a combined positive score (CPS) ≥ 10 and who have received prior systemic therapy, based on the results from study KEYNOTE-181: an international, randomized, open-label phase 3 trial of pembrolizumab versus the investigator's choice of paclitaxel, docetaxel, or irinotecan in participants with advanced/metastatic adenocarcinoma or squamous cell carcinoma of the oesophagus, or advanced/metastatic Siewert type I adenocarcinoma of the oesophagogastric junction. As a consequence, sections 4.1, 4.2, and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 25.1) are updated accordingly

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

5.3.32. Propranolol - HEMANGIOL (CAP) - EMEA/H/C/002621/II/0019

Applicant: Pierre Fabre Dermatologie

PRAC Rapporteur: Eva Segovia

Scope: Submission of the results of a drug utilisation study (DUS) performed in Germany and France to evaluate off-label use and effectiveness of risk minimisation measures (RMM) in a real-life clinical setting (MEA 002). As a consequence, the package leaflet is updated to strengthen the warning on hypoglycaemia and bronchospasm. The RMP (version 3.1) is updated accordingly. In addition, the MAH took the opportunity to introduce some editorial changes in section 4.4 of the SmPC as well as changes in the package leaflet in accordance with the latest quality review document (QRD) template (version 10.0)

Action: For adoption of PRAC Assessment Report

5.3.33. Ranibizumab - LUCENTIS (CAP) - EMEA/H/C/000715/II/0074/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) extension of indication to include a new indication for the vial presentation 'treatment of retinopathy of prematurity (ROP) in preterm infants'. As a consequence, sections 2, 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet, labelling and the RMP (version 18.0) are updated accordingly; 2) introduction of a low volume high accuracy syringe, as a stand-alone medical device for the administration of the Lucentis (ranibizumab) 0.2 mg paediatric dose (corresponding to 0.02 mL of the Lucentis 10 mg/mL solution for injection in vial presentation)

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

5.3.34. Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0162

Applicant: Roche Registration GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Extension of indication to include the treatment of paediatric patients (aged ≥ 2 to <18 years old) with active polyangiitis (Wegener's) (GPA) and microscopic polyangiitis (MPA) for the 100 mg and 500 mg concentrate for solution based on efficacy and safety data from study WA25615: a phase 2A, international, multicentre, open-label, uncontrolled study to evaluate the safety and pharmacokinetics of 4×375 mg/m² intravenous rituximab in paediatric patients with severe granulomatosis with polyangiitis (Wegener's) or microscopic polyangiitis (PePRS). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC is updated. The package leaflet and the RMP (version 20.0) are updated accordingly. In addition, the product information is brought in line with the latest quality review document (QRD) template (version 10) and the opportunity is taken to combine the SmPC and package leaflet for the 100 mg and 500 mg concentrate for solution presentations. Furthermore, the MAH took the opportunity to implement minor editorial changes in the SmPC

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

5.3.35. Rituximab - RIXATHON (CAP) - EMEA/H/C/003903/WS1599/0020; RIXIMYO (CAP) - EMEA/H/C/004729/WS1599/0020

Applicant: Sandoz GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final report from study GP13-301 (listed as a category 3 study in the RMP): a randomized, controlled double-blind phase 3 trial to compare the efficacy, safety and pharmacokinetics of Rixathon/Riximyo (GP2013 – rituximab biosimilars) plus cyclophosphamide, vincristine, prednisone vs. MabThera (rituximab) plus cyclophosphamide, vincristine, prednisone, followed by Rixathon/Riximyo (GP2013 - rituximab biosimilars) or MabThera (rituximab) maintenance therapy in patients with previously untreated advanced stage follicular lymphoma. The RMP (version 4.0) is updated accordingly

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

5.3.36. Ruxolitinib - JAKAVI (CAP) - EMEA/H/C/002464/II/0040

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Update of section 5.3 of the SmPC in order to update the preclinical safety information based on the final results from juvenile toxicity studies 1570143 (dose range finding juvenile study) and 157014 (juvenile development study). The RMP (version 10) is updated accordingly. Furthermore, the RMP is updated to revise the safety specification as requested in the outcome of the PSUR single assessment procedure (PSUSA/00010015/201802) finalised in September 2018 as well as 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 RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.37. Ruxolitinib - JAKAVI (CAP) - EMEA/H/C/002464/II/0041

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Submission of the final results of drug-drug interaction (DDI) study INC4242A2106: an open-label, crossover study evaluating the effect of multiple doses of fluconazole on the pharmacokinetics (PK) of ruxolitinib administered as a single dose in healthy subjects (fulfilment of post-authorisation measures (PAM) MEA 016). The RMP (version 10) is updated accordingly and brought in line with revision 2 of GVP module V on 'Risk management systems' 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

5.3.38. 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

5.3.39. Tafamidis - VYNDAQEL (CAP) - EMEA/H/C/002294/X/0049/G, Orphan

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Ghania Chamouni

Scope: Grouped application consisting of: extension application to introduce a new strength (61 mg soft capsules, pack-size of 30 and 90 capsules) including an extension of indication to include treatment of transthyretin amyloidosis in adult patients with wild-type or hereditary cardiomyopathy to reduce all-cause mortality and cardiovascular-related hospitalisation (ATTR-CM); update of section 4.6 of the SmPC of 20 mg soft capsules to reflect some wording pertaining to the Tafamidis Enhanced Surveillance for Pregnancy Outcomes (TESPO) programme. The RMP (version 9.0) is updated accordingly, including a reclassification of the safety concerns and the removal of healthcare professional (HCP) educational leaflet. Annex II is updated in accordance. In addition, the MAH proposed to update the information in Braille of Annex III-A on 'Labelling' to differentiate between the dosage forms

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

5.3.40. Trastuzumab emtansine - KADCYLA (CAP) - EMEA/H/C/002389/II/0045

Applicant: Roche Registration GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Extension of indication to include the adjuvant treatment of adult patients with human epidermal growth factor receptor 2 (HER2)-positive early breast cancer. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 9.0) are updated accordingly. In addition, the MAH took the opportunity to introduce editorial changes

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

5.3.41. [Varenicline - CHAMPIX \(CAP\) - EMEA/H/C/000699/II/0074](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of sections 4.2, 5.1 and 5.2 of the SmPC in order to reflect results of paediatric study A3051073 (MEA 047): a phase 4, twelve-week, randomized, double-blind, placebo-controlled, parallel-group, dose-ranging study with follow-up, evaluating the safety and efficacy of varenicline for smoking cessation in healthy adolescent smokers. The package leaflet and the RMP (version 11.0) are updated accordingly

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

5.3.42. [Venetoclax - VENCLYXTO \(CAP\) - EMEA/H/C/004106/II/0020, Orphan](#)

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Update of sections 4.2 and 5.2 of the SmPC in order to include that a 50% dose reduction of venetoclax is recommended in patients with severe hepatic impairment, based on the final results from study M15-342 (listed as a category 3 study in the RMP): a study to evaluate the safety and pharmacokinetics of a single dose of venetoclax in female subjects with mild, moderate, or severe hepatic impairment. The package leaflet and the RMP (version 3.4) are updated accordingly

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

6. Periodic safety update reports (PSURs)

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

6.1.1. [Adefovir - HEPSERA \(CAP\) - PSUSA/00000060/201809](#)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Axicabtagene ciloleucel - YESCARTA (CAP) - PSUSA/00010703/201810

Applicant: Kite Pharma EU B.V., ATMP¹⁰

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.3. Bezlotoxumab - ZINPLAVA (CAP) - PSUSA/00010576/201810

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Cariprazine - REAGILA (CAP) - PSUSA/00010623/201810

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Ceftaroline fosamil - ZINFORO (CAP) - PSUSA/00010013/201810

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Ceritinib - ZYKADIA (CAP) - PSUSA/00010372/201810

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Cerliponase alfa - BRINEURA (CAP) - PSUSA/00010596/201810

Applicant: BioMarin International Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁰ Advanced therapy medicinal product

6.1.8. [Cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA \(CAP\) - PSUSA/00010449/201811](#)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. [Conestat alfa - RUCONEST \(CAP\) - PSUSA/00000873/201810](#)

Applicant: Pharming Group N.V

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. [Daclizumab - ZINBRYTA¹¹ - PSUSA/00010518/201811](#)

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.1.11. [Dapagliflozin - EDISTRIDE \(CAP\); FORXIGA \(CAP\) - PSUSA/00010029/201810](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. [Deferasirox - EXJADE \(CAP\) - PSUSA/00000939/201810](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. [Defibrotide - DEFITELIO \(CAP\) - PSUSA/00010086/201810](#)

Applicant: Gentium S.r.l.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

¹¹ European Commission (EC) decision on the marketing authorisation (MA) withdrawal dated 27 March 2018

Action: For adoption of recommendation to CHMP

6.1.14. Delamanid - DELTYBA (CAP) - PSUSA/00010213/201810

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Durvalumab - IMFINZI (CAP) - PSUSA/00010723/201810

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Edoxaban - LIXIANA (CAP); ROTEAS (CAP) - PSUSA/00010387/201810

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Flutemetamol (¹⁸F) - VIZAMYL (CAP) - PSUSA/00010293/201810

Applicant: GE Healthcare AS

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Gemtuzumab ozogamicin - MYLOTARG (CAP) - PSUSA/00010688/201810

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Granisetron¹² - SANCUSO (CAP) - PSUSA/00010101/201810

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

¹² Transdermal patch only

Action: For adoption of recommendation to CHMP

6.1.20. [Hepatitis A \(inactivated\), hepatitis B \(rDNA\) vaccine \(adsorbed\) - AMBIRIX \(CAP\); TWINRIX ADULT \(CAP\); TWINRIX PAEDIATRIC \(CAP\) - PSUSA/00001593/201809](#)

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. [Herpes zoster vaccine \(recombinant, adjuvanted\) - SHINGRIX \(CAP\) - PSUSA/00010678/201810](#)

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. [Idarucizumab - PRAXBIND \(CAP\) - PSUSA/00010435/201810](#)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. [Insulin detemir - LEVEMIR \(CAP\) - PSUSA/00001750/201810](#)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. [Irinotecan¹³ - ONIVYDE \(CAP\) - PSUSA/00010534/201810](#)

Applicant: Les Laboratoires Servier

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. [Letermovir - PREVYMIS \(CAP\) - PSUSA/00010660/201811](#)

Applicant: Merck Sharp & Dohme B.V.

¹³ Liposomal formulations only

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. [Lopinavir, ritonavir - ALUVIA \(Art 58¹⁴\); KALETRA \(CAP\) - PSUSA/00001905/201809](#)

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. [Macitentan - OPSUMIT \(CAP\) - PSUSA/00010115/201810](#)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. [Measles, mumps, rubella, varicella vaccines \(live\) - PROQUAD \(CAP\) - PSUSA/00001936/201809](#)

Applicant: MSD Vaccins

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. [Memantine - AXURA \(CAP\); EBIXA \(CAP\); MEMANTINE MERZ \(CAP\) - PSUSA/00001967/201809](#)

Applicant(s): Merz Pharmaceuticals GmbH (Axura, Memantine Merz), H. Lundbeck A/S (Ebixa)

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. [Meningococcal group B vaccine \(recombinant, adsorbed\) - TRUMENBA \(CAP\) - PSUSA/00010607/201810](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

¹⁴ Article 58 of Regulation (EC) No 726/2004 allows the Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO) on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Micafungin - MYCAMINE (CAP) - PSUSA/00002051/201810

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Midostaurin - RYDAPT (CAP) - PSUSA/00010638/201810

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Miglustat - ZAVESCA (CAP) - PSUSA/00002062/201810

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Netupitant, palonosetron - AKYNZEO (CAP) - PSUSA/00010393/201810

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Nintedanib¹⁵ - VARGATEF (CAP) - PSUSA/00010318/201810

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Agni Kapou

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Nintedanib¹⁶ - OFEV (CAP) - PSUSA/00010319/201810

Applicant: Boehringer Ingelheim International GmbH

¹⁵ Oncology indication(s) only

¹⁶ Respiratory indication(s) only

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Obinutuzumab - GAZYVARO (CAP) - PSUSA/00010279/201810

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Ocriplasmin - JETREA (CAP) - PSUSA/00010122/201810

Applicant: Oxurion NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Ofatumumab - ARZERRA¹⁷ - PSUSA/00002202/201810

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.1.40. Olaratumab - LARTRUVO (CAP) - PSUSA/00010541/201810

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Oseltamivir - TAMIFLU (CAP) - PSUSA/00002225/201809

Applicant: Roche Registration GmbH (Tamiflu)

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁷ European Commission (EC) decision on the marketing authorisation (MA) withdrawal dated 25 February 2019

6.1.42. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - FOCLIVIA (CAP); prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - AFLUNOV (CAP) - PSUSA/00010008/201810

Applicant: Seqirus S.r.l

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Para-aminosalicylic acid¹⁸ - GRANUPAS (CAP) - PSUSA/00010171/201810

Applicant: Eurocept International B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Parathyroid hormone - NATPAR (CAP) - PSUSA/00010591/201810

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Pasireotide - SIGNIFOR (CAP) - PSUSA/00009253/201810

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Patiromer - VELTASSA (CAP) - PSUSA/00010618/201810

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

6.1.47. Pazopanib - VOTRIENT (CAP) - PSUSA/00002321/201810

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

¹⁸ Centrally authorised product(s) only

Action: For adoption of recommendation to CHMP

6.1.48. Sofosbuvir, ledipasvir - HARVONI (CAP) - PSUSA/00010306/201810

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. Stiripentol - DIACOMIT (CAP) - PSUSA/00002789/201811

Applicant: Biocodex

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Talimogene laherparepvec - IMLYGIC (CAP) - PSUSA/00010459/201810

Applicant: Amgen Europe B.V., ATMP¹⁹

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.51. Thalidomide - THALIDOMIDE CELGENE (CAP) - PSUSA/00002919/201810

Applicant: Celgene Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Tofacitinib - XELJANZ (CAP) - PSUSA/00010588/201811

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Trastuzumab - HERCEPTIN (CAP); HERZUMA (CAP); KANJINTI (CAP); ONTRUZANT (CAP); TRAZIMERA (CAP) - PSUSA/00003010/201809

Applicant(s): Roche Registration GmbH (Herceptin), Celltrion Healthcare Hungary Kft. (Herzuma), Amgen Europe B.V., Breda (Kanjinti), Samsung Bioepis NL B.V. (Ontruzant), Pfizer Europe MA EEIG (Trazimera)

¹⁹ Advanced therapy medicinal product

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. [Turoctocog alfa - NOVOEIGHT \(CAP\) - PSUSA/00010138/201810](#)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.55. [Vinflunine - JAVLOR \(CAP\) - PSUSA/00003123/201809](#)

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Eva Segovia

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. [Carbidopa, entacapone, levodopa - CORBILTA \(CAP\); LEVODOPA/CARBIDOPA/ENTACAPONE ORION \(CAP\); STALEVO \(CAP\); NAP - PSUSA/00000547/201810](#)

Applicant(s): Orion Corporation (Corbilta, Levodopa/Carbidopa/Entacapone Orion, Stalevo), various

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. [Chenodeoxycholic acid - CHENODEOXYCHOLIC ACID LEADIANT \(CAP\); NAP - PSUSA/00010590/201810](#)

Applicant(s): Leadiant GmbH (Chenodeoxycholic acid Leadiant), various

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. [Enoxaparin²⁰ - INHIXA \(CAP\); THORINANE \(CAP\); NAP - PSUSA/00010553/201810](#)

Applicant(s): Techdow Europe AB (Inhixa), Techdow Pharma Netherlands B.V. (Thorinane),

²⁰ Biosimilar(s) only

various

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. [Epoetin alfa - ABSEAMED \(CAP\); BINOCRIT \(CAP\); EPOETIN ALFA HEXAL \(CAP\); NAP - PSUSA/00001237/201808](#)

Applicant(s): Medice Arzneimittel Pütter GmbH & Co. KG (Abseamed), Sandoz GmbH (Binocrit), Hexal AG (Epoetin alfa Hexal), various

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. [Filgrastim - ACCOFIL \(CAP\); FILGRASTIM HEXAL \(CAP\); GRASTOFIL \(CAP\); NIVESTIM \(CAP\); RATIOGRASTIM \(CAP\); TEVAGRASTIM \(CAP\); ZARZIO \(CAP\); NAP - PSUSA/00001391/201809](#)

Applicant(s): Accord Healthcare S.L.U. (Accofil), Hexal AG (Filgrastim Hexal), Apotex Europe BV (Grastofil), Pfizer Europe MA EEIG (Nivestim), ratiopharm GmbH (Ratiograstim), TEVA GmbH (Tevagrastim), Sandoz GmbH (Zarzio), various

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.6. [Sodium oxybate²¹ - XYREM \(CAP\); NAP - PSUSA/00010612/201810](#)

Applicant(s): UCB Pharma S.A. (Xyrem), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.7. [Teriparatide - FORSTEO \(CAP\); MOVYMIA \(CAP\); TERROSA \(CAP\); NAP - PSUSA/00002903/201809](#)

Applicant(s): Eli Lilly Nederland B.V. (Forsteo), Stada Arzneimittel AG (Movymia), Gedeon Richter Plc. (Terrosa), various

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

²¹ For oral use only

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

6.3.1. Acetylcysteine (NAP) - PSUSA/00000034/201809

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Alfentanil (NAP) - PSUSA/00000082/201809

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Asparaginase²² (NAP), crisantaspase (NAP), pegaspargase²³ (NAP) - PSUSA/00003161/201808

Applicant(s): various

PRAC Lead: Roxana Stefania Stroe

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Baclofen²⁴ (NAP) - PSUSA/00000294/201809

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Carmustine²⁵ (NAP) - PSUSA/00010348/201809

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

²² Nationally authorised product(s) only

²³ Nationally authorised product(s) only

²⁴ For oral use only

²⁵ Implant only

6.3.6. Clenbuterol (NAP) - PSUSA/00000794/201809

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Dermatophagoides pteronyssinus, dermatophagoides farina^{26 27} (NAP) - PSUSA/00010582/201809

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Diclofenac²⁸ (NAP) - PSUSA/00001048/201809

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Diclofenac²⁹ (NAP) - PSUSA/00010342/201809

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Diclofenac, omeprazole (NAP) - PSUSA/00010461/201809

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Dienogest, estradiol³⁰ (NAP) - PSUSA/00010444/201809

Applicant(s): various

²⁶ Allergen for therapy for oromucosal use only

²⁷ Mutual recognition procedure (MRP) and decentralised procedure (DCP) only

²⁸ Systemic formulation(s) only

²⁹ Topical formulation(s) only

³⁰ Contraception indication(s) only

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Etonogestrel (NAP) - PSUSA/00001331/201809

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Indoramin (NAP) - PSUSA/00001740/201809

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Isotretinoin³¹ (NAP); isotretinoin, erythromycin (NAP) - PSUSA/00010487/201808

Applicant(s): various

PRAC Lead: Tatiana Magalova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Levofloxacin³² (NAP) - PSUSA/00001854/201810

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Meropenem (NAP) - PSUSA/00001989/201808

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

³¹ Topical formulation(s) only

³² Except for centrally authorised product(s)

6.3.17. Mirtazapine (NAP) - PSUSA/00002068/201808

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Permethrin (NAP) - PSUSA/00002355/201808

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Phloroglucinol (NAP); phloroglucinol, trimethylphloroglucinol (NAP) - PSUSA/00010355/201809

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Sodium oxybate³³ (NAP) - PSUSA/00010613/201810

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Zidovudine (NAP) - PSUSA/00003143/201809

Applicant(s): various

PRAC Lead: Jana Lukačšínová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Fluticasone furoate - AVAMYS (CAP) - EMEA/H/C/000770/LEG 027

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Adam Przybylkowski

³³ For intravenous use only

Scope: Cumulative review of cases of respiratory, thoracic and mediastinal disorders together with a cumulative review of lower respiratory tract infections, as requested in the conclusions of PSUSA/009154/201804 adopted in December 2018

Action: For adoption of advice to CHMP

6.4.2. Fluticasone furoate - AVAMYS (CAP) - EMEA/H/C/000770/LEG 028

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Cumulative review of cases of drug dependence, as requested in the conclusions of PSUSA/009154/201804 adopted in December 2018

Action: For adoption of advice to CHMP

6.4.3. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/LEG 066.2

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to LEG 066.1 [detailed study report of the retrospective analysis of extended interval dosing (EID) versus standard interval dosing (SID), a proposal for further investigation of efficacy and safety in terms of progressive multifocal leukoencephalopathy (PML) risk reduction with EID relative to SID, and updated pharmacokinetic/pharmacodynamic (PK/PD) modelling taking into account body weight and extended dosing intervals, as requested in the conclusions of PSUSA/00002127/201708 adopted by PRAC in March 2018] as per the request for supplementary information (RSI) adopted in January 2019

Action: For adoption of advice to CHMP

6.4.4. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/LEG 055

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Cumulative hepatotoxicity drug safety reports (DSR), as requested in the conclusions of PSUSA/00002980/201804 adopted at the November 2018 PRAC

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

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

7.1.1. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/PSP/S/0079

Applicant: Kite Pharma EU B.V., ATMP³⁵

PRAC Rapporteur: Anette Kirstine Stark

³⁴ In accordance with Article 107n of Directive 2001/83/EC

³⁵ Advanced therapy medicinal product

Scope: Protocol for a long-term, non-interventional study in patients taking Yescarta (axicabtagene ciloleucel) for the treatment of relapsed or refractory diffuse large B-cell lymphoma and primary mediastinal B-cell lymphoma to evaluate the safety of patients, including secondary malignancies, cytokine release syndrome (CRS), neurologic events, serious infections, prolonged cytopenias, hypogammaglobulinaemia and pregnancy outcomes in female patients of childbearing potential

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)³⁶

7.2.1. Brigatinib - ALUNBRIG (CAP) - EMEA/H/C/004248/MEA 002

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Protocol for study Brigatinib-5007: a cohort study to describe the occurrence of early-onset pulmonary events in patients with anaplastic lymphoma kinase-positive (ALS+) advance non-small cell lung cancer (NSCLC) treated with brigatinib

Action: For adoption of advice to CHMP

7.2.2. Brodalumab - KYNTHEUM (CAP) - EMEA/H/C/003959/MEA 002.3

Applicant: LEO Pharma A/S

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 002.2 [protocol for study NIS-KYNTHEUM-1345: an observational PASS of suicidal behaviour, serious infections, major adverse cardiovascular events (MACE) and malignancy in psoriasis patients treated with brodalumab. The brodalumab assessment of hazards: a multinational safety (BRAHMS) study in electronic healthcare databases [final report expected in Q3 2030]] as per the request for supplementary information (RSI) adopted in December 2018

Action: For adoption of advice to CHMP

7.2.3. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/MEA 001.2

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to MEA 001.1 [protocol for study GO40162: a PASS based on the European Haemophilia Safety Surveillance (EUHASS) registry to characterise the safety profile of patients with haemophilia A exposed to emicizumab under real-world conditions, including an estimate of event rates of the following important risks: thromboembolic events, thrombotic microangiopathy, systemic hypersensitivity, anaphylaxis and anaphylactoid events [final clinical study report: (CSR) expected in June 2024]] as per the request for supplementary information (RSI) adopted in December 2018

Action: For adoption of advice to CHMP

³⁶ 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. Mexiletine - NAMUSCLA (CAP) - EMEA/H/C/004584/MEA 001

Applicant: Lupin Europe GmbH

PRAC Rapporteur: Eva Jirsová

Scope: Protocol for a registry study to determine the long-term safety and tolerability of Namuscla (mexiletine) for the symptomatic treatment of myotonia in adult patients with non-dystrophic myotonic disorder (from the initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.5. Niraparib - ZEJULA (CAP) - EMEA/H/C/004249/MEA 003.2

Applicant: Tesaro Bio Netherlands B.V.

PRAC Rapporteur: Jan Neuhauser

Scope: MAH's response to MEA 003.1 [protocol and statistical analysis plan for a non-interventional non-imposed PASS: a pooled analysis of the incidence of acute myelogenous leukaemia, myelodysplastic syndrome, and other secondary primary malignancies in patients treated with niraparib] as per the request for supplementary information (RSI) adopted in December 2018

Action: For adoption of advice to CHMP

7.2.6. Radium-223 – XOFIGO (CAP) - EMEA/H/C/2653/MEA 014

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Protocol for a drug utilisation study (DUS) of Xofigo (radium-223) under routine clinical practice in Europe to investigate the risk of off-label use, as requested in the conclusions of the referral procedure on Xofigo (radium-223) under Article 20 of Regulation (EC) No 726/2004 (EMA/H/A-20/1459) finalised in 2018

Action: For adoption of advice to CHMP

7.2.7. Sirolimus - RAPAMUNE (CAP) - EMEA/H/C/000273/MEA 054.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 054 [protocol for study B1741224: a non-interventional observational PASS to present additional long-term safety and effectiveness data on patients with sporadically lymphangioliomyomatosis (S-LAM) treated with sirolimus], as per the request for supplementary information (RSI) adopted in January 2019

Action: For adoption of advice to CHMP

7.2.8. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 007.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 007.2 [protocol for a non-interventional PASS study A3921298 (listed as a category 3 study in the RMP) evaluating the effectiveness of additional risk minimisation measures (aRMM) for Xeljanz (tofacitinib) in the European Union via a survey of healthcare professionals (HCPs) considered as an additional pharmacovigilance activity in the RMP] as per the request for supplementary information (RSI) adopted in January 2019

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)³⁷

7.3.1. Valproate (NAP) - EMEA/H/N/PSR/J/0021

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

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Results for a joint drug utilisation study (DUS) of valproate and related substances, in Europe, using databases to describe the prescribing practices before and after the dissemination of risk minimisations measures (RMMs) (i.e. educational materials and direct healthcare professional communication (DHPC) between December 2014 and June 2015) and to assess the effectiveness of these measures, as imposed 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)³⁸

7.4.1. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0074/G

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) submission of the final report from study RA0021 (Anti-Rheumatic Therapies in Sweden (ARTIS) registry) (listed as a category 3 study in the RMP): registry to gather short- and long-term safety data from the use of certolizumab pegol (CZP) in Sweden for rheumatoid arthritis (RA) patients; 2) submission of the final report from study RA005 (NBD registry) (listed as a category 3 study in the RMP): registry to gather safety and outcome data in RA patients receiving CZP and other RA treatments. In addition, the MAH submitted interim results for two ongoing registries studies, namely: study RA0020 - Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT): a German long-term observation of biologics/disease-modifying antirheumatic drugs (DMARD) in RA; and study RA0022 - British Society of Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR): a longitudinal observational study of patients with RA treated with biologic agents, and prospective surveillance study for adverse events

Action: For adoption of PRAC Assessment Report

³⁷ In accordance with Article 107p-q of Directive 2001/83/EC

³⁸ 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. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/II/0059

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Submission of the final clinical study report (CSR) for study H80-MC-B016: a modified prescription-event monitoring programme (modified PEM) to be conducted in the UK enrolling patients with type 2 diabetes mellitus (T2DM) to quantify the incidence of acute pancreatitis in the first 12 months after initiating treatment with prescription exenatide once weekly. The RMP (version 33) is updated accordingly (fulfilment of post-authorisation measures (PAM) MEA 010.5)

Action: For adoption of PRAC Assessment Report

7.4.3. Florbetaben (¹⁸F) - NEURACEQ (CAP) - EMEA/H/C/002553/II/0028

Applicant: Life Radiopharma Berlin GmbH

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from non-interventional PASS study FBB-01_02_13 (listed as a category 3 study in the RMP): a prospective observational study to assess the effectiveness of the training and risk minimisation measures recommended for the usage of NeuraCeq (florbetaben (¹⁸F)) in the post-authorisation clinical settings. The RMP (version 3.9) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.4. Idelalisib - ZYDELIG (CAP) - EMEA/H/C/003843/II/0046

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Martin Huber

Scope: Submission of the final clinical study report (CSR) for study GS-EU-313-4226 (listed as a category 3 study in the RMP): a cross-sectional PASS to assess healthcare provider awareness of risks associated with Zydelig (idelalisib) in the European Union. The study assesses the effectiveness of additional risk minimisation measures (RMM) by determining the level of knowledge of haematologists and oncologists on the infection risks associated with Zydelig (idelalisib) treatment and the corresponding recommendation to minimise these risks (fulfilment of post-authorisation measures (PAM) MEA 016)

Action: For adoption of PRAC Assessment Report

7.4.5. Indacaterol, glycopyrronium - ULTIBRO BREEZHALER (CAP) - EMEA/H/C/002679/WS1543/0029; ULUNAR BREEZHALER (CAP) - EMEA/H/C/003875/WS1543/0029; XOTERNA BREEZHALER (CAP) - EMEA/H/C/003755/WS1543/0033

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final study report of study CQVA149A2402 (listed as a category 1 study): a multinational database cohort study in Europe in chronic obstructive pulmonary disease (COPD) patients to assess the incidence rates and hazard ratios of various safety

outcomes in new users of indacaterol/glycopyrronium compared to new users of comparator drugs (at the drug-class level). The product information is updated to remove the black triangle and reflect the relevant amendments in Annex II.D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product'. The RMP (version 5.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.6. [Insulin lispro - HUMALOG \(CAP\) - EMEA/H/C/000088/WS1596/0172;](#) [LIPROLOG \(CAP\) - EMEA/H/C/000393/WS1596/0133](#)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Annika Folin

Scope: Submission of the final report from an on-going review of adverse drug events related to Humalog (insulin lispro) (MEA 028) and Liprolog (insulin lispro) (MEA 021) (listed as a category 3 study in the RMP): a post approval safety surveillance programme for lot-specific adverse event review to evaluate any potential change in frequency of hypersensitivity, immunogenicity, and lack of drug effect (LODE) events for insulin lispro synthesized via streamlined lispro drug substance process (sKPB)

Action: For adoption of PRAC Assessment Report

7.4.7. [Teriparatide - FORSTEO \(CAP\) - EMEA/H/C/000425/II/0050/G](#)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Grouped variations consisting of the submission of the final study reports of the European Union (EU) components of two PASS; namely study B3DMC-GHBX (2.2) and study B3D-MC-GHBX (2.3b) both US population-based comparative cohort studies undertaken to evaluate a potential association between teriparatide and adult osteosarcoma. The RMP (version 7.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.8. [Vardenafil - LEVITRA \(CAP\) - EMEA/H/C/000475/WS1536/0064;](#) [VIVANZA \(CAP\) - EMEA/H/C/000488/WS1536/0060](#)

Applicant: Bayer AG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final clinical study report (CSR) for study 12912: (listed as category 3 study in the RMP) a non-interventional PASS to investigate the risk of non-arteritic anterior ischemic optic neuropathy (NAION) associated with phosphodiesterase type 5 (PDE5) inhibitors. The RMP (version 6.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

7.5.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/MEA 048.7

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Annual update report on recruitment for study IM101240: an observational registry of abatacept in patients with juvenile idiopathic arthritis (JIA registry) to explore the long-term safety of abatacept treatment for JIA in routine clinical practice by quantifying the incidence rates of serious infections, autoimmune disorders and malignancies [final registry report expected by 2029]

Action: For adoption of advice to CHMP

7.5.2. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 065.9

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Tenth interim annual report for study P10-023, a psoriasis patient registry: a 10-year, post-marketing observational study to assess the long term safety of Humira (adalimumab) in adult patients with chronic plaque psoriasis (PS)) [final registry report expected in February 2023]

Action: For adoption of advice to CHMP

7.5.3. Bazedoxifene - CONBRIZA (CAP) - EMEA/H/C/000913/MEA 012.13

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Sixth annual report for PASS B1781044: a cohort study of venous thromboembolism and other clinical endpoints among osteoporotic women prescribed bazedoxifene, bisphosphonates or raloxifene in Europe [final clinical study report (CSR) expected in April 2020]

Action: For adoption of advice to CHMP

7.5.4. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/MEA 001.4

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Fourth annual interim report for EuroSIDA PASS study 201177 (listed as a category 3 study in the RMP): a prospective observational cohort study in patients receiving dolutegravir to investigate the risk of hypersensitivity reactions (HSR), hepatotoxicity and serious rash (division of acquired immune deficiency syndrome (DAIDS) grading scale category 3 or 4)

Action: For adoption of advice to CHMP

7.5.5. Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/MEA 007.4

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Fourth annual interim report for EuroSIDA PASS study 201177 (listed as a category 3 study in the RMP): a prospective observational cohort study in patients receiving dolutegravir to investigate the risk of hypersensitivity reactions (HSR), hepatotoxicity and serious rash (division of acquired immune deficiency syndrome (DAIDS) grading scale category 3 or 4)

Action: For adoption of advice to CHMP

7.5.6. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 007.4

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fourth annual report for study CNTO148ART4001: a pregnancy research initiative to study the exposure to golimumab during pregnancy in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis: a review and analysis of birth outcomes from the Swedish, Danish, and Finnish medical birth registers; together with the study summary reports for study CNTO148ART4001 and for study CNTO148ART4002: a pregnancy research initiative to study the exposure to golimumab during pregnancy using a US health insurance claims database

Action: For adoption of advice to CHMP

7.5.7. Lesinurad - ZURAMPIC (CAP) - EMEA/H/C/003932/ANX 002.2

Applicant: Grunenthal GmbH

PRAC Rapporteur: Eva Segovia

Scope: Annual progress report for an observational PASS of lesinurad patients (SATURATES) to further assess cardiovascular (CV) safety with a focus on major adverse cardiovascular events (MACE) in gout patients treated with Zurampic (lesinurad) in combination with a xanthine oxidase inhibitor (XOI)

Action: For adoption of advice to CHMP

7.5.8. Levofloxacin - QUINSAIR (CAP) - EMEA/H/C/002789/ANX 004.3

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: First interim report for a post-marketing, open-label, observational safety study of Quinsair (nebulised levofloxacin hemihydrate) in patients with cystic fibrosis and chronic *Pseudomonas aeruginosa* infection, using data collected through European cystic fibrosis registries

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Febuxostat - ADENURIC (CAP) - EMEA/H/C/000777/MEA 005.12

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Seventh interim annual report for the FAST study: a prospective, randomised, comparative, open-label phase 4 cardiovascular safety study in patients exposed to febuxostat or allopurinol in the clinical settings [final clinical study report (CSR) expected in Q4 2019]

Action: For adoption of advice to CHMP

7.6.2. Indacaterol, glycopyrronium - ULTIBRO BREEZHALER (CAP) - EMEA/H/C/002679/LEG 007

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's clarification following the temporary halt of study CIDD001D2402: a 24-week randomised, controlled, multicentre, open-label study to evaluate the effect of reminder notifications and motivational/adaptive messaging on treatment adherence of chronic obstructive pulmonary disease (COPD) subjects receiving Ultibro Breezhaler (indacaterol/glycopyrronium) treatment using the concept 2 inhaler for dose administration and tracking

Action: For adoption of advice to CHMP

7.6.3. Prucalopride - RESOLOR (CAP) - EMEA/H/C/001012/REC 022

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Report from the FDA³⁹ on study SPD555-802: a retrospective cohort (observational) study measuring the incidence of major adverse cardiovascular events (MACE; non-fatal acute myocardial infarction, non-fatal stroke, or in-hospital cardiovascular death) in five European data sources, as requested in the conclusions of variation II/42 concluded in September 2018

Action: For adoption of advice to CHMP

7.6.4. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/MEA 005.2

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 005.1 [protocol for study WA40404 (listed as category 3 study in the RMP): a phase 3b multicentre, randomised, double-blind, placebo controlled study to evaluate the efficacy and safety of ocrelizumab in adults with primary progressive multiple sclerosis later in their disease course] as per the request for supplementary

³⁹ US Food & Drug Administration

information (RSI) adopted in December 2018

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

None

8.2. Conditional renewals of the marketing authorisation

8.2.1. Nalotimagene carmaleucel - ZALMOXIS (CAP) - EMEA/H/C/002801/R/0015 (with RMP)

Applicant: MolMed S.p.A, ATMP⁴⁰

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Acridinium, formoterol fumarate dihydrate - BRIMICA GENUAIR (CAP) - EMEA/H/C/003969/R/0026 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

⁴⁰ Advanced therapy medicinal product

8.3.2. [Aclidinium, formoterol fumarate dihydrate - DUAKLIR GENUAIR \(CAP\) - EMEA/H/C/003745/R/0026 \(without RMP\)](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. [Ataluren - TRANSLARNA \(CAP\) - EMEA/H/C/002720/R/0051 \(with RMP\)](#)

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. [Darunavir, cobicistat - REZOLSTA \(CAP\) - EMEA/H/C/002819/R/0031 \(without RMP\)](#)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. [Dronedarone - MULTAQ \(CAP\) - EMEA/H/C/001043/R/0042 \(with RMP\)](#)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. [Duloxetine - DULOXETINE LILLY \(CAP\) - EMEA/H/C/004000/R/0015 \(without RMP\)](#)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. [Flutemetamol \(¹⁸F\) - VIZAMYL \(CAP\) - EMEA/H/C/002557/R/0017 \(without RMP\)](#)

Applicant: GE Healthcare AS

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Insulin glargine - ABASAGLAR (CAP) - EMEA/H/C/002835/R/0023 (without RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Ketoconazole - KETOCONAZOLE HRA (CAP) - EMEA/H/C/003906/R/0014 (with RMP)

Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Željana Margan Koletić

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Ledipasvir, sofosbuvir - HARVONI (CAP) - EMEA/H/C/003850/R/0080 (without RMP)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/R/0028 (without RMP)

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Ronan Grimes

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Nintedanib - OFEV (CAP) - EMEA/H/C/003821/R/0025 (without RMP)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - ADJUPANRIX (CAP) - EMEA/H/C/001206/R/0062 (with RMP)

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.14. Ramucirumab - CYRAMZA (CAP) - EMEA/H/C/002829/R/0031 (without RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.15. Tadalafil - TADALAFIL MYLAN (CAP) - EMEA/H/C/003787/R/0014 (without RMP)

Applicant: Mylan S.A.S

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.16. Tilmanocept - LYMPHOSEEK (CAP) - EMEA/H/C/002085/R/0016 (with RMP)

Applicant: Norgine B.V.

PRAC Rapporteur: Rugile Pilviniene

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

10.1.1. Febuxostat - ADENURIC (CAP) - EMEA/H/C/000777/II/0051

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Jan Neuhauser

Scope: PRAC follow-up consultation in a variation to update section 5.1 of the SmPC in order to include the results of the clinical safety study CARES (TMX-67_301) to compare the cardiovascular outcomes of febuxostat and allopurinol in subjects with gout and cardiovascular comorbidities. This is a multicentre, randomized, active-control, phase 3B study. In addition, the MAH took the opportunity to provide a consolidated Module 2.7.6 in order to list all the synopsis of individual studies in a unique tabular format

Action: For adoption of advice to CHMP

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Azithromycin (NAP) - FI/H/xxxx/WS/035

Applicant(s): Pfizer (Zithromax)

PRAC Lead: Kimmo Jaakkola

Scope: PRAC consultation on a national worksharing variation assessing the final study report of study A0661209: a registry based study estimating the relative and absolute cardiovascular risk amongst adult azithromycin users compared to amoxicillin users, within 5 days and within 6-10 days of dispensed prescription, using the Kaiser Permanente in Northern California (KPNC) and Kaiser Permanente in Southern California (KPSC) databases, on request of Finland

Action: For adoption of advice to Member States

11.1.2. Leuprorelin (NAP) - DE/H/0580/001-003/II/077, DE/H/0580/001-003/II/078

Applicant(s): Astellas Pharma (Eligard)

PRAC Lead: Martin Huber

Scope: PRAC follow-up consultation on national variations on RMP updates proposing the removal of additional risk minimisation measure (aRMM) on the development of a new product presentation, the addition of new risk minimisation measures and

pharmacovigilance activities updating the product information with monitoring the response to Eligard (leuprorelin) by measuring the serum concentrations of testosterone, following PRAC advice adopted in February 2019, on request of Germany

Action: For adoption of advice to Member States

11.2. Other request

11.2.1. Ulipristal acetate - AT/H/0862/001/DC, AT/H/0863/001/DC

PRAC Lead: Jan Neuhauser

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

Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Brexit preparedness – extension of the period under Article 50 of Treaty on the European Union (EU)

Action: For information

12.4.2. European Commission (EC) report on pharmacovigilance tasks from the European Union (EU) Member States and the European Medicines Agency (EMA) - 2015-2018

Action: For discussion

12.5. Cooperation with International Regulators

12.5.1. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)-E19 on 'optimisation of safety data collection' – draft guideline

Action: For adoption

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional 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 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

12.15.3. Post-authorisation Safety Studies - Guidance for assessors to request the conduct of a PASS

PRAC lead: Ulla Wändel Liminga

Action: For discussion

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 - draft technical specifications for EMA funded impact research

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/