3 April 2017
EMA/PRAC/227083/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 3-6 April 2017

Chair: June Raine – Vice-Chair: Almath Spooner

3 April 2017, 13:00 – 19:30, room 3/A

4 April 2017, 08:30 – 19:30, room 3/A

5 April 2017, 08:30 – 19:30, room 3/A

6 April 2017, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

20 April 2017, 09:00 - 12:00, room 7/B, via adobe connect

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 scope listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also change during the course of the review. Additional details on some of these procedures will be published in the PRAC meeting highlights once the procedures are finalised.

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

Note on access to documents

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

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Table of contents

1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 3-6 April 2017. See April 2017 PRAC minutes (to be published post May 2017 PRAC meeting).

1.2. Adoption of agenda of the meeting of 3-6 April 2017

Action: For adoption

1.3. Adoption of the minutes of the previous meeting of 6-9 March 2017

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

2.4. Planned public hearings

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.4. Article 5(3) of Regulation (EC) No 726/2004: PRAC advice on CHMP request

See 10.3.1.

3.5. Others

3.5.1. Gadolinium-containing contrast agents (GdCA): gadobenic acid (NAP); gadobutrol (NAP); gadodiamide (NAP); gadopentetic acid (NAP); gadoteric acid (NAP); gadoteridol (NAP); gadoxetic acid (NAP); gadoversetamide – OPTIMARK (CAP) - EMEA/H/A-31/1437

Applicant: Mallinckrodt Deutschland GmbH (Optimark); various

PRAC Rapporteur: To be appointed; PRAC Co-rapporteur: To be appointed

Scope: Request for re-examination of the review of the benefit-risk balance following notification by the European Commission of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

Action: For discussion

4. Signals assessment and prioritisation[1]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Gefitinib – IRESSA (CAP)

Applicant (s): AstraZeneca AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of recall phenomenon

Action: For adoption of PRAC recommendation

EPITT 18857 – New signal

Lead Member State(s): SE

4.1.2. Meningococcal group B vaccine (rDNA, component, adsorbed) - BEXSERO (CAP)

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of arthritis and synovitis

Action: For adoption of PRAC recommendation

EPITT 18764 – New signal

Lead Member State(s): SE

4.1.3. Methotrexate – NORDIMET (CAP); NAP

Applicant(s): Nordic Group B.V. (Nordimet), various

PRAC Rapporteur: To be appointed

Scope: Signal of pulmonary alveolar haemorrhage

Action: For adoption of PRAC recommendation

EPITT 18850 – New signal

Lead Member State(s): DE

4.1.4. Pramipexole – MIRAPEXIN (CAP), SIFROL (CAP), OPRYMEA (CAP), PRAMIPEXOLE TEVA (CAP), PRAMIPEXOLE ACCORD (CAP); NAP

Applicant(s): Boehringer Ingelheim International GmbH (Mirapexin, Sifrol), Krka, d.d., Novo mesto (Oprymea), Teva B.V. (Pramipexole Teva), Accord Healthcare Ltd (Pramipexole Accord); various

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

PRAC Rapporteur: To be appointed

Scope: Signal of dystonia

Action: For adoption of PRAC recommendation

EPITT 18866 – New signal

Lead Member State(s): DK

4.2. New signals detected from other sources

4.2.1. Azithromycin (NAP); tobramycin[2] – TOBI PODHALER (CAP), VANTOBRA (CAP); NAP

Applicant(s): Novartis Europharm Ltd (Tobi Podhaler), PARI Pharma GmbH (Vantobra); various

PRAC Rapporteur: To be appointed

Scope: Signal of possible interaction between tobramycin and azithromycin leading to lower effectiveness of tobramycin

Action: For adoption of PRAC recommendation

EPITT 18855 – New signal

Lead Member State(s): NL, SE

4.2.2. Flucloxacillin (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of high anion gap metabolic acidosis (HAGMA)

Action: For adoption of PRAC recommendation

EPITT 18844 – New signal

Lead Member State(s): PT

4.2.3. Mesalazine (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of risk of photosensitivity reactions

Action: For adoption of PRAC recommendation

EPITT 18869 – New signal

Lead Member State(s): UK

[2] For inhalation use only

4.3. Signals follow-up and prioritisation

4.3.1. Albiglutide – EPERZAN (CAP) - EMEA/H/C/002735/SDA/010

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Julie Williams

Scope: Signal of acute kidney injury

Action: For adoption of PRAC recommendation

EPITT 18778 – Follow up to December 2016

4.3.2. Docetaxel – TAXOTERE (CAP), DOCETAXEL ACCORD (CAP), TAXESPIRA (CAP)

Applicant(s): Aventis Pharma S.A. (Taxotere), Accord Healthcare Ltd (Docetaxel Accord), Hospira UK Limited (Taxespira), various

PRAC Rapporteur: Claire Ferard

Scope: Signal of unexpected seriousness of reported adverse drug reactions with docetaxel and suspicion of an increase in adverse drug reactions (ADR) reporting rate in France with docetaxel-containing products

Action: For adoption of PRAC recommendation

EPITT 12059 – Follow up to March 2017

4.3.3. Intravenous fluids containing electrolytes and/or carbohydrates (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of hyponatremia

Action: For adoption of PRAC recommendation

EPITT 18631 – Related to March 2016

4.3.4. Leflunomide – ARAVA (CAP) - EMEA/H/C/000235/SDA/057, LEFLUNOMIDE MEDAC (CAP) - EMEA/H/C/001227/SDA/012, LEFLUNOMIDE WINTHROP (CAP) - EMEA/H/C/001129/SDA/025; teriflunomide – AUBAGIO - EMEA/H/C/002514/SDA/003 (CAP)

Applicant: Sanofi-aventis Deutschland GmbH (Arava, Leflunomide Winthrop), Sanofi-Aventis Groupe (Aubagio); Medac Gesellschaft fur klinische Spezialpraparate GmbH (Leflunomide Medac)

PRAC Rapporteur: Sabine Straus

Scope: Signal of falsely decreased ionised calcium levels

Action: For adoption of PRAC recommendation

EPITT 18787 – Follow up to December 2016

4.3.5. Selexipag - UPTRAVI (CAP) – EMEA/H/C/003774/SDA/004

Applicant: Actelion Registration Ltd.

PRAC Rapporteur: Julie Williams

Scope: Signal of fatal cases in patients with pulmonary arterial hypertension (PAH)

Action: For adoption of PRAC recommendation

EPITT 18833 – Follow up to February 2017

4.3.6. Temozolomide - TEMODAL (CAP) - EMEA/H/C/000229/SDA/041; NAPs

Applicant: Merck Sharp & Dohme Limited; various

PRAC Rapporteur: Martin Huber

Scope: Signal of meningoencephalitis herpetic

Action: For adoption of PRAC recommendation

EPITT 18785 – Follow up to December 2016

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Adalimumab - EMEA/H/C/004279

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

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

5.1.2. Atezolizumab - EMEA/H/C/004143

Scope: Treatment of locally advanced or metastatic urothelial carcinoma and non-small cell lung carcinoma (NSCLC)

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

5.1.3. Brodalumab – EMEA/H/C/003959

Scope: Treatment of moderate to severe plaque psoriasis

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

5.1.4. Ciclosporin - EMEA/H/C/004411, Orphan

Applicant: Santen Oy

Scope, accelerated assessment: Treatment of severe vernal keratoconjunctivitis (VKC)

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

5.1.5. Cladribine - EMEA/H/C/004230

Scope: Treatment of highly active relapsing-remitting multiple sclerosis (MS)

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

5.1.6. Glecaprevir, pibrentasvir - EMEA/H/C/004430

Scope, accelerated assessment: Treatment of chronic hepatitis C virus (HCV) infection in adults

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

5.1.7. Insulin lispro - EMEA/H/C/004303

Scope: Treatment of diabetes mellitus

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

5.1.8. Midostaurin - EMEA/H/C/004095, Orphan

Applicant: Novartis Europharm Ltd

Scope: Treatment of mastocytosis and treatment of acute myeloid leukaemia

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

5.1.9. Ribociclib - EMEA/H/C/004213

Scope: Treatment of breast cancer

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

5.1.10. Sofosbuvir, velpatasvir, voxilaprevir - EMEA/H/C/004350

Scope, accelerated assessment: Treatment of chronic hepatitis C virus in adults (HCV) infection in adults

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

5.1.11. Telotristat ethyl - EMEA/H/C/003937, Orphan

Applicant: Ipsen Pharma

Scope: Treatment of carcinoid syndrome

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. Eribulin - HALAVEN (CAP) - EMEA/H/C/002084/II/0033

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 4.2) to reflect the revised protocol for a PASS to capture data on the frequency of resolution and time to resolution of eribulin-induced or aggravated peripheral neuropathy from study E7389-A001-303 (ACCRU: a randomized phase III study of eribulin compared to standard weekly paclitaxel as first- or second-line therapy for locally recurrent or metastatic breast cancer) to an observational post authorisation, single-arm, prospective multicentre cohort study E7389-M044-504 (IRENE). The submission date of the corresponding study report to EMA remains unchanged and is planned in 2019

Action: For adoption of PRAC Assessment Report

5.2.2. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/II/0042

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of the RMP (version 25) following closure and final summary of the exenatide pregnancy registry (a prospective, observational study conducted in the United States that actively collected information on exposure to antidiabetic medication during pregnancy and the associated pregnancy outcomes in patients with type 2 diabetes mellitus (T2DM)). Moreover, the MAH included additional minor updates to the RMP

Action: For adoption of PRAC Assessment Report

5.2.3. Human alpha 1-proteinase inhibitor - RESPREEZA (CAP) - EMEA/H/C/002739/II/0013

Applicant: CSL Behring GmbH

PRAC Rapporteur: Eva Segovia

Scope: Update of the RMP (version 3.1) in order to include the final safety data from study CE1226_3001 (an open-label, non-controlled, multicentre, multinational study to evaluate the efficacy and safety of human alpha1-proteinase inhibitor administration in chronic augmentation and maintenance therapy in subjects with emphysema due to alpha 1-proteinase inhibitor deficiency who completed clinical study CE1226_4001) assessed within EMEA/H/C/002739/II/0002 procedure. Further adjustments in the non-clinical safety specification part are included

Action: For adoption of PRAC Assessment Report

5.2.4. Vildagliptin - GALVUS (CAP) - EMEA/H/C/000771/WS1088/0048; JALRA (CAP) - EMEA/H/C/001048/WS1088/0048; XILIARX (CAP) - EMEA/H/C/001051/WS1088/0047 Vildagliptin, metformin hydrochloride - EUCREAS (CAP) - EMEA/H/C/000807/WS1088/0057; ICANDRA (CAP) -

EMEA/H/C/001050/WS1088/0058; ZOMARIST (CAP) EMEA/H/C/001049/WS1088/0058

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of the RMPs (version 14) for Galvus, Jalra, Xiliarx, Eucreas, Icandra and Zomarist in order to reflect the outcome of the recently finalised procedure for metformin-containing products under Article 31 of Directive 2001/83/EC (EMEA/H/A-31/1432) in order to implement a targeted questionnaire for cases of lactic acidosis

Action: For adoption of PRAC Assessment Report

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

5.3.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/II/0017

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and long term use information in the posology following final results from study CAMMS03409: an extension protocol for multiple sclerosis (MS) patients who participated in Genzyme-sponsored studies of alemtuzumab to evaluate the long term safety and efficacy of alemtuzumab in MS patients who received alemtuzumab during prior company-sponsored studies. The Package Leaflet and the RMP (version 3.0) are updated accordingly. In addition, the MAH took the opportunity to bring the Product Information in line with the latest QRD template (version 10.0) and to introduce editorial corrections

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

5.3.2. Aliskiren - RASILEZ (CAP) - EMEA/H/C/000780/WS1026/0110; Aliskiren, hydrochlorothiazide - RASILEZ HCT (CAP) - EMEA/H/C/000964/WS1026/0080

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of section 5.1 of the SmPC in order to reflect the results of study SPP100F2301 (ATMOSPHERE): a multicentre, randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of both aliskiren monotherapy and aliskiren/enalapril combination therapy compared to enalapril monotherapy, on morbidity and mortality in patients with chronic heart failure (New York Heart Association (NYHA) Class II-IV). The RMP (version 13) is updated accordingly

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

5.3.3. Bevacizumab - AVASTIN (CAP) - EMEA/H/C/000582/II/0092

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Extension of indication to include the use of Avastin in combination with paclitaxel and carboplatin for the treatment of adult patients with first recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated with efficacy and safety information from study GOG-0213 (a phase III randomized controlled clinical trial of carboplatin and paclitaxel (or gemcitabine) alone or in combination with bevacizumab followed by bevacizumab and secondary cytoreductive surgery in platinum-sensitive, recurrent ovarian, peritoneal primary and fallopian tube cancer). The Package Leaflet and the RMP (version 27) are updated accordingly

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

5.3.4. Bimatoprost, timolol - GANFORT (CAP) - EMEA/H/C/000668/II/0026

Applicant: Allergan Pharmaceuticals Ireland

PRAC Rapporteur: Torbjorn Callreus

Scope: Update of section 4.8 of the SmPC to revise and simplify the undesirable effects section as per the PRAC recommendation following PSUSA assessment (EMEA/H/C/PSUSA/00002961/2015). The Package Leaflet and the RMP (version 3.2) are updated accordingly. In addition, the MAH took the opportunity to update the Product Information in line with the QRD template (version 10.0) to implement the unique identifier 2D bar code and include some editorial corrections

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

5.3.5. Daptomycin - CUBICIN (CAP) - EMEA/H/C/000637/II/0061

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to extend the *S. aureus* bacteraemia indication to include paediatric patients 1 to 17 years of age. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet, Labelling and the RMP (version 10.0) are updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 10) and to combine the SmPCs for both strengths (350 and 500 mg)

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

5.3.6. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0062

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.4 and 4.8 of the SmPC to update the safety information and reflect the possible occurrence of multiple vertebral fractures (MVF) particularly in patients with a history of vertebral fracture following discontinuation of Prolia treatment. This results from an analysis of osteoporosis-related fracture data in subjects who discontinued

investigational product and remained on study in either the Prolia phase III pivotal fracture study (study 20030216: evaluation of denosumab in the treatment of postmenopausal osteoporosis FREEDOM (fracture reduction evaluation of denosumab in osteoporosis every 6 months)) or its study extension (study 20060289: open label, single arm, extension study to evaluate the long term safety and sustained efficacy of denosumab in the treatment of postmenopausal osteoporosis) to better understand the incidence of fracture following treatment discontinuation. The Package Leaflet is updated accordingly. The RMP (version 16) is also updated to reflect MVF as a new important risk. In addition, the Product Information is updated in line with the QRD template latest version and corrected to remove typographical errors and implement minor changes in the list of local representatives

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

5.3.7. Efavirenz - STOCRIN (CAP) - EMEA/H/C/000250/WS1117/0110/G; SUSTIVA (CAP) - EMEA/H/C/000249/WS1117/0139/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Grouped work-sharing variations on: 1) update of sections 4.4, 4.5 and 5.1 of the SmPC in order to add a warning and update the safety information on QTc prolongation based on the final results from study AI266959: an interventional study to determine the concentration-electrocardiographic effects of efavirenz in healthy subjects enriched for CYP2B6[3] polymorphisms. The Package Leaflet and the RMP (version 8) are updated accordingly; 2) update of sections 4.4 and 4.8 of the SmPC to add catatonia as a psychiatric symptom following an assessment of cases of catatonia reported in the literature and via the United States (US) Food and Drug Administration adverse event reporting system (FAERS)

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

5.3.8. Efavirenz, emtricitabine, tenofovir disoproxil - ATRIPLA (CAP) - EMEA/H/C/000797/WS1133/0121/G; emtricitabine, tenofovir alafenamide - DESCOVY (CAP) –EMEA/H/C/004094/WS1133/0015/G; emtricitabine, rilpivirine, tenofovir disoproxil - EVIPLERA (CAP) - EMEA/H/C/002312/WS1133/0081/G; elvitegravir, cobicistat, emtricitabine, tenofovir - GENVOYA (CAP) - EMEA/H/C/004042/WS1133/0029/G; STRIBILD (CAP) - EMEA/H/C/002574/WS1133/0080/G; emtricitabine, rilpivirine, tenofovir alafenamide - ODEFSEY (CAP) - EMEA/H/C/004156/WS1133/0011/G; emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/WS1133/0136/G; tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/WS1133/0174/G

Applicants: Bristol-Myers Squibb and Gilead Sciences Ltd. (Atripla), Gilead Sciences International Ltd (Eviplera, Genvoya, Odefsey, Stribild, Truvada, Viread, Descovy)

PRAC Rapporteur: Amelia Cupelli

Scope: Grouped variations including: 1) update of sections 4.4 and 4.5 of the SmPC of tenofovir disoproxil fumarate (TDF)-containing products (Viread, Truvada, Atripla, Eviplera, Stribild) following the results from study GS-US-342-1167 (phase 1 study to evaluate the potential drug-drug interaction between sofosbuvir/velpatasvir (SOF/VEL) tablets and human

[3] Cytochrome P450 2B6

immunodefficiency virus antiretrovirals (HIV ARVs): efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/FTC/TDF; Atripla), emtricitabine/riplivirine/tenofovir disoproxil fumarate (FTC/RPV/TDF; Complera), dolutegravir (DTG; Tivicay) or elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide fumarate (EVG/COBI/FTC/TAF) in healthy subjects) and study GS-US-342-1326 (phase 1 study to evaluate the pharmacokinetic (PK) drug-drug interaction between SOF/VEL and HIV ARVs: elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (EVG/COBI/FTC/TDF), ritonavir-boosted darunavir (DRV/r) plus emtricitabine/tenofovir disoproxil fumarate (FTC/TDF), ritonavir-boosted atazanavir (ATV/r) plus FTC/TDF, ritonavir/boosted lopinavir (LPV/r) plus FTC/TDF or raltegravir plus FTC/TDF in healthy subjects); 2) update of section 4.5 for the tenofovir alafenamide (TAF)-containing products (Genvoya, Descovy, Odefsey) following the results from study GS-US-342-1167. The Package Leaflets and RMPs are updated accordingly

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

5.3.9. Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/WS1134/0137; Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/WS1134/0175

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Caroline Laborde

Scope: Worksharing variation to update section 4.5 of the SmPC for Viread and Truvada with data on interaction between emtricitabine (FTC), tenofovir disoproxil fumarate (TDF), ledipasvir, sofosbuvir and dolutegavir based on new clinical pharmacology data from study GS-US-377-1501. This is a Phase 1, open-label, multiple-dose study that evaluated the pharmacokinetic drug-drug interaction potential between Harvoni (ledipasvir [LDV]/sofosbuvir [SOF]) and FTC/TDF+dolutegravir (DTG). The RMP version 22 for Viread and version 14 for Truvada have also been submitted

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

5.3.10. Fluticasone furoate, vilanterol - RELVAR ELLIPTA (CAP) - EMEA/H/C/002673/WS0992/0022/G; REVINTY ELLIPTA (CAP) - EMEA/H/C/002745/WS0992/0017/G

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Grouped worksharing variation to update sections 4.4, 4.8 and 5.1 of the SmPC in order to include data from study HZC113782 (SUMMIT): clinical outcomes study comparing the effect of fluticasone furoate/vilanterol inhalation powder 100/25mcg with placebo on survival in subjects with moderate chronic obstructive pulmonary disease (COPD) and a history of or at increased risk for cardiovascular disease. In addition, section 4.8 of the SmPC is updated to add 'paradoxical bronchospasm' to the list of adverse reactions as well as section 5.1 of the SmPC to correct an error identified in the pharmacodynamic section. The Package Leaflet, Labelling and RMP (version 8.1) are updated accordingly

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

5.3.11. Fluticasone furoate, vilanterol - RELVAR ELLIPTA (CAP) - EMEA/H/C/002673/WS1101/0029; REVINTY ELLIPTA (CAP) - EMEA/H/C/002745/WS1101/0025

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of section 5.1 of the SmPC in order to update the safety information with the results of HZC115151 study: a 12-month, open label, randomised, effectiveness study to evaluate fluticasone furoate/vilanterol inhalation powder delivered once daily via a novel dry powder inhaler (NDPI) compared with the existing chronic obstructive pulmonary disease (COPD) maintenance therapy alone in subjects with COPD (Annex II condition) of the Relvar Ellipta and Revinty Ellipta (92/22mcg strength only). The RMP (version 8.3) is updated accordingly

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

5.3.12. Insulin detemir - LEVEMIR (CAP) - EMEA/H/C/000528/II/0084

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Doris Stenver

Scope: Submission of the summary analysis report on the incidence of neoplasms with the combination of liraglutide and insulin detemir from the cardiovascular outcome trial for Victoza (liraglutide): study EX2211-3748 (LEADER: liraglutide effect and action in diabetes): a long-term, multicentre, international, randomised double-blind, placebo-controlled trial to determine liraglutide effects on cardiovascular events. The RMP (version 18) is updated accordingly to delete the important potential risk of malignant neoplasms following combination treatment with insulin detemir + liraglutide + metformin

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

5.3.13. Miglustat - ZAVESCA (CAP) - EMEA/H/C/000435/II/0056, Orphan

Applicant: Actelion Registration Ltd.

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the eighth Niemann-Pick type C (NPC) registry report and update of Annex II-D of the Product Information to delete the NPC Registry listed as an obligation to the marketing authorisation. The RMP (version 12.1) is updated accordingly. In addition, the MAH took the opportunity to introduce minor changes and bring the Product Information and Annex A in line with the latest QRD template (version 10)

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

5.3.14. Pasireotide - SIGNIFOR (CAP) - EMEA/H/C/002052/X/0030/G, Orphan

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Line extension to introduce two new strengths for the 'powder and solvent for

suspension for injection pharmaceutical form' (10 mg and 30 mg) grouped with a type II variation to extend the indication to include the 'treatment of adult patients with Cushing's disease for whom surgery is not an option or for whom surgery has failed' to the intramuscular injection formulations. The RMP (version 5.0) is updated accordingly

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

5.3.15. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0018/G

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Grouped variation to update section 5.1 of the SmPC to reflect the data from the post-authorisation efficacy studies (PAES) in melanoma study P001 (phase I study of pembrolizumab alone in patients with progressive locally advanced or metastatic carcinoma, melanoma, and non-small cell lung carcinoma), study P002 (randomized, phase II study of pembrolizumab versus chemotherapy in patients with advanced melanoma) and study P006 (a multicentre, randomized, controlled, three-arm, phase III study to evaluate the safety and efficacy of two dosing schedules of pembrolizumab compared to ipilimumab in patients with advanced melanoma). Annex II and the RMP (version 6.0) are updated accordingly

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

5.3.16. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0025

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC to add a warning on the risk of severe skin reactions and to communicate that Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), including fatal cases, have been reported in patients treated with pembrolizumab. The Package Leaflet and the RMP (version 8.0) are updated accordingly. The submission includes a proposed DHPC and communication plan

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

5.3.17. Rilpivirine - EDURANT (CAP) - EMEA/H/C/002264/II/0024

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.2, 4.4, 4.6, 5.1 and 5.2 of the SmPC in order to include information: use of rilpivirine in combination with a background regimen for the treatment of HIV-1 infection during pregnancy and postpartum, without dose adjustment following final results from study TMC114HIV3015 listed as a category 3 study in the RMP. This is a single arm, open-label trial to assess the pharmacokinetics of darunavir/ritonavir, etravirine, and rilpivirine in HIV-1-infected pregnant women. The Package Leaflet is updated accordingly. The RMP version 7.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce the latest renewal date in section 9 of the SmPC and the physical address of the Netherlands Local Representative in the PIL section 6.

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

5.3.18. Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/II/0017/G

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variation including: 1) update of sections 4.2, 4.8 and 5.1 of the SmPC to reflect available data from previously untreated patients (PUP) based on the interim report of interventional study GENA-05 (an immunogenicity, efficacy and safety of treatment with human cell line-derived recombinant factor VIII (human-cl-rhFVIII) in previously untreated patients with severe haemophilia A). The Package Leaflet and the RMP (version 8.0) are updated accordingly. In addition, the MAH took the opportunity to update the Product Information throughout to bring it in line with the core Summary of Product Characteristics for human plasma-derived and recombinant coagulation factor VIII products (EMA/CHMP/BPWP/1619/1999 rev. 2) and with the latest QRD template (version 10). Moreover, the MAH proposed to combine the SmPC for all strengths and to update Annex A with detailed information on the packaging

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

5.3.19. Sitagliptin - JANUVIA (CAP) - EMEA/H/C/000722/WS1141/0056; RISTABEN (CAP) - EMEA/H/C/001234/WS1141/0048; TESAVEL (CAP) - EMEA/H/C/000910/WS1141/0056; XELEVIA (CAP) - EMEA/H/C/000762/WS1141/0060

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 4.4 of the SmPC in order to add 'bullous pemphigoid' as a warning following the PRAC outcome for EMEA/H/C/PSUSA/2711/201408 procedure. The Labelling and the RMP (version 7) are updated accordingly

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

5.3.20. Sitagliptin, metformin hydrochloride - EFFICIB (CAP) - EMEA/H/C/000896/WS1130/0081/G; JANUMET (CAP) - EMEA/H/C/000861/WS1130/0081/G; RISTFOR (CAP) - EMEA/H/C/001235/WS1130/0068/G; VELMETIA (CAP) - EMEA/H/C/000862/WS1130/0084/G

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variation including: 1) update of section 4.4 of the SmPC in order to add 'bullous pemphigoid' as a warning following the PRAC outcome for EMEA/H/C/PSUSA/2711/201408 procedure. The Labelling and the RMP (version 7) are updated accordingly; 2) The RMP (version 7) is updated to add a targeted questionnaire related to lactic acidosis as part of the outcome of referral procedure EMEA/H/A-31/1432 on metformin-containing medicines completed in 2016

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

5.3.21. Sofosbuvir, ledipasvir - HARVONI (CAP) - EMEA/H/C/003850/II/0039

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication to add treatment of chronic hepatitis C in adolescents aged 12 to <18 years. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add information on posology, warnings, safety, efficacy and pharmacokinetics. The Package Leaflet and RMP (version 2) are updated accordingly

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

5.3.22. Teduglutide - REVESTIVE (CAP) - EMEA/H/C/002345/X/0029, Orphan

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Line extension to add a new strength of 1.25 mg (paediatric formulation). The RMP (version 7.4) is updated accordingly

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

5.3.23. Tolvaptan - SAMSCA (CAP) - EMEA/H/C/000980/X/0024

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Line extension to add a new strength of 7.5 mg tablets. The RMP (version 13.0) is updated accordingly

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

5.3.24. Varenicline - CHAMPIX (CAP) - EMEA/H/C/000699/II/0064

Applicant: Pfizer Limited

PRAC Rapporteur: Doris Stenver

Scope: Update of sections 4.5 and 5.1 of the SmPC in order to update the safety information based on the final results from study A3051078: a varenicline pregnancy cohort study (a prospective population-based cohort study to examine whether varenicline use during pregnancy is associated with an increased risk of major congenital malformations in infants above that associated with smoking during pregnancy). The Package Leaflet and the RMP (version 10.1) are updated accordingly. In addition, the MAH took the opportunity to bring the Product Information in line with the latest QRD template (version 10)

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

5.3.25. Vismodegib - ERIVEDGE (CAP) - EMEA/H/C/002602/II/0032

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 5.3 of the SmPC in order to reflect non-clinical carcinogenicity studies (MEA 003): 1) study 13-0322: a 26-week oral gavage carcinogenicity study with vismodegib in hemizygous CByB6F1-Tg(HRAS)2Jic mice; 2) study 13-0323: a 104-week and 52-week with a 12-week recovery phase oral gavage carcinogenicity study with vismodegib in Sprague Dawley rats. The RMP (version 12.0) is updated accordingly. Furthermore, additional routine changes (including some resulting from the assessment of RMP version 11) have been introduced

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 procedures including centrally authorised products (CAPs) only

6.1.1. Afatinib - GIOTRIF (CAP) - PSUSA/00010054/201609

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Albiglutide - EPERZAN (CAP) - PSUSA/00010175/201609

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Alemtuzumab - LEMTRADA (CAP) - PSUSA/00010055/201609

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Alirocumab - PRALUENT (CAP) - PSUSA/00010423/201609

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Apremilast - OTEZLA (CAP) - PSUSA/00010338/201609

Applicant: Celgene Europe Limited

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Bedaquiline - SIRTURO (CAP) - PSUSA/00010074/201609

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Bivalirudin - ANGIOX (CAP) - PSUSA/00000421/201609

Applicant: The Medicines Company UK Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Canagliflozin - INVOKANA (CAP); canagliflozin, metformin - VOKANAMET (CAP) - PSUSA/00010077/201609

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Cangrelor - KENGREXAL (CAP) - PSUSA/00010360/201609

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Ceftolozane, tazobactam - ZERBAXA (CAP) - PSUSA/00010411/201609

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Cholic acid[4] - KOLBAM (CAP) - PSUSA/00010182/201609

Applicant: Retrophin Europe Ltd

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Cholic acid[5] - ORPHACOL (CAP) - PSUSA/00010208/201609

Applicant: Laboratoires CTRS - Boulogne Billancourt

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Ciclosporin[6] - IKERVIS (CAP) - PSUSA/00010362/201609

Applicant: Santen Oy

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Dabigatran - PRADAXA (CAP) - PSUSA/00000918/201609

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Daptomycin - CUBICIN (CAP) - PSUSA/00000931/201609

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[4] Treatment of inborn errors in primary bile acid synthesis due to sterol 27-hydroxylase (presenting as cerebrotendinous xanthomatosis, CTX) deficiency, 2- (or α-) methylacyl-CoA racemase (AMACR) deficiency or cholesterol 7α-hydroxylase (CYP7A1) deficiency indications only

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

[6] For topical use only

6.1.16. Denosumab[7] - PROLIA (CAP) - PSUSA/00000954/201609

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Denosumab[8] - XGEVA (CAP) - PSUSA/00009119/201609

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Dexamethasone[9] - NEOFORDEX (CAP) - PSUSA/00010480/201609

Applicant: Laboratoires CTRS

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Dulaglutide - TRULICITY (CAP) - PSUSA/00010311/201609

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Eftrenonacog alfa - ALPROLIX (CAP) - PSUSA/00010499/201609

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Etravirine - INTELENCE (CAP) - PSUSA/00001335/201609

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Caroline Laborde

[7] Treatment of osteoporosis and for bone loss associated with hormone ablation in prostate cancer indications only
[8] Treatment of skeletal related events associated with bone metastases and of giant cell tumour of bone indications only
[9] Treatment of symptomatic multiple myeloma indication for centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Ferric citrate coordination complex - FEXERIC (CAP) - PSUSA/00010418/201609

Applicant: Keryx Biopharma UK Ltd.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Glycopyrronium bromide[10] - ENUREV BREEZHALER (CAP); SEEBRI BREEZHALER (CAP); TOVANOR BREEZHALER (CAP) - PSUSA/00010047/201609 (with RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Guanfacine - INTUNIV (CAP) - PSUSA/00010413/201609

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Human coagulation factor X - COAGADEX (CAP) - PSUSA/00010481/201609

Applicant: Bio Products Laboratory Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Idebenone[11] - RAXONE (CAP) - PSUSA/00010412/201609

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[10] Treatment of chronic obstructive pulmonary disease indication only
[11] Centrally authorised product(s) only

6.1.27. Indacaterol, glycopyrronium bromide - ULTIBRO BREEZHALER (CAP); ULUNAR BREEZHALER (CAP); XOTERNA BREEZHALER (CAP) - PSUSA/00010105/201609 (with RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Infliximab[12] - REMICADE (CAP) - PSUSA/00010231/201608

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Insulin human[13] - INSUMAN (CAP) - PSUSA/00010107/201609

Applicant: Sanofi-aventis Deutschland GmbH

PRAC Rapporteur: Jean-Michel Dogne

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Isavuconazole - CRESEMBA (CAP) - PSUSA/00010426/201609

Applicant: Basilea Medical Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Ixekizumab - TALTZ (CAP) - PSUSA/00010493/201609

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[12] Biosimilars excluded
[13] Intraperitoneal route of administration

6.1.32. Leflunomide - ARAVA (CAP); LEFLUNOMIDE MEDAC (CAP); LEFLUNOMIDE WINTHROP (CAP) - PSUSA/00001837/201609

Applicant: Sanofi-aventis Deutschland GmbH (Arava, Leflunomide Winthrop), Medac Gesellschaft fur klinische Spezialpraparate GmbH (Leflunomide medac)

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Mepolizumab - NUCALA (CAP) - PSUSA/00010456/201609

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Midazolam[14] - BUCCOLAM (CAP) - PSUSA/00010118/201609

Applicant: Shire Services BVBA

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Moroctocog alfa - REFACTO AF (CAP) - PSUSA/00002089/201608

Applicant: Pfizer Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Naloxegol - MOVENTIG (CAP) - PSUSA/00010317/201609

Applicant: Kyowa Kirin Limited

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Naltrexone, bupropion - MYSIMBA (CAP) - PSUSA/00010366/201609

Applicant: Orexigen Therapeutics Ireland Limited

[14] Oromucosal solution, treatment of prolonged, acute, convulsive seizures indication(s) only

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Oritavancin - ORBACTIV (CAP) - PSUSA/00010368/201609

Applicant: The Medicines Company UK Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Pembrolizumab - KEYTRUDA (CAP) - PSUSA/00010403/201609

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Pyronaridine, artesunate - PYRAMAX (Art 58[15]) - EMEA/H/W/002319/PSUV/0014

Applicant: Shin Poong Pharmaceutical Co., Ltd.

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.41. Raltegravir - ISENTRESS (CAP), raltegravir, lamivudine - DUTREBIS (CAP) - PSUSA/00010373/201609

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Regorafenib - STIVARGA (CAP) - PSUSA/00010133/201609

Applicant: Bayer Pharma AG

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

[15] Article 58 of Regulation (EC) No 726/2004 allows the Agency's 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)

Action: For adoption of recommendation to CHMP

6.1.43. Retigabine - TROBALT (CAP) - PSUSA/00002624/201609

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Riociguat - ADEMPAS (CAP) - PSUSA/00010174/201609

Applicant: Bayer Pharma AG

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Ritonavir - NORVIR (CAP) - PSUSA/00002651/201608

Applicant: AbbVie Ltd.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Rivaroxaban - XARELTO (CAP) - PSUSA/00002653/201609

Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Telavancin - VIBATIV (CAP) - PSUSA/00002879/201609

Applicant: Theravance Biopharma Ireland Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Telbivudine - SEBIVO (CAP) - PSUSA/00002880/201608

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Teriflunomide - AUBAGIO (CAP) - PSUSA/00010135/201609 (with RMP)

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Tobramycin[16] - VANTOBRA (CAP) - PSUSA/00010370/201609

Applicant: PARI Pharma GmbH

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Trabectedin - YONDELIS (CAP) - PSUSA/00003001/201609

Applicant: Pharma Mar, S.A.

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Trastuzumab - HERCEPTIN (CAP) - PSUSA/00003010/201609 (with RMP)

Applicant: Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Vinflunine - JAVLOR (CAP) - PSUSA/00003123/201609

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

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

6.2.1. Anagrelide - XAGRID (CAP); NAP - PSUSA/00000208/201609

Applicant(s): Shire Pharmaceutical Contracts Ltd. (Xagrid), various

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Zoledronic acid[17] - ZOLEDRONIC ACID HOSPIRA (CAP); ZOLEDRONIC ACID MEDAC (CAP); ZOMETA (CAP); NAP - PSUSA/00003149/201608

Applicant(s): Hospira UK Limited (Zoledronic acid Hospira), Medac Gesellschaft fur klinische Spezialpraparate GmbH (Zoledronic acid medac), Novartis Europharm Ltd (Zometa), various

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Ajmaline (NAP) - PSUSA/00000072/201608

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Budesonide, formoterol (NAP) - PSUSA/00000450/201608

Applicant(s): various

PRAC Lead: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Buserelin (NAP) - PSUSA/00000462/201608

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

[17] Treatment of cancer and fractures indication(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Cilostazol (NAP) - PSUSA/00010209/201608

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Ethinylestradiol, gestodene[18] (NAP) - PSUSA/00010145/201608

Applicant(s): various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Finasteride (NAP) - PSUSA/00001392/201608

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Fluocinolone acetonide[19] (NAP) - PSUSA/00010224/201608

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Fosfomycin[20] (NAP) - PSUSA/00010336/201607

Applicant(s): various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[18] Transdermal application
[19] Intravitreal implant in applicator
[20] Intravenous (IV) formulation

6.3.9. Fosfomycin[21] (NAP) - PSUSA/00010326/201607

Applicant(s): various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Human plasma protease C1 inhibitor[22] (NAP) - PSUSA/00010163/201608

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Lisdexamfetamine (NAP) - PSUSA/00010289/201608

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Paricalcitol (NAP) - PSUSA/00002316/201608

Applicant(s): various

PRAC Lead: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Timolol[23] (NAP) - PSUSA/00010439/201607

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[21] Oral formulation
[22] Nationally authorised products
[23] Ocular preparations

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Betaine anhydrous - CYSTADANE (CAP) - EMEA/H/C/000678/LEG 023

Applicant: Orphan Europe S.A.R.L.

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of MAH's response to PSUSA/00000390/201602 (analysis of the data on patients with remethylation disorders with baseline and follow-up measures with methionine and homocysteine plasma level, issued from the Cystadane Surveillance Programme (CSP))

Action: For adoption of advice to CHMP

6.4.2. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/LEG 039.1

Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of MAH's response to LEG 039 (cumulative review on cases of liver-related events (hepatotoxicity) as requested in the recommendation of PSUSA/00002653/201509 adopted by PRAC in April 2016) as per request for supplementary information (RSI) adopted in November 2016

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[24]

7.1.1. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/PSA/S/0016

Applicant: Celgene Europe Limited

PRAC Rapporteur: Claire Ferard

Scope: MAH's request for a 2-months extension to respond to the amendment of PASS protocol MDS-012: a retrospective drug-utilisation study to describe patterns of Revlimid use

Action: For discussion

7.1.2. Levofloxacin - QUINSAIR (CAP) - EMEA/H/C/PSP/S/0049.2

Applicant: Horizon Pharma Europe B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Updated PASS protocol for an open-label, observational safety study of Quinsair (nebulised levofloxacin hemihydrate) in patients with cystic fibrosis and chronic

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

Pseudomonas aeruginosa infection, using data collected through European cystic fibrosis registries as per the request for supplementary information (RSI) adopted at PRAC in December 2016

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

7.1.3. Ethinylestradiol (NAP); levonorgestrel, ethinylestradiol (NAP) - EMEA/H/N/PSP/J/0054

Applicant(s): Teva Pharma B.V. (Seasonique), various

PRAC Rapporteur: Claire Ferard

Scope: PASS protocol for a drug utilisation study of Seasonique in Europe with the aim to assess both safety outcomes and drug utilisation patterns

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

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

7.2.1. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/MEA 019.2

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 019.1: revised protocol for a drug utilisation study (DUS) of alirocumab in Europe to assess the effectiveness of the dosing recommendation to avoid very low low-density lipoprotein (LDL)-C levels (study OBS14697), as per the request for supplementary information (RSI) adopted in December 2016

Action: For adoption of advice to CHMP

7.2.2. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 012

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Valerie Strassmann

Scope: PASS protocol for an epidemiological study to evaluate the risk of acute pancreatitis in patients with type 2 diabetes mellitus (T2DM) newly exposed to canagliflozin containing products compared to patients with T2DM exposed to non-SGLT2 inhibitor anti-hyperglycaemic agents

Action: For adoption of advice to CHMP

7.2.3. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 011

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: PASS protocol of an epidemiological study to evaluate the risk of acute pancreatitis

[25] 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

in patients with type 2 diabetes mellitus (T2DM) newly exposed to canagliflozin containing products compared to patients with T2DM exposed to non-SGLT2 inhibitor anti-hyperglycaemic agents

Action: For adoption of advice to CHMP

7.2.4. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/MEA 067.1

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: MAH's response to MEA 067: revised PASS protocol and questionnaire for a cross sectional physician survey (study N6987) to assess the impact of educational materials on prescribers' awareness of doses and biological monitoring recommendations and also to assess the awareness and appropriate use of both formulations (orodispersible tablets and film-coated tablets) as requested as part of X/43 (RMP, category 3 study), as per the request for supplementary information (RSI) adopted in December 2016

Action: For adoption of advice to CHMP

7.2.5. Necitumumab - PORTRAZZA (CAP) - EMEA/H/C/003886/MEA 001.2

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 001.1 on a revised PASS protocol for a survey to assess physicians'/oncologists' understanding of the key conditions for the safe use of necitumumab, as per the request for supplementary information (RSI) adopted in November 2016

Action: For adoption of advice to CHMP

7.2.6. Necitumumab - PORTRAZZA (CAP) - EMEA/H/C/003886/MEA 002.2

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 002.1 on a revised PASS protocol for an observational prospective study to assess the incidence, severity, and sequelae of all serious life-threatening identified and potential risks for necitumumab treatment in the approved indication, as per the request for supplementary information (RSI) adopted by PRAC and CHMP in November 2016

7.2.7. Reslizumab - CINQAERO (CAP) - EMEA/H/C/003912/MEA 004

Applicant: Teva Pharmaceuticals Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: PASS protocol for study C38072-AS-50026, a non-interventional phase IV study: effect of reslizumab exposure on pregnancy outcomes: active pregnancy surveillance

Action: For adoption of advice to CHMP

7.2.8. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/MEA 001.2

Applicant: Actelion Registration Ltd.

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 001.1: revised protocol for a non-interventional non-imposed PASS (AC-065A401): an observational cohort study of pulmonary arterial hypertension (PAH) patients exposed and unexposed to selexipag in routine clinical practice, as per the request for supplementary information (RSI) adopted in February 2017

Action: For adoption of advice to CHMP

7.2.9. Sodium oxybate - XYREM (CAP) - EMEA/H/C/000593/MEA 019

Applicant: UCB Pharma Ltd.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Protocol for study NA0001 (EU PAS register EUPAS15024): a non-interventional PASS on the effectiveness of the educational materials

Action: For adoption of advice to CHMP

7.2.10. Tocilizumab – ROACTEMRA (CAP) - EMEA/H/C/000955/MEA/045.3

Applicant: Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of MAH proposal to include additional data-sets along with the British Society of Rheumatology Biologics Register (BSRBR) data to complete the post-authorisation measure. This non-interventional post-authorisation safety study aims to collect further safety data, including data about hypersensitivity, in patients who switch route of tocilizumab administration from intravenous to subcutaneous pharmaceutical forms

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[26]

7.3.1. Cyproterone, ethinylestradiol (NAP) - EMEA/H/N/PSR/J/0005.1

Applicant: Bayer Pharma AG (Diane 35); various

PRAC Rapporteur: Menno van der Elst

Scope: Addendum to final study results, with additional French data on the drug utilisation study (DUS) (survey) designed to characterize the prescribing behaviours for cyproterone acetate/ethinylestradiol (CPA/EE) in five European countries: Austria, Czech Republic, France, the Netherlands and Spain

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

Action: For adoption of revised PRAC Assessment Report

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

7.4.1. Collagenase Clostridium histolyticum - XIAPEX (CAP) - EMEA/H/C/002048/II/0089

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Martin Huber

Scope: Submission of the final clinical study report for study B1531005, a non-interventional study to evaluate the outcomes (clinical treatment success measured by goniometry assessment, recurrence rate measured by goniometry assessment, subject and physician global assessment of treatment satisfaction, complications resulting from the procedure based on the adverse event/serious adverse event (AE/SAE)) of 3 various treatment options for Dupuytren's contracture, listed as a category 3 study in the RMP. The RMP (version 13.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.2. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/II/0009

Applicant: Samsung Bioepis UK Limited (SBUK)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final clinical study report (CSR) of study SB2-G31-RA: a randomised, double-blind, parallel group, multicentre clinical study to evaluate the efficacy, safety, pharmacokinetics and immunogenicity of Flixabi compared to Remicade in subjects with moderate to severe rheumatoid arthritis despite methotrexate therapy. The RMP (version 4) is updated to reflect the results from the 78 weeks CSR, to exclude 2 of the 5 registries of the pharmacovigilance plan and update the due date for the prospective observational cohort study of Flixabi in ankylosing spondylitis (AS) and Crohn's disease (CD) patients

Action: For adoption of PRAC Assessment Report

7.4.3. Liraglutide - SAXENDA (CAP) - EMEA/H/C/003780/WS0943/0009; VICTOZA (CAP) - EMEA/H/C/001026/WS0943/0041

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final results from a RMP category 3 study NNN2211-3784: liraglutide safety and surveillance programme using the Optum research database study and its sub-study on breast cancer. The RMP (version 26) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

7.4.4. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/II/0101

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final clinical study report for TYGRIS, a post-marketing safety observational cohort programme designed to obtain long-term safety data (approximately 5 years) in subjects with multiple sclerosis (MS) treated with natalizumab, and comprising parallel studies 101MS402 (United States and Canada) and 101MS403 (rest of World). The RMP (version 23) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.5. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/II/0102

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final clinical study report for study STRATIFY-2 (101JC402), an observational, longitudinal cohort study designed to gather post-marketing data on the incidence of progressive multifocal leukoencephalopathy (PML) in natalizumab-treated subjects with MS. The RMP (version 23) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

7.5.1. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 056.2

Applicant: Genzyme Europe BV

PRAC Rapporteur: Caroline Laborde

Scope: MAH's response to MEA 056.1: interim report from a healthcare pofessional survey that measure the effectiveness of the approved safety information packet (SIP) as per the request for supplementary information (RSI) adopted in December 2016

Action: For adoption of advice to CHMP

7.5.2. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/MEA 003.2

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a yearly report for study BEL115467/HGS1006-C1113: a randomized, double-blind placebo-controlled large safety study, based on a protocol agreed with CHMP, evaluating over a minimum of 1 year the incidence of all-cause mortality and adverse events of special interest in patients with systemic lupus

Action: For adoption of advice to CHMP

7.5.3. Insulin detemir - LEVEMIR (CAP) - EMEA/H/C/000528/MEA 045.6

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Doris Stenver

Scope: Third progress report covering the period from November 2015 until October 2016 for PASS NN304-4016 (EVOLVE study): an international non-interventional prospective cohort registry to evaluate the safety of treatment with Levemir (insulin detemir) in pregnant women with diabetes mellitus

Action: For adoption of advice to CHMP

7.5.4. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/MEA 265.7

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Caroline Laborde

Scope: MAH's response to MEA 265.6: interim results for study GS-EU-174-1403, a pharmacoepidemiology study to define the long-term safety profile of tenofovir disoproxil fumarate and describe the management of tenofovir-associated renal and bone toxicity in chronic hepatitis B-infected adolescents aged 12 to <18 years in Europe as per the request for supplementary information (RSI) adopted in October 2016

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 005.11

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Valerie Strassmann

Scope: Sixth independent data monitoring committee (IDMC) status report for DIA 3008 (CANVAS: a randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of JNJ-28431754 (canagliflozin) on cardiovascular outcomes in adult subjects with type 2 diabetes mellitus (T2DM)) and DIA4003 (CANVAS-R: a randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of canagliflozin on renal endpoints in adult subjects with T2DM) studies

Action: For adoption of advice to CHMP

7.6.2. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 004.11

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Sixth independent data monitoring committee (IDMC) status report for DIA 3008 (CANVAS: a randomized, multicentre, double-blind, parallel, placebo-controlled study of the effects of JNJ-28431754 (canagliflozin) on cardiovascular outcomes in adult subjects with type 2 diabetes mellitus (T2DM)) and DIA4003 (CANVAS-R: a randomized, multicentre,

double-blind, parallel, placebo-controlled study of the effects of canagliflozin on renal endpoints in adult subjects with T2DM) studies

Action: For adoption of advice to CHMP

7.6.3. Edoxaban - LIXIANA (CAP) - EMEA/H/C/002629/MEA 005.3

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 005.3: evaluation of a statistical analysis plan for study DSE-EDO-01-14-EU: a drug utilisation study (DUS) for exploring edoxaban prescription patterns in Europe: a retrospective drug utilisation chart review study, as per the request for supplementary information (RSI) adopted in September 2016

Action: For adoption of advice to CHMP

7.6.4. Edoxaban - LIXIANA (CAP) - EMEA/H/C/002629/MEA 006.3

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 006.3: evaluation of a statistical analysis plan for study DSE-EDO-04-14-EU ETNA-AF: a non-interventional study on edoxaban treatment in routine clinical practice for patients with non valvular atrial fibrillation, as per the request for supplementary information (RSI) adopted in September 2016

Action: For adoption of advice to CHMP

7.6.5. Edoxaban - LIXIANA (CAP) - EMEA/H/C/002629/MEA 007.3

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 007.3: evaluation of a statistical analysis plan for study DSE-EDO-05-14-EU ETNA-AF: a non-interventional study on edoxaban treatment in routine clinical practice in patients with venous thromboembolism in Europe, as per the request for supplementary information (RSI) adopted in September 2016

Action: For adoption of advice to CHMP

7.6.6. Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/MEA 093.4

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: MAH's responses on the statistical analysis plan (SAP) to MEA 093.3: revised PASS registry protocol for a long-term surveillance study of rituximab (Mabthera)-treated patients with granulomatosis, with polyangiitis (GPA) or microscopic polyangiitis (MPA) (RIVAS) as per request for supplementary information adopted in November 2016

Action: For adoption of advice to CHMP

7.6.7. Valproate (NAP) - EMEA/H/N/PSI/J/0001

Applicant(s): Sanofi; various

PRAC Rapporteur: Sabine Straus

Scope: Submission of the first interim study report of a non-interventional imposed PASS, designed to assess the effectiveness of risk minimisation measures in the outpatient setting, including the 3-year data collected for the pre-implementation period in 4 out of 5 countries (France, Germany, Spain, Sweden and United Kingdom) versus the 6-month data collected for the post-implementation period and submission of the final study report of the Joint PASS survey among Health Care to assess their knowledge and attitudes on prescribing conditions of valproate in France, Germany, Spain, Sweden and United Kingdom.

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/S/0011 (without RMP)

Applicant: Clinuvel (UK) Limited

PRAC Rapporteur: Valerie Strassmann

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Cholic acid - KOLBAM (CAP) - EMEA/H/C/002081/S/0020 (without RMP)

Applicant: Retrophin Europe Ltd

PRAC Rapporteur: Patrick Batty

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/S/0020 (without RMP)

Applicant: Gentium S.r.l.

PRAC Rapporteur: Julie Williams

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/S/0005 (without RMP)

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Carmela Macchiarulo

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - ZALMOXIS (CAP) - EMEA/H/C/002801/R/0003 (without RMP)

Applicant: MolMed SpA, ATMP[28]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.2.2. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/R/0032 (without RMP)

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Anidulafungin - ECALTA (CAP) - EMEA/H/C/000788/R/0033 (without RMP)

Applicant: Pfizer Limited

[28] Advanced therapy medicinal product

PRAC Rapporteur: Sabine Straus

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Capecitabine - CAPECITABINE MEDAC (CAP) - EMEA/H/C/002568/R/0017 (without RMP)

Applicant: Medac Gesellschaft fuer klinische Spezialpraeparate GmbH

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/R/0042 (without RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Nelarabine - ATRIANCE (CAP) - EMEA/H/C/000752/R/0037 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Orlistat - ALLI (CAP) - EMEA/H/C/000854/R/0054 (with RMP)

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Teglutide - REVESTIVE (CAP) - EMEA/H/C/002345/R/0038 (with RMP)

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Torbjorn Callreus

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

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

10.3.1. Desloratadine - AERIUS (CAP); AZOMYR (CAP); DASSELTA (CAP); DESLORATADINE ACTAVIS (CAP); DESLORATADINE RATIOPHARM (CAP); DESLORATADINE TEVA (CAP); NEOCLARITYN (CAP); NAP – EMEA/H/A-5(3)/1431

Applicant(s): Merck Sharp & Dohme Limited (Aerinaze, Aerius, Azomyr, Neoclarityn), Krka, d.d., Novo mesto (Dasselta), Actavis Group PTC ehf (Desloratadine Actavis), Ratiopharm GmbH (Desloratadine Ratiopharm), Teva B.V. (Desloratadine Teva), various

PRAC Rapporteur: Jean-Michel Dogne; PRAC Co-rapporteur: Jan Neuhauser

Scope: PRAC consultation on an ongoing CHMP review under Article 5(3) of Regulation (EC) No 726/2004 evaluating the possible switch of the prescription status of nationally-authorised desloratadine-containing products from 'medicinal products subject to prescription' to 'medicinal products not subject to prescription' (also known as OTC-over-the-counter)

Action: For adoption of advice to CHMP

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC Best Practice guide on efficiency – implementation quantitative goals – Q1 2017 statistics

PRAC lead: Martin Huber, Ulla Wändel Liminga, Menno van der Elst, Tatiana Magalova, Albert van der Zeijden, Marianne Lunzer, Jan Neuhauser

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh

None

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

12.3.1. Guideline on safety and efficacy follow-up – risk management plan of advanced therapy medicinal products (ATMP) – revision

Action: For discussion

12.4. Cooperation within the EU regulatory network

None

12.5. Cooperation with International Regulators

12.5.1. Direct oral anticoagulants (DOAC) EMA-founded study - update on study protocol and international collaboration

Action: For discussion

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

12.6.1. Patient registry initiative - update and organisation of a workshop on cystic fibrosis (CF) on 14 June 2017 and a workshop on multiple-sclerosis (MS) on 7 July 2017

Action: For discussion

12.7. PRAC work plan

None

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system - PRAC work tracking including quarterly workload measures and performance indicators for the last three months - predictions

Action: For discussion

12.8.2. Marketing authorisation applications (MAA) expected for 2017 – Q1 2017 update

Action: For discussion

12.8.3. PRAC workload statistics - Q1 2017

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Sabine Straus

Action: For discussion

12.11.2. Signal management – handling of MAHs' signals following the go-live of the new EudraVigilance system

PRAC lead: Sabine Straus

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring – impact on pharmacovigilance performance

Action: For discussion

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- EudraVigilance auditable requirement project update

Action: For discussion

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.14.3. Strategy on measuring the impact of pharmacovigilance activities - effectiveness of risk minimisation measures: diclofenac and hydroxyzine impact study protocols

Action: For discussion

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. Antiretroviral Pregnancy Registry (APR) – participation of generic[29] medicinal products – follow-up

PRAC lead: Julie Williams

[29] Article 10 (1) of Directive 2001/83/EC

Action: For adoption

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. Serious cutaneous adverse reactions (SCARs) - regulatory perspective

PRAC lead: Sabine Straus, Herve Le Louet, Zane Neikena

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/