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Inspections, Human Medicines Pharmacovigilance and Committees Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 09-12 April 2018

Chair: June Raine – Vice-Chair: Almath Spooner

09 April 2018, 13:00 – 19:30, room 3/A

10 April 2018, 08:30 – 19:30, room 3/A

11 April 2018, 08:30 – 19:30, room 3/A

12 April 2018, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

26 April 2018, 09:00-12:00, room 9/B, via teleconference

Health and safety information

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

Disclaimers

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

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

Note on access to documents

Some documents mentioned in the agenda cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents ([EMA/127362/2006, Rev. 1](http://www.ema.europa.eu/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 09-12 April 2018. See April 2018 PRAC minutes (to be published post May 2018 PRAC meeting).

1.2. Agenda of the meeting on 09-12 April 2018

Action: For adoption

1.3. Minutes of the previous meeting on 05-08 March 2018

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

3.1.1. Methotrexate¹ - JYLAMVO (CAP); NAP - EMEA/H/A-31/1463

Applicants: Therakind Limited (Jylamvo), various

¹ For oral use

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

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 questions (LoQ)

3.2. Ongoing procedures

3.2.1. Ulipristal acetate - ESMYA (CAP) - EMEA/H/A-20/1460

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga; PRAC Co-rapporteur: Menno van der Elst

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

Action: For adoption of a list of experts (LoE) for an ad-hoc expert group meeting

3.3. Procedures for finalisation

None

3.4. Re-examination procedures²

None

3.5. Others

None

4. Signals assessment and prioritisation³

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Alemtuzumab – LEMTRADA (CAP)

Applicant(s): Genzyme Therapeutics Ltd

PRAC Rapporteur: Anette Stark

Scope: Signal of cytomegalovirus (CMV) infection

Action: For adoption of PRAC recommendation

² Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC

³ Each signal refers to a substance or therapeutic class. The route of marketing authorisation is indicated in brackets (CAP for centrally authorised products; NAP for nationally authorised products including products authorised via mutual recognition procedures and decentralised procedure). Product names are listed for reference centrally authorised products (CAP) only. PRAC recommendations will specify the products concerned in case of any regulatory action required

EPITT 19193 – New signal

Lead Member State: DK

4.1.2. Belimumab – BENLYSTA (CAP)

Applicant(s): Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of lupus nephritis

Action: For adoption of PRAC recommendation

EPITT 19174 – New signal

Lead Member State: SE

4.1.3. Daratumumab – DARZALEX (CAP)

Applicant(s): Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Signal of encephalopathy

Action: For adoption of PRAC recommendation

EPITT 19176 – New signal

Lead Member State: PT

4.1.4. Dimethyl fumarate – TECFIDERA (CAP)

Applicant(s): Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: Signal of immune thrombocytopenic purpura, thrombocytopenia

Action: For adoption of PRAC recommendation

EPITT 19192 – New signal

Lead Member State: DE

4.1.5. Parathyroid hormone – NATPAR (CAP)

Applicant(s): Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Almath Spooner

Scope: Signal of nephrolithiasis

Action: For adoption of PRAC recommendation

EPITT 19177 – New signal

Lead Member State: IE

4.1.6. Pegfilgrastim – NEULASTA (CAP)

Applicant(s): Amgen Europe B.V.

PRAC Rapporteur: To be appointed

Scope: Signal of pulmonary haemorrhage

Action: For adoption of PRAC recommendation

EPITT 19181 – New signal

Lead Member State: UK

4.1.7. Sitagliptin – JANUVIA (CAP), RISTABEN (CAP), TESAVEL (CAP), XELEVIA (CAP); sitagliptin, metformin hydrochloride – JANUMET (CAP), EFFICIB (CAP), RISTFOR (CAP), VELMETIA (CAP)

Angiotensin-converting-enzyme (ACE)-inhibitors: benazepril (NAP); captopril (NAP); cilazapril (NAP); delapril (NAP); enalapril (NAP); fosinopril (NAP); imidapril (NAP); lisinopril (NAP); moexipril (NAP); perindopril (NAP); quinapril (NAP); ramipril (NAP); spirapril (NAP); trandolapril (NAP); zofenopril (NAP); zofenopril, hydrochlorothiazide (NAP)

Applicant(s): Merck Sharp & Dohme Limited, various

PRAC Rapporteur: To be appointed

Scope: Signal of potential drug interaction between sitagliptin and angiotensin-converting-enzyme (ACE)-inhibitors leading to an increased risk of angioedema

Action: For adoption of PRAC recommendation

EPITT 17608 – New signal

Lead Member State: NL

4.1.8. Tocilizumab – ROACTEMRA (CAP)

Applicant(s): Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of hypofibrinogenaemia

Action: For adoption of PRAC recommendation

EPITT 19179 – New signal

Lead Member State: DE

4.2. New signals detected from other sources

4.2.1. Dienogest, ethinylestradiol (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: New information on the known risk of venous thromboembolism with combined

hormonal contraceptives (CHCs) containing dienogest and ethinylestradiol (DNG/EE)

Action: For adoption of PRAC recommendation

EPITT 17409 – New signal

Lead Member State: DE

4.2.2. Emicizumab – HEMLIBRA (CAP)

Applicant(s): Roche Registration Limited

PRAC Rapporteur: Amelia Cupelli

Scope: New information on the known risk of haemorrhagic events

Action: For adoption of PRAC recommendation

EPITT 19214 – New signal

Lead Member State: IT

4.2.3. Duloxetine – ARICLAIM (CAP), CYMBALTA (CAP), DULOXETINE LILLY (CAP), DULOXETINE MYLAN (CAP), DULOXETINE ZENTIVA (CAP), XERISTAR (CAP), YENTREVE (CAP); NAP

Applicant(s): Eli Lilly Nederland B.V. (Ariclaim, Cymbalta, Duloxetine Lilly, Xeristar, Yentreve), Generics UK Limited (Duloxetine Mylan), Zentiva k.s. (Duloxetine Zentiva), various

PRAC Rapporteur: To be appointed

Scope: Signal of interstitial lung disease

Action: For adoption of PRAC recommendation

EPITT 19175 – New signal

Lead Member State: ES

4.2.4. Olanzapine – ZALASTA (CAP), ZYPADHERA (CAP), ZYPREXA (CAP), ZYPREXA VELOTAB (CAP); NAP

Applicant(s): Eli Lilly Nederland B.V. (Zypadhera, Zyprexa, Zyprexa Velotab), KRKA d.d. (Zalasta), various

PRAC Rapporteur: To be appointed

Scope: Signal of somnambulism

Action: For adoption of PRAC recommendation

EPITT 19202 – New signal

Lead Member State: FI

4.3. Signals follow-up and prioritisation

4.3.1. Adalimumab – AMGEVITA (CAP), CYLTEZO (CAP), HUMIRA (CAP), IMRALDI (CAP), SOLYMBIC (CAP); infliximab – FLIXABI (CAP), INFLECTRA (CAP), REMICADE (CAP), REMSIMA (CAP)

Applicant(s): AbbVie Limited (Humira), Amgen Europe B.V. (Amgevita, Solymbic), Boehringer Ingelheim International GmbH (Cyltezo), Celltrion Healthcare Hungary Kft. (Remsima), Hospira UK Limited (Inflectra), Janssen Biologics B.V. (Remicade), Samsung Bioepis UK Limited (Flixabi, Imraldi)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of risk of lymphoma in patients with inflammatory bowel disease

Action: For adoption of PRAC recommendation

EPITT 19121 – Follow-up to January 2018

4.3.2. Amitriptyline (NAP)

Applicant(s): various

PRAC Rapporteur: Agni Kapou

Scope: Signal of dry eye

Action: For adoption of PRAC recommendation

EPITT 19173 – Follow-up to March 2018

4.3.3. Azithromycin (NAP)

Applicant(s): various

PRAC Rapporteur: Kimmo Jaakkola

Scope: Signal of increased rate of relapses of haematological malignancies and mortality in hematopoietic stem cell transplantation (HSCT) patients with azithromycin

Action: For adoption of PRAC recommendation

EPITT 18907 – Follow-up to September 2017

4.3.4. Dasatinib – SPRYCEL (CAP)

Applicant(s): Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Doris Stenver

Scope: Signal of cytomegalovirus (CMV) reactivation

Action: For adoption of PRAC recommendation

EPITT 19111 – Follow-up to December 2017

4.3.5. Human normal immunoglobulin – FLEBOGAMMA DIF (CAP), HIZENTRA (CAP), HYQVIA (CAP), KIOVIG (CAP), PRIVIGEN (CAP); NAP

Applicant(s): Baxalta Innovations GmbH (HyQvia), Baxter AG (Kiovig), CSL Behring GmbH (Privigen, Hizentra), Instituto Grifols, S.A. (Flebogamma DIF), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of lupus-like syndrome and related terms

Action: For adoption of PRAC recommendation

EPITT 19098 – Follow-up to December 2017

4.3.6. Lapatinib – TYVERB (CAP)

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of pulmonary hypertension

Action: For adoption of PRAC recommendation

EPITT 19089 – Follow-up to December 2017

4.3.7. Phenprocoumon (NAP)

Applicant(s): various

PRAC Rapporteur: Martin Huber

Scope: Signal related to risk of birth defects and foetal loss following first trimester exposure as a function of the time of withdrawal

Action: For adoption of PRAC recommendation

EPITT 18902 – Follow-up to December 2017

4.3.8. Vortioxetine – BRINTELLIX (CAP)

Applicant(s): H. Lundbeck A/S

PRAC Rapporteur: Laurence de Fays

Scope: Signal of angioedema and urticaria

Action: For adoption of PRAC recommendation

EPITT 19099 – Follow-up to December 2017

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Abemaciclib - EMEA/H/C/004302

Scope: Treatment of hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer

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

5.1.2. Adalimumab - EMEA/H/C/004429

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

5.1.3. Axicabtagene ciloleucel - EMEA/H/C/004480, Orphan

Applicant: Kite Pharma EU B.V., ATMP⁴

Scope: Treatment of diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL) and transformed follicular lymphoma (TFL)

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

5.1.4. Fexinidazole Art 58⁵ - EMEA/H/W/002320

Scope (accelerated assessment): Treatment of human African trypanosomiasis (HAT)

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

5.1.5. Lesinurad, allopurinol - EMEA/H/C/004412

Scope: Treatment of hyperuricaemia in gout patients

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

5.1.6. Patisiran - EMEA/H/C/004699, Orphan

Applicant: Alnylam UK Limited

Scope (accelerated assessment): Treatment of hereditary transthyretin-mediated amyloidosis

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

⁴ Advanced therapy medicinal product

⁵ 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)

5.1.7. Trastuzumab - EMEA/H/C/004463

Scope: Treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)

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

5.1.8. Vigabatrin - EMEA/H/C/004534, PUMA⁶

Scope: Treatment in monotherapy of infantile spasms (West's syndrome) and resistant partial epilepsy in infants and children

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

5.1.9. Volanesorsen - EMEA/H/C/004538, Orphan

Applicant: Akcea Therapeutics UK Ltd.

Scope: Adjunct to diet for the treatment of patients with familial chylomicronemia syndrome (FCS)

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

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

5.2.1. Adalimumab - IMRALDI (CAP) - EMEA/H/C/004279/II/0004

Applicant: Samsung Bioepis UK Limited (SBUK)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Updated RMP (version 2.1) in order to indicate changes in the distribution method for the Imraldi patient alert card (PAC) from its inclusion in Annex IIIa of the product information to be provided to patients by healthcare professionals by including the PAC in the physician educational material. Annex IIIa is updated accordingly

Action: For adoption of PRAC Assessment Report

5.2.2. Ceftazidime, avibactam - ZAVICEFTA (CAP) - EMEA/H/C/004027/II/0008

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Updated RMP (version 2.0) in order to incorporate data from the REPROVE study (already submitted in procedure II/02), align the RMP with the current EU template, and add current post-marketing experience relative to the RMP data lock point (DLP)(24/8/2017). REPROVE is a phase 3 randomized, multicentre, double-blind, double-dummy, parallel group comparative study to determine the efficacy, safety and tolerability of ceftazidime/avibactam (CAZ-AVI) (2,000 mg ceftazidime/500 mg avibactam) vs meropenem (1,000 mg) in the treatment of nosocomial pneumonia (NP), including

⁶ Paediatric-use marketing authorisation(s)

ventilator associated pneumonia (VAP), in hospitalised adults 18 years of age or older

Action: For adoption of PRAC Assessment Report

5.2.3. [Dasabuvir - EXVIERA \(CAP\) - EMEA/H/C/003837/WS1342/0034;](#)
[ombitasvir, paritaprevir, ritonavir - VIEKIRAX \(CAP\) -](#)
[EMEA/H/C/003839/WS1342/0041](#)

Applicant: AbbVie Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Updated RMP (version 4) to incorporate changes requested by PRAC (in procedures PSUSA/00010363/201701 and PSUSA/00010367/201701 finalised in September 2017): addition of a new potential risk of depression and suicide as newly identified safety concerns; removal of off-label use and medication error as potential risks; renaming of the potential risk of development of resistance to lack of efficacy/risk of development of resistance. In addition, the commitment dates for four ongoing studies (on-going and planned additional pharmacovigilance studies/activities in the pharmacovigilance plan) have been revised

Action: For adoption of PRAC Assessment Report

5.2.4. [Defibrotide - DEFITELIO \(CAP\) - EMEA/H/C/002393/II/0027, Orphan](#)

Applicant: Gentium S.r.l.

PRAC Rapporteur: Julie Williams

Scope: Updated RMP (version 4.0) in order to re-classify an imposed non-interventional PASS listed as a category 2 study in the RMP (specific obligation) to a study listed as a category 3 in the RMP (required additional pharmacovigilance activities). This study is an observational registry (DF-VOD2013-03-REG) aiming at recording safety and outcome data in patients diagnosed with severe veno-occlusive disease (VOD) following haematopoietic stem cell transplantation (HSCT) treated or not with Defitelio (defibrotide). Annex II of the product information is updated accordingly

Action: For adoption of PRAC Assessment Report

5.2.5. [Follitropin alfa - BEMFOLA \(CAP\) - EMEA/H/C/002615/II/0016](#)

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Menno van der Elst

Scope: Updated RMP (version 2) based on a phase 3 multicentre study conducted to compare the efficacy and safety of two recombinant human follicle stimulating hormone (r-hFSH) formulations in normal ovulatory women 35 to 42 years of age undergoing in-vitro fertilisation (IVF) (CSR FIN3002)

Action: For adoption of PRAC Assessment Report

5.2.6. [Follitropin alfa, lutropin alfa - PERGOVERIS \(CAP\) - EMEA/H/C/000714/II/0055](#)

Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Julie Williams

Scope: Updated RMP (version 5.1) in order to revise the epidemiology section based on the recent literature data, to revise the non-clinical part of the safety specification section with the data available from recombinant human follicle stimulating hormone (r-hFSH), recombinant human luteinizing hormone (r-hLH) and Pergoveris (follitropin alfa/lutropin alfa) as well as to revise the clinical trial section for clinical studies for r-hFSH/r-hLH for ovulation induction (OI) and assisted reproductive technologies (ART). In addition, the patient exposure data is updated and a reference is added to the recently approved pharmaceutical forms (solution for injection in pre-filled pen (300IU/150IU, 450IU/225IU and 900IU/450IU)). Finally, the RMP is aligned with GVP module V on 'Risk management systems', revision 1

Action: For adoption of PRAC Assessment Report

5.2.7. [Nilotinib - TASIGNA \(CAP\) - EMEA/H/C/000798/II/0092, Orphan](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Doris Stenver

Scope: Updated RMP (version 21.0) in order to delete 'myelosuppression' as an important identified risk and to reclassify 'cardiac failure' from an important potential to an important identified risk. In addition, changes in the definition of the identified risks 'hepatotoxicity' and 'fluid retention' have been implemented

Action: For adoption of PRAC Assessment Report

5.2.8. [Rituximab - MABTHERA \(CAP\) - EMEA/H/C/000165/II/0144](#)

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

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

Action: For adoption of PRAC Assessment Report

5.2.9. [Sitagliptin - JANUVIA \(CAP\) - EMEA/H/C/000722/WS1357/0063, RISTABEN \(CAP\) - EMEA/H/C/001234/WS1357/0055, TESAVEL \(CAP\) - EMEA/H/C/000910/WS1357/0063, XELEVIA \(CAP\) - EMEA/H/C/000762/WS1357/0067; sitagliptin, metformin hydrochloride - EFFICIB \(CAP\) - EMEA/H/C/000896/WS1357/0089, JANUMET \(CAP\) - EMEA/H/C/000861/WS1357/0089, RISTFOR \(CAP\) - EMEA/H/C/001235/WS1357/0076, VELMETIA \(CAP\) - EMEA/H/C/000862/WS1357/0092](#)

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Menno van der Elst

Scope: Updated RMP (version 10) in order to remove 'theoretic carcinogenic potential' currently classified as missing information from the list of safety concerns

Action: For adoption of PRAC Assessment Report

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

5.3.1. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/II/0037, Orphan

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include a new population: children from 2 to less than 5 years of age. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 7.1) 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/II/0004

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Update of section 4.8 of the SmPC in order to update the safety information based on the primary results from study IMvigor211 in order to fulfil ANX 002 (submission of the final clinical study report (CSR) is listed as an imposed post-authorisation efficacy study (PAES) in Annex II.D). This is a phase 3, open-label, multicentre, randomized study to investigate the efficacy and safety of atezolizumab (anti-programme death-ligand 1 (PD-L1) antibody) compared with chemotherapy in patients with locally advanced or metastatic urothelial bladder cancer after failure with platinum-containing chemotherapy. The package leaflet and the RMP (version 3.0) are updated accordingly. In addition, the MAH took the opportunity to implement some editorial changes throughout the product information

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

5.3.3. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0011, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include the treatment of adults with minimal residual disease (MRD) positive B-cell precursor acute lymphoblastic leukaemia (ALL). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, and amend the safety information. The labelling and the RMP (version 4.0) are updated accordingly

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

5.3.4. Dabigatran etexilate - PRADAXA (CAP) - EMEA/H/C/000829/II/0111

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Doris Stenver

Scope: Update of section 5.1 of the SmPC to reflect the phase II outcome results from the 'global registry on long-term oral antithrombotic treatment in patients with atrial fibrillation' (GLORIA-AF) with the main objective 'to collect real-world data on important outcome events of antithrombotic treatments for the prevention of stroke' for patients taking Pradaxa (dabigatran etexilate). In addition, the results of the Medicare study (P14-15648) are proposed to be included in section 5.1 with further information on the effectiveness and safety of Pradaxa in patients with non-valvular atrial fibrillation (NVAf) in a real-world setting. The RMP (version 35.0) is updated accordingly

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

5.3.5. Darunavir, cobicistat, emtricitabine, tenofovir alafenamide - SYMTUZA (CAP) - EMEA/H/C/004391/II/0003/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: Grouped variations consisting of: 1) update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to reflect the week-48 results from two studies listed as category 3 studies in the RMP, namely study TMC114FD2HTX3001: evaluation of the 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 (DRV/COBI) fixed dose combination (FDC) co-administered with emtricitabine/tenofovir alafenamide (FTC/TDF) FDC in antiretroviral (ARV) treatment-naïve human immunodeficiency virus 1 (HIV-1) infected subjects; and study TMC114IFD3013: evaluation of 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 RMP (version 2.0) is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to make minor editorial revision in the product information

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

5.3.6. Dasatinib - SPRYCEL (CAP) - EMEA/H/C/000709/X/0056/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Doris Stenver

Scope: Grouped application consisting of: 1) extension application (line extension) to introduce a new pharmaceutical form (powder for oral suspension) associated with a new strength (10 mg/mL); 2) extension of indication to include the treatment of children and adolescents aged 1 year to 18 years with Philadelphia chromosome-positive (Ph+) chronic phase in chronic myeloid leukaemia (CML). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, to add a warning on effects on growth and development in the paediatric population and to update the safety information. The package leaflet and the RMP (version

15.0) are updated accordingly

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

5.3.7. [Defibrotide - DEFITELIO \(CAP\) - EMEA/H/C/002393/II/0026, Orphan](#)

Applicant: Gentium S.r.l.

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the frequencies of adverse reactions included in the tabulated list of adverse reactions and to update the clinical efficacy and safety information based on the results from study 2006-05 (listed as a category 3 in the RMP): a phase 3, open-label expanded access study designed to provide access to defibrotide as an investigational new drug to patients with severe hepatic veno-occlusive disease. The package leaflet and the RMP (version 3.0) are updated accordingly. In addition, the MAH took the opportunity to bring the SmPC in line with the latest QRD template (version 10), to update the list of local representatives in the package leaflet and to correct a translation error in the Polish, Finnish, Danish and Latvian versions

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

5.3.8. [Denosumab - PROLIA \(CAP\) - EMEA/H/C/001120/II/0068](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at increased risk of fracture as well as the prevention of osteoporosis in women and men at increased risk of fracture who are starting or have recently started long-term glucocorticoid therapy. As a consequence, sections 4.1 and 5.1 of the SmPC are updated to reflect the new indications based on the analysis of the data from the pivotal study glucocorticoid-induced osteoporosis (GIOP): study 20101217: a randomized, double-blind, active controlled study evaluating the efficacy and safety of denosumab compared with risedronate in glucocorticoid-treated individuals. The package leaflet and the RMP (version 19.0) are updated accordingly

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

5.3.9. [Denosumab - XGEVA \(CAP\) - EMEA/H/C/002173/II/0059](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information and to revise the special warnings, precautions for use and undesirable effects based on cases of clinically significant hypercalcemia following discontinuation of denosumab in patients with growing skeletons (i.e. adolescent subject with giant-cell tumour of bone (GCTB) in study 20062004: an open label, multicentre, phase 2 study of denosumab in subjects with GCTB) and in post-marketing reports of paediatric patients treated with denosumab for GCTB or for unapproved indications previously determined as an important identified risk. 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

5.3.10. [Dexmedetomidine - DEXDOR \(CAP\) - EMEA/H/C/002268/II/0026](#)

Applicant: Orion Corporation

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to include the 'sedation of non-intubated adult patients prior to and/or during diagnostic or surgical procedures requiring sedation, i.e. procedural/awake sedation' for Dexdor (dexmedetomidine). As a consequence, section 4.1, 4.2, 4.4, 4.6, 4.7, 4.8 and 5.1 of the SmPC are updated. In addition, the package leaflet and the RMP (version 7.0) are updated accordingly

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

5.3.11. [Eliglustat - CERDELGA \(CAP\) - EMEA/H/C/003724/II/0015/G, Orphan](#)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Dolores Montero Corominas

Scope: Grouped variations consisting of an update of sections 4.2, 4.3, 4.4, 4.5 and 5.2 of the SmPC based on the final data from: 1) study POP13777: an open-label pharmacokinetic and tolerability study of eliglustat tartrate given as a single dose in subjects with mild and moderate hepatic impairment, and in matched subjects with normal hepatic function (MEA003.3) and; 2) study POP13778: an open-label two-stage pharmacokinetic and tolerability study of eliglustat tartrate given as a single dose in subjects with mild, moderate and severe renal impairment, and in matched subjects with normal renal function (MEA004.3). Annex II D, the package leaflet and the RMP (version 5.0) are updated accordingly

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

5.3.12. [Exenatide - BYDUREON \(CAP\) - EMEA/H/C/002020/X/0048/G](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped application consisting of: 1) extension application to introduce a new pharmaceutical form (prolonged-release suspension for injection (in autoinjector)); 2) variation to align the product information for the approved Bydureon formulations (powder and solvent for prolonged-release suspension for injection, powder and solvent for prolonged-release suspension for injection in pre-filled pen) with the product information proposed for the new pharmaceutical form (prolonged-release suspension for injection (in autoinjector)). In addition, the MAH took the opportunity to introduce minor editorial changes in the SmPC. The RMP (version 28) is updated accordingly

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

5.3.13. [Fluticasone furoate, vilanterol - RELVAR ELLIPTA \(CAP\) - EMEA/H/C/002673/WS1343/0036, REVINTY ELLIPTA \(CAP\) - EMEA/H/C/002745/WS1343/0032](#)

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of the results of the Salford lung study (SLS)-asthma (HZA115150): an interventional post-authorisation safety category 1 open-label comparative study to further investigate the risk of pneumonia (ANX005). The RMP (version 9.2) is updated accordingly to reflect additional information following the completion of the study. In addition, the RMP is updated to amend the important identified risk of pneumonia with regards findings from the study, and to provide a justification for the removal of the important potential risk of asthma related intubations and deaths and a justification for removal of missing information related to long term use in asthma (>1 year). Consequently, the Annex II condition of the product information is updated accordingly

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

5.3.14. [Human normal immunoglobulin - PRIVIGEN \(CAP\) - EMEA/H/C/000831/II/0129](#)

Applicant: CSL Behring GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.3 of the SmPC to remove the contraindication on hyperprolineamia based on a comprehensive data survey of data from all available sources. The package leaflet and RMP (version 6.0) are updated accordingly

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

5.3.15. [Infliximab - REMICADE \(CAP\) - EMEA/H/C/000240/II/0212](#)

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.4 to include a warning recommending adult patients to be brought up to date with all vaccinations if possible prior to initiating Remicade (infliximab) therapy, in line with the current warning for children, and to clarify that patients on infliximab may receive concurrent vaccinations, except for live vaccines. The package leaflet and the RMP (version 15.1) are updated accordingly. The MAH took the opportunity to include minor editorial changes in the product information

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

5.3.16. [Ipilimumab - YERVOY \(CAP\) - EMEA/H/C/002213/II/0054](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Update of section 5.1 of the SmPC to update the overall survival data of ipilimumab 3mg/kg monotherapy pooled across studies based on the final results of study CA184332

and CA184338 (listed as category 3 studies in the RMP), in order to fulfil MEA 035 and MEA 030.1 respectively. Study CA184332 is a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab as first line therapy in a community practice setting and study CA184438 is a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab as first line therapy. The RMP (version 18.4) is updated accordingly

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

5.3.17. [Ipilimumab - YERVOY \(CAP\) - EMEA/H/C/002213/II/0055](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include the treatment of advanced (unresectable or metastatic) melanoma in adults in combination with nivolumab for Yervoy (ipilimumab). 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 20.0) are updated accordingly. In addition, the MAH took the opportunity to update the contact details of the Irish local representative in the package leaflet

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

5.3.18. [Lenalidomide - REVLIMID \(CAP\) - EMEA/H/C/000717/II/0098, Orphan](#)

Applicant: Celgene Europe Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Update of Annex II to amend the key elements of the risk minimisation programme with information on prescription duration and to revise due dates of two post-authorisation non-interventional, safety studies CC-5013-MDS-10 and CC-5013-MDS-1 on patients with myelodysplastic syndromes (MDS) treated with lenalidomide to gather safety data on the use of lenalidomide in MDS patients and monitor off-label use. Section 4.4 of the SmPC is updated accordingly. The RMP (version 35) is updated in line with GVP module V on 'Risk management systems' revision 1, in order to reclassify and/or rename known safety concerns associated with the use of Revlimid (lenalidomide). As a consequence, Annex IID is updated

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

5.3.19. [Levetiracetam - KEPPRA \(CAP\) - EMEA/H/C/000277/II/0169/G](#)

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Laurence de Fays

Scope: Grouped variations consisting of: 1) update of section 4.8 of the SmPC to add the adverse drug reaction (ADR) 'gait disturbance' to address the CHMP recommendation from P46/085; 2) update of section 4.2 of the SmPC to add dysgeusia as a potential experience post administration and update of section 4.5 of the SmPC to remove drug interaction with methotrexate in accordance with the latest levetiracetam company core data sheet; 3) update of section 4.6 to add information on 'women of childbearing potential' and to update

the pregnancy section to address the PRAC recommendation from LEG 084.1. The package leaflet and the RMP (version 8) are updated accordingly

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

5.3.20. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0039

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of adult patients with advanced or recurrent gastric or gastroesophageal junction (GEJ) cancer after two or more prior systemic therapies, based on data from study ONO-4538-12: a Phase 3 study, multicentre, double-blind, randomized study in patients with unresectable advanced or recurrent gastric cancer. As a consequence, sections 4.1, 4.4, 4.8, and 5.1 of the SmPC are updated. Annex II, 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

5.3.21. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0041

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include adjuvant treatment of adults and adolescents of 12 years of age and older with completely resected stage III and IV melanoma. 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 efficacy and safety information from pivotal study CA209238: a phase 3, randomized, double-blind study of adjuvant immunotherapy with nivolumab versus ipilimumab after complete resection of stage IIIb/c or stage IV melanoma in subjects who are at high risk for recurrence. The package leaflet and the RMP (version 12.0) are updated accordingly. The MAH also took the opportunity to revise the due dates for two category 4 studies, namely study CA209172: a single-arm, open-label, multicentre clinical trial with nivolumab for subjects with histologically confirmed stage III (unresectable) or stage IV melanoma progressing post prior treatment containing an anti-cytotoxic T lymphocyte-associated antigen (CTLA-4) monoclonal antibody; and study CA209171: an open-label, multicentre clinical trial with nivolumab monotherapy in subjects with advanced or metastatic squamous cell (Sq) non-small cell lung cancer (NSCLC) who have received at least one prior systemic regimen for the treatment of stage IIIb/IV SqNSCLC. In addition, the MAH took the opportunity to make minor editorial changes to the product information

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

5.3.22. Nusinersen - SPINRAZA (CAP) - EMEA/H/C/004312/II/0004, Orphan

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of section 4.8 of the SmPC to include new safety information related to hydrocephalus. The package leaflet and the RMP (version 7.0) are updated accordingly. In addition, the MAH took the opportunity to correct some typographical errors in section 5.1

of the SmPC

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

5.3.23. [Octocog alfa - ADVATE \(CAP\) - EMEA/H/C/000520/II/0091](#)

Applicant: Baxter AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.2 of the SmPC in order to remove a statement mentioning that 'the use of the 2 mL presentation has not been documented for paediatric subjects below 2 years of age'. This update follows the final results from study 061101 (listed as a category 3 study in the RMP): a prospective, non-interventional, post-marketing surveillance study that assessed the safety and efficacy of Advate (octocog alfa) reconstituted in 2 mL of sterile water for injection during routine clinical practice in the EU. The package leaflet and the RMP (version 15.1) are updated accordingly

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

5.3.24. [Osimertinib - TAGRISSO \(CAP\) - EMEA/H/C/004124/II/0019](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) whose tumours have epidermal growth factor receptor exon 19 deletions or exon 21 (L858R) substitution mutations, based on data from FLAURA study (D5160C00007): a phase 3, double-blind, randomised study to assess the efficacy and safety of osimertinib versus a standard of care epidermal growth factor receptor-tyrosine kinase inhibitor as first-line treatment in patients with epidermal growth factor receptor mutation-positive, locally-advanced or metastatic NSCLC. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC are updated. The package leaflet and the RMP (version 8) are updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the SmPC and package leaflet. As part of this application, the MAH requested an additional year of market protection

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

5.3.25. [Pembrolizumab - KEYTRUDA \(CAP\) - EMEA/H/C/003820/II/0042](#)

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include treatment as monotherapy of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) on or after platinum-containing chemotherapy based on the results from KEYNOTE-040 (KN040) with supportive data from two additional single arm studies (KEYNOTE-012: a phase Ib multi-cohort study of pembrolizumab on subjects with advanced solid tumours; KEYNOTE-055: a phase II clinical trial of single agent pembrolizumab in subjects with recurrent or metastatic head). KN040 is a randomized, multicentre, pivotal phase 3 study investigating Keytruda (pembrolizumab) as a monotherapy versus standard treatment (methotrexate, docetaxel or

cetuximab) in patients with recurrent or metastatic HNSCC who have previously progressed on prior platinum. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 15.1) are updated accordingly. In addition, the MAH took the opportunity to include in SmPC section 5.2 the description of pembrolizumab pharmacokinetic (PK) results on time-dependent change in clearance using a time-dependent pharmacokinetic (TDPK) model structure rather than the static PK model structure

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

5.3.26. [Pertuzumab - PERJETA \(CAP\) - EMEA/H/C/002547/II/0034](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Extension of indication for Perjeta (pertuzumab) in combination with trastuzumab and chemotherapy for the adjuvant treatment of adult patients with human epidermal growth factor receptor 2 (HER2)-positive early breast cancer. The submission is based on the primary analysis of efficacy and safety data from the pivotal phase 3 study BIG-4-11/BO25126/TOC4939g (APHINITY): a randomized multicentre, double-blind, placebo-controlled comparison of chemotherapy plus trastuzumab plus placebo versus chemotherapy plus trastuzumab plus pertuzumab as adjuvant therapy in patients with operable HER2-positive primary breast cancer. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. Annex II-D (fulfilment of the obligation to include a neoadjuvant indication), the package leaflet and the RMP (version 10.0) are updated accordingly

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

5.3.27. [Pneumococcal polysaccharide conjugate vaccine \(13-valent, adsorbed\) - PREVENAR 13 \(CAP\) - EMEA/H/C/001104/II/0161](#)

Applicant: Pfizer Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the final study report from effectiveness study B1851041: a phase 4 post marketing study to determine 'national trends in ambulatory care visits for otitis media in children under the age of five in the United States'. The RMP (version 12) is updated accordingly

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

5.3.28. [Rituximab - RIXATHON \(CAP\) - EMEA/H/C/003903/WS1335/0010; RIXIMYO \(CAP\) - EMEA/H/C/004729/WS1335/0010](#)

Applicant: Sandoz GmbH

PRAC Rapporteur: Doris Stenver

Scope: Submission of the final clinical study reports (CSR) for: 1) study GP13-302: a randomized, double-blind, parallel-group safety study with the aim to specifically address a potential safety risk of a switch from treatment with originator rituximab containing product

to treatment with GP2013 (biosimilar rituximab containing products); 2) study GP13-201: a 52-week multicentre, randomized, double-blind, parallel-arm, comparative study in patients with active rheumatoid arthritis (RA) refractory or intolerant to standard disease modifying anti-rheumatic drugs (DMARDs) and one or up to three anti-tumour necrosis factor (TNF) therapies. The RMP (version 3.0) is updated accordingly

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

5.3.29. Sapropterin - KUVAN (CAP) - EMEA/H/C/000943/II/0052, Orphan

Applicant: BioMarin International Limited

PRAC Rapporteur: Almath Spooner

Scope: Update of section 4.4 of the SmPC to add a warning regarding gastritis and update of section 4.8 to add the following adverse events regarding gastrointestinal tract and respiratory irritation: oropharyngeal pain, oesophageal pain, dyspepsia, nausea, gastritis and pharyngitis. The package leaflet and the RMP (version 13.0) are updated accordingly

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

5.3.30. Siltuximab - SYLVANT (CAP) - EMEA/H/C/003708/II/0026/G, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of an update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to update the product information following final results from: 1) study CNTO328MCD2001: a randomized, double blind, placebo controlled study to assess the efficacy and safety of siltuximab plus best supportive care compared with best supportive care in subjects with multicentric Castleman's disease; 2) study CNTO328MCD2002: an open-label, multicentre study to evaluate the safety of long-term treatment with siltuximab in subjects with multicentric Castleman's disease, both listed as imposed obligations in Annex II. The package leaflet and the RMP (version 4.0) are updated accordingly

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

5.3.31. Sirolimus - RAPAMUNE (CAP) - EMEA/H/C/000273/II/0164

Applicant: Pfizer Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the treatment of patients with lymphangioliomyomatosis. As a consequence, section 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 6.0) are updated accordingly. In addition, the MAH took the opportunity to make very minor formatting changes in the labelling

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

5.3.32. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0006

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include treatment of adult patients with active psoriatic arthritis who have had an inadequate response or who have been intolerant to a prior disease-modifying anti-rheumatic drug (DMARD) therapy, based on data from study A3921091: a phase 3, randomized, double-blind, placebo-controlled study of the efficacy and safety of 2 doses of tofacitinib or adalimumab in subjects with active psoriatic arthritis; study A3921092: a long term, open label extension study of tofacitinib for the treatment of psoriatic arthritis; study A3921125: a phase 3, randomized, double-blind, placebo-controlled study of the efficacy and safety of 2 doses of tofacitinib in subjects with active psoriatic arthritis and an inadequate response to at least one tumour necrosis factor (TNF) inhibitor. 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 3.0) are updated accordingly. In addition, the MAH took the opportunity to update Annex II with minor editorial changes

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

5.3.33. Tolvaptan - JINARC (CAP) - EMEA/H/C/002788/II/0009

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Extension of indication based on the results of a completed post-authorisation efficacy study (PAES), study 156-13-210: a phase 3b, multicentre, randomized-withdrawal, placebo-controlled, double-blind, parallel-group trial to compare the efficacy and safety of tolvaptan (45 to 120 mg/day, split-dose) in subjects with chronic kidney disease (CKD) between late stage 2 to early stage 4 due to autosomal dominant polycystic kidney disease. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC and Annex II are updated. The package leaflet and the RMP (version 13.2) are updated accordingly. The MAH took the opportunity to introduce minor editorial changes to the product information

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

5.3.34. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/II/0008, Orphan

Applicant: AbbVie Limited

PRAC Rapporteur: Patrick Batty

Scope: Extension of indication to include Venclyxto (venetoclax) in combination with rituximab for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. This is based on the results from the MURANO study: a multicentre, phase 3, open-label, randomised study in relapsed/refractory patients with CLL to evaluate the benefit of venetoclax plus rituximab compared with bendamustine plus rituximab. Annex II, the package leaflet and the RMP (version 3.0) 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. Afatinib - GIOTRIF (CAP) - PSUSA/00010054/201709

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. Alemtuzumab - LEMTRADA (CAP) - PSUSA/00010055/201709

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Anette Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Alirocumab - PRALUENT (CAP) - PSUSA/00010423/201709

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Aliskiren - RASILEZ (CAP); aliskiren, hydrochlorothiazide - RASILEZ HCT (CAP) - PSUSA/00000089/201709

Applicant: Noden Pharma DAC

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Azilsartan medoxomil - EDARBI (CAP) - PSUSA/00000280/201708

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Aztreonam⁷ - CAYSTON (CAP) - PSUSA/00000283/201709

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Bedaquiline - SIRTURO (CAP) - PSUSA/00010074/201709

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Bivalirudin - ANGIOX (CAP) - PSUSA/00000421/201709

Applicant: The Medicines Company UK Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Ceftolozane, tazobactam - ZERBAXA (CAP) - PSUSA/00010411/201709

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Cholic acid⁸ - KOLBAM (CAP) - PSUSA/00010182/201709

Applicant: Retrophin Europe Ltd

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

⁷ For inhalation use only

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

6.1.11. Cholic acid⁹ - ORPHACOL (CAP) - PSUSA/00010208/201709

Applicant: Laboratoires CTRS

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Ciclosporin¹⁰ - IKERVIS (CAP) - PSUSA/00010362/201709

Applicant: Santen Oy

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Dabigatran - PRADAXA (CAP) - PSUSA/00000918/201709

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Daclizumab beta – ZINBRYTA¹¹ – PSUSA/00010518/201711

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.1.15. Dapagliflozin - EDISTRIDE (CAP), FORXIGA (CAP) - PSUSA/00010029/201710

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Daptomycin - CUBICIN (CAP) - PSUSA/00000931/201709

Applicant: Merck Sharp & Dohme Limited

⁹ Treatment of inborn errors in primary bile acid synthesis due to 3 β -hydroxy- Δ 5-C27-steroid oxidoreductase deficiency or Δ 4-3-oxosteroid-5 β -reductase indications only

¹⁰ For topical use only

¹¹ European Commission (EC) decision on the MA withdrawal of Zinbryta dated 27 March 2018

PRAC Rapporteur: Julie Williams
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.17. [Deferiprone - FERRIPROX \(CAP\) - PSUSA/00000940/201708 \(with RMP\)](#)

Applicant: Apotex Europe BV
PRAC Rapporteur: Ghania Chamouni
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.18. [Denosumab¹² - PROLIA \(CAP\) - PSUSA/00000954/201709](#)

Applicant: Amgen Europe B.V.
PRAC Rapporteur: Ulla Wändel Liminga
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.19. [Denosumab¹³ - XGEVA \(CAP\) - PSUSA/00009119/201709](#)

Applicant: Amgen Europe B.V.
PRAC Rapporteur: Ulla Wändel Liminga
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.20. [Dexamethasone¹⁴ - NEOFORDEX \(CAP\) - PSUSA/00010480/201709](#)

Applicant: Laboratoires CTRS
PRAC Rapporteur: Ghania Chamouni
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.21. [Dibotermin alfa - INDUCTOS \(CAP\) - PSUSA/00001034/201709](#)

Applicant: Medtronic BioPharma B.V.
PRAC Rapporteur: Menno van der Elst
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

¹² Indicated for osteoporosis and for bone loss associated with hormone ablation in prostate cancer

¹³ Indicated for skeletal related events associated with bone metastases and for giant cell tumour of bone

¹⁴ Centrally authorised product(s) indicated in symptomatic multiple myeloma

6.1.22. [Dulaglutide - TRULICITY \(CAP\) - PSUSA/00010311/201709](#)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. [Eculizumab - SOLIRIS \(CAP\) - PSUSA/00001198/201710](#)

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. [Eftrenonacog alfa - ALPROLIX \(CAP\) - PSUSA/00010499/201709](#)

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. [Eltrombopag - REVOLADE \(CAP\) - PSUSA/00001205/201709 \(with RMP\)](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. [Eluxadoline - TRUBERZI \(CAP\) - PSUSA/00010528/201709](#)

Applicant: Allergan Pharmaceuticals International Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. [Emtricitabine, rilpivirine, tenofovir alafenamide - ODEFSEY \(CAP\) - PSUSA/00010514/201708](#)

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Emtricitabine, tenofovir alafenamide - DESCOVY (CAP) - PSUSA/00010515/201710

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Etravirine - INTELENCE (CAP) - PSUSA/00001335/201709

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Ferric citrate coordination complex - FEXERIC (CAP) - PSUSA/00010418/201709

Applicant: Keryx Biopharma UK Ltd.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Glycopyrronium¹⁵ - SIALANAR (CAP) - PSUSA/00010529/201709

Applicant: Proveca Limited

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Guanfacine - INTUNIV (CAP) - PSUSA/00010413/201709

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Human coagulation factor X - COAGADDEX (CAP) - PSUSA/00010481/201709

Applicant: Bio Products Laboratory Limited

¹⁵ For centrally authorised product(s) indicated for the treatment of severe siallorrhea

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. [Idebenone¹⁶ - RAXONE \(CAP\) - PSUSA/00010412/201709](#)

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. [Indacaterol, glycopyrronium bromide - ULTIBRO BREEZHALER \(CAP\), ULUNAR BREEZHALER \(CAP\), XOTERNA BREEZHALER \(CAP\) - PSUSA/00010105/201709 \(with RMP\)](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. [Indinavir - CRIXIVAN \(CAP\) - PSUSA/00001733/201709](#)

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. [Insulin aspart - FIASP \(CAP\), NOVOMIX \(CAP\), NOVORAPID \(CAP\) - PSUSA/00001749/201709](#)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. [Insulin degludec - TRESIBA \(CAP\); insulin degludec, insulin aspart - RYZODEG \(CAP\) - PSUSA/00010036/201709](#)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

¹⁶ Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. [Insulin degludec, liraglutide - XULTOPHY \(CAP\) - PSUSA/00010272/201709](#)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. [Insulin human¹⁷ - INSUMAN \(CAP\) - PSUSA/00010107/201709](#)

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. [Isavuconazole - CRESEMBA \(CAP\) - PSUSA/00010426/201709](#)

Applicant: Basilea Medical Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. [Ixekizumab - TALTZ \(CAP\) - PSUSA/00010493/201709 \(with RMP\)](#)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. [Mecasermin - INCRELEX \(CAP\) - PSUSA/00001942/201708](#)

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁷ Intraperitoneal route of administration only

6.1.44. [Mepolizumab - NUCALA \(CAP\) - PSUSA/00010456/201709](#)

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. [Naloxegol - MOVENTIG \(CAP\) - PSUSA/00010317/201709](#)

Applicant: Kyowa Kirin Limited

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. [Naltrexone, bupropion - MYSIMBA \(CAP\) - PSUSA/00010366/201709](#)

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. [Oritavancin - ORBACTIV \(CAP\) - PSUSA/00010368/201709](#)

Applicant: The Medicines Company UK Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. [Pandemic influenza vaccine \(H5N1\) \(whole virion, vero cell derived, inactivated\) - PANDEMIC INFLUENZA VACCINE H5N1 BAXTER \(CAP\); prepandemic influenza vaccine \(H5N1\) \(whole virion, vero cell derived, inactivated\) - VEPACEL \(CAP\) - PSUSA/00002282/201708](#)

Applicant: Nanotherapeutics UK Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. [Panitumumab - VECTIBIX \(CAP\) - PSUSA/00002283/201709](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Pembrolizumab - KEYTRUDA (CAP) - PSUSA/00010403/201709

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Pitolisant - WAKIX (CAP) - PSUSA/00010490/201709

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Raltegravir - ISENTRESS (CAP) - PSUSA/00010373/201709

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Regorafenib - STIVARGA (CAP) - PSUSA/00010133/201709

Applicant: Bayer AG

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Retigabine - TROBALT (CAP) - PSUSA/00002624/201709

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.55. Riociguat - ADEMPAS (CAP) - PSUSA/00010174/201709

Applicant: Bayer AG

PRAC Rapporteur: Julie Williams
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.56. [Rivaroxaban - XARELTO \(CAP\) - PSUSA/00002653/201709](#)

Applicant: Bayer AG
PRAC Rapporteur: Qun-Ying Yue
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.57. [Rolapitant - VARUBY \(CAP\) - PSUSA/00010592/201708](#)

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

6.1.58. [Sirolimus - RAPAMUNE \(CAP\) - PSUSA/00002710/201709](#)

Applicant: Pfizer Limited
PRAC Rapporteur: Ulla Wändel Liminga
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.59. [Tasonermin - BEROMUN \(CAP\) - PSUSA/00002850/201708](#)

Applicant: Boehringer Ingelheim International GmbH
PRAC Rapporteur: Doris Stenver
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.60. [Telavancin - VIBATIV¹⁸ - PSUSA/00002879/201709](#)

Applicant: Theravance Biopharma Ireland Ltd
PRAC Rapporteur: Julie Williams
Scope: Evaluation of a PSUSA procedure
Action: For information

¹⁸ European Commission (EC) decision on the MA withdrawal of Vibativ dated 23 March 2018

6.1.61. Teriflunomide - AUBAGIO (CAP) - PSUSA/00010135/201709

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.62. Tobramycin¹⁹ - VANTOBRA (CAP) - PSUSA/00010370/201709

Applicant: PARI Pharma GmbH

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.63. Trabectedin - YONDELIS (CAP) - PSUSA/00003001/201709

Applicant: Pharma Mar, S.A.

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.64. Trifluridine, tipiracil - LONSURF (CAP) - PSUSA/00010517/201709

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.65. Vernakalant - BRINAVESS (CAP) - PSUSA/00003109/201708

Applicant: Cardiome UK Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.66. Vortioxetine - BRINTELLIX (CAP) - PSUSA/00010052/201709

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Laurence de Fays

¹⁹ Nebuliser solution, centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.2.1. Anagrelide - XAGRID (CAP); NAP - PSUSA/00000208/201709

Applicants: Shire Pharmaceutical Contracts Limited (Xagrid), various

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Duloxetine - ARICLAIM (CAP), CYMBALTA (CAP), DULOXETINE LILLY (CAP), XERISTAR (CAP), YENTREVE (CAP); NAP - PSUSA/00001187/201708

Applicants: Eli Lilly Nederland B.V. (Ariclaim, Cymbalta, Duloxetine Lilly, Xeristar, Yentreve), various

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Leflunomide - ARAVA (CAP), LEFLUNOMIDE MEDAC (CAP), LEFLUNOMIDE WINTHROP (CAP); NAP - PSUSA/00001837/201709

Applicants: Medac Gesellschaft für klinische Spezialpräparate mbH (Leflunomide medac), Sanofi-Aventis Deutschland GmbH (Arava, Leflunomide Winthrop), various

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Pantoprazole - CONTROLOC CONTROL (CAP), PANTOLOC CONTROL (CAP), PANTOZOL CONTROL (CAP), SOMAC CONTROL (CAP); NAP - PSUSA/00002285/201708

Applicants: Takeda GmbH, various

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. [Zoledronic acid²⁰- ZOLEDRONIC ACID HOSPIRA \(CAP\), ZOLEDRONIC ACID MEDAC \(CAP\), ZOMETA \(CAP\); NAP - PSUSA/00003149/201708](#)

Applicants: Hospira UK Limited (Zoledronic acid Hospira), Medac Gesellschaft für klinische Spezialpräparate mbH (Zoledronic acid medac), Novartis Europharm Limited (Zometa), various

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. [Aciclovir, hydrocortisone \(NAP\) - PSUSA/00009004/201707](#)

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. [Adenosine \(NAP\) - PSUSA/00000062/201708](#)

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. [Alprostadil²¹ \(NAP\) - PSUSA/00000111/201707](#)

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. [Anastrozole \(NAP\) - PSUSA/00000210/201708](#)

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

²⁰ Indicated for cancer and fractures only

²¹ Indicated in peripheral arterial occlusive diseases only

Action: For adoption of recommendation to CMDh

6.3.5. Buprenorphine (NAP) - PSUSA/00000459/201707

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Clindamycin phosphate, tretinoin (NAP) - PSUSA/00010080/201707

Applicant(s): various

PRAC Lead: Tatiana Magalova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Dexamfetamine (NAP) - PSUSA/00000986/201709

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. Diphtheria, tetanus, poliomyelitis (inactivated) vaccine (adsorbed, reduced antigens(s) content) (NAP) - PSUSA/00001127/201708

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Ethinylestradiol, gestodene²² (NAP) - PSUSA/00010145/201708

Applicant(s): various

PRAC Lead: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

²² Transdermal application only

6.3.10. Ethinylestradiol, norethisterone (NAP) - PSUSA/00001312/201708

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Etoposide (NAP) - PSUSA/00001333/201708

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Fenofibrate (NAP) - PSUSA/00001362/201707

Applicant(s): various

PRAC Lead: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Finasteride (NAP) - PSUSA/00001392/201708

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Fludarabine (NAP) - PSUSA/00001406/201708

Applicant(s): various

PRAC Lead: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Fluocinolone acetonide²³ (NAP) - PSUSA/00010224/201708

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

²³ Intravitreal implant in applicator only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Fluvoxamine (NAP) - PSUSA/00001458/201707

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Human tetanus immunoglobulin (NAP) - PSUSA/00002909/201708

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Ketoprofen²⁴ (NAP) - PSUSA/00001809/201707

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Leuprorelin (NAP) - PSUSA/00001844/201707

Applicant(s): various

PRAC Lead: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Naproxen (NAP) - PSUSA/00002125/201708

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

²⁴ All formulations except topical

6.3.21. Norethisterone (NAP) - PSUSA/00002188/201708

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Permethrin (NAP) - PSUSA/00002355/201707

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Pilocarpine²⁵ (NAP) - PSUSA/00002409/201707

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Quetiapine (NAP) - PSUSA/00002589/201707

Applicant(s): various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Quinagolide (NAP) - PSUSA/00002590/201707

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Suxamethonium (NAP) - PSUSA/00002834/201708

Applicant(s): various

PRAC Lead: Julie Williams

²⁵ All formulations except ophthalmic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.27. Triazolam (NAP) - PSUSA/00003023/201707

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.28. Typhoid polysaccharide vaccine (NAP) - PSUSA/00003065/201708

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/LEG 027

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Cumulative review of cases of headache, dizziness, and abdominal pain/gastrointestinal (GI) pain from all available sources (post marketing cases, clinical trial data and literature) as requested in the conclusions of PSUSA/00000226/201705 adopted at the December 2017 PRAC

Action: For adoption of advice to CHMP

6.4.2. Decitabine - DACOGEN (CAP) - EMEA/H/C/002221/LEG 009

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ghania Chamouni

Scope: Cumulative review of cases of hepatic failure, fibrosis, cirrhosis and other liver damage-related conditions from all available sources (post marketing cases, clinical trial data and literature) as requested in the conclusions of PSUSA/00009118/201705 adopted at the December 2017 PRAC

Action: For adoption of advice to CHMP

6.4.3. Ibritumomab tiuxetan - ZEVALIN (CAP) - EMEA/H/C/000547/LEG 046

Applicant: Spectrum Pharmaceuticals B.V.

PRAC Rapporteur: Doris Stenver

Scope: Detailed review of cases of myelodysplastic syndrome/acute myeloid leukaemia (MDS/AML), analysis of types of multiple cytogenetic abnormalities at individual patient level in order to identify whether specific abnormalities are present in relation to treatment with Zevalin (ibritumomab tiuxetan), number of patients who, in addition to complex cytogenetics, have cytogenetic abnormalities normally associated with poor prognostic groups or therapy-related MDS/AML as well as a detailed review on whether these patient characteristics differ between treatment and control groups, as requested in the conclusions of PSUSA/00001704/201702 adopted at the October 2017 PRAC

Action: For adoption of advice to CHMP

6.4.4. Meningococcal group A, C, W135 and Y conjugate vaccine - MENVEO (CAP) - EMEA/H/C/001095/LEG 037

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Menno van der Elst

Scope: Detailed review investigating the root cause of the observed peak in reconstitution errors reporting within the EU, including proposals for appropriate measures as applicable as part of routine risk minimisation as requested in the conclusions of PSUSA/00001969/201703 adopted at the November 2017 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)²⁶

7.1.1. Direct acting antivirals (DAAV) indicated for the treatment of hepatitis C: Daclatasvir – DAKLINZA (CAP); dasabuvir - EXVIERA (CAP); elbasvir, grazoprevir – ZEPATIER (CAP); glecaprevir, pibrentasvir – MAVIRET (CAP); ledipasvir, sofosbuvir - HARVONI (CAP); ombitasvir, paritaprevir, ritonavir – VIEKIRAX (CAP); simeprevir - OLYSIO (CAP); sofosbuvir – SOVALDI (CAP); sofosbuvir, velpatasvir – EPCLUSA (CAP); sofosbuvir, velpatasvir, voxilaprevir - VOSEVI - EMEA/H/C/PSA/J/0028

Applicant(s): AbbVie Limited (Exviera, Maviret, Viekirax), Bristol-Myers Squibb Pharma EEIG (Daklinza), Gilead Sciences International Ltd (Epclusa, Harvoni, Sovaldi, Vosevi), Janssen-Cilag International NV (Olysio), Merck Sharp & Dohme Limited (Zepatier)

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Substantial amendment to the previously agreed joint protocol in January 2018 for a non-interventional imposed PASS on early recurrence of hepatocellular carcinoma (HCC) in hepatitis C virus (HCV)-infected patients after direct-acting antiviral (DAAV) therapy in order to estimate the risk of early HCC recurrence (within 24 months after the first HCC-free image) associated with DAAV therapy exposure relative to no DAAV therapy exposure during routine clinical care of HCV-infected patients with successfully treated HCC, as

²⁶ In accordance with Article 107n of Directive 2001/83/EC

required in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMA/H/A-20/1438)

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)²⁷

7.2.1. Dapagliflozin - EDISTRIDE (CAP) - EMA/H/C/004161/MEA 006.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Protocol amendment to study MB102-103 ST/D1690R00008 - (EUPAS12113): a pharmacoepidemiology study assessing the risk of severe complications of urinary tract infections (UTI) and evaluating severe complications of UTI [final clinical study report (CSR) due in 2019]

Action: For adoption of advice to CHMP

7.2.2. Dapagliflozin - EDISTRIDE (CAP) - EMA/H/C/004161/MEA 007.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Protocol amendment to study MB102-110 ST/D1690R00004 - (EUPAS11684): a pharmacoepidemiology observational study assessing the risk of acute renal failure and evaluating the risk of acute kidney injury [final clinical study report (CSR) due in 2019]

Action: For adoption of advice to CHMP

7.2.3. Dapagliflozin - EDISTRIDE (CAP) - EMA/H/C/004161/MEA 008.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Protocol amendment to study MB102-104 ST/D1690R00005 - (EUPAS12110): a pharmacoepidemiology observational study assessing the risk of acute hepatic failure and evaluating the risk of acute liver injury [final clinical study report (CSR) due in 2019]

Action: For adoption of advice to CHMP

7.2.4. Dapagliflozin - EDISTRIDE (CAP) - EMA/H/C/004161/MEA 009.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Protocol amendment to study MB102-118 ST/D1690R00007 - (EUPAS12116): a

²⁷ 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

pharmacoepidemiology study assessing the risk of cancer [final clinical study report (CSR) due in 2024]

Action: For adoption of advice to CHMP

7.2.5. [Dapagliflozin - FORXIGA \(CAP\) - EMEA/H/C/002322/MEA 001.6](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Protocol amendment to study MB102-103 ST/D1690R00008 - (EUPAS12113): a pharmacoepidemiology study assessing the risk of severe complications of urinary tract infections (UTI) and evaluating severe complications of UTI [Final clinical study report (CSR) due in 2019]

Action: For adoption of advice to CHMP

7.2.6. [Dapagliflozin - FORXIGA \(CAP\) - EMEA/H/C/002322/MEA 002.6](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Protocol amendment to study MB102-110 ST/D1690R00004 - (EUPAS11684): a pharmacoepidemiology observational study assessing the risk of acute renal failure and evaluating the risk of acute kidney injury [final clinical study report (CSR) due in 2019]

Action: For adoption of advice to CHMP

7.2.7. [Dapagliflozin - FORXIGA \(CAP\) - EMEA/H/C/002322/MEA 003.5](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Protocol amendment to study MB102-104 ST/D1690R00005 - (EUPAS12110): a pharmacoepidemiology observational study assessing the risk of acute hepatic failure and evaluating the risk of acute liver injury [final clinical study report (CSR) due in 2019]

Action: For adoption of advice to CHMP

7.2.8. [Dapagliflozin - FORXIGA \(CAP\) - EMEA/H/C/002322/MEA 004.6](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Protocol amendment to study MB102-118 ST/D1690R00007 - (EUPAS12116): a pharmacoepidemiology study assessing the risk of cancer [final clinical study report (CSR) due in 2024]

Action: For adoption of advice to CHMP

7.2.9. [Dapagliflozin, metformin - EBYMECT \(CAP\) - EMEA/H/C/004162/MEA 005.1](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Protocol amendment to study MB102-103 ST/D1690R00008 - (EUPAS12113): a pharmacoepidemiology study assessing the risk of severe complications of urinary tract infections (UTI) and evaluating severe complications of UTI [Final clinical study report (CSR) due in 2019]

Action: For adoption of advice to CHMP

7.2.10. [Dapagliflozin, metformin - EBYMECT \(CAP\) - EMEA/H/C/004162/MEA 006.1](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Protocol amendment to study MB102-110 ST/D1690R00004 - (EUPAS11684): a pharmacoepidemiology observational study assessing the risk of acute renal failure and evaluating the risk of acute kidney injury [final clinical study report (CSR) due in 2019]

Action: For adoption of advice to CHMP

7.2.11. [Dapagliflozin, metformin - EBYMECT \(CAP\) - EMEA/H/C/004162/MEA 007.1](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Protocol amendment to study MB102-104 ST/D1690R00005 - (EUPAS12110): a pharmacoepidemiology observational study assessing the risk of acute hepatic failure and evaluating the risk of acute liver injury [final clinical study report (CSR) due in 2019]

Action: For adoption of advice to CHMP

7.2.12. [Dapagliflozin, metformin - EBYMECT \(CAP\) - EMEA/H/C/004162/MEA 008.1](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Protocol amendment to study MB102-118 ST/D1690R00007 - (EUPAS12116): a pharmacoepidemiology study assessing the risk of cancer [final clinical study report (CSR) due in 2024]

Action: For adoption of advice to CHMP

7.2.13. [Dapagliflozin, metformin - XIGDUO \(CAP\) - EMEA/H/C/002672/MEA 008.1](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Protocol amendment to study MB102-103 ST/D1690R00008 - (EUPAS12113): a

pharmacoepidemiology study assessing the risk of severe complications of urinary tract infections (UTI) and evaluating severe complications of UTI [Final clinical study report (CSR) due in 2019]

Action: For adoption of advice to CHMP

7.2.14. Dapagliflozin, metformin - XIGDUO (CAP) - EMEA/H/C/002672/MEA 009.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Protocol amendment to study MB102-110 ST/D1690R00004 - (EUPAS11684): a pharmacoepidemiology observational study assessing the risk of acute renal failure and evaluating the risk of acute kidney injury [final clinical study report (CSR) due in 2019]

Action: For adoption of advice to CHMP

7.2.15. Dapagliflozin, metformin - XIGDUO (CAP) - EMEA/H/C/002672/MEA 010.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Protocol amendment to study MB102-104 ST/D1690R00005 - (EUPAS12110): a pharmacoepidemiology observational study assessing the risk of acute hepatic failure and evaluating the risk of acute liver injury [final clinical study report (CSR) due in 2019]

Action: For adoption of advice to CHMP

7.2.16. Dapagliflozin, metformin - XIGDUO (CAP) - EMEA/H/C/002672/MEA 011.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Protocol amendment to study MB102-118 ST/D1690R00007 - (EUPAS12116): a pharmacoepidemiology study assessing the risk of cancer [final clinical study report (CSR) due in 2024]

Action: For adoption of advice to CHMP

7.2.17. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/MEA 003

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Protocol for study R668-AD-1639 pregnancy registry: a safety study to monitor pregnancy and infant outcomes following administration of dupilumab during planned or unexpected pregnancy in North America

Action: For adoption of advice to CHMP

7.2.18. Guanfacine - INTUNIV (CAP) - EMEA/H/C/003759/MEA 005.1

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's response to MEA 005 [Protocol for a non-imposed, non-interventional PASS safety study: a drug utilisation study (DUS) of Intuniv (guanfacine extended release) in European countries (DUS-database) and protocol for a prescriber survey (DUS-survey) conducted in European countries] as per the request for supplementary information (RSI) adopted at the November 2017 PRAC meeting

Action: For adoption of advice to CHMP

7.2.19. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 007.1

Applicant: Samsung Bioepis UK Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 007 [Protocol for study SB2-G41-AS; SB2-G42-CD: a prospective observational cohort study in ankylosing spondylitis (AS) and Crohn's disease (CD) for two years to observe safety, efficacy and immunogenicity of Flixabi with active comparator in AS and CD] as per the request for supplementary information (RSI) adopted at the November 2017 PRAC meeting

Action: For adoption of advice to CHMP

7.2.20. Lutetium (¹⁷⁷Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/MEA 001

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Protocol for study A-LUT-T-E02-402 (SALUS) (a category 3 study in the RMP): an international post-authorisation safety registry to assess the long-term safety of Lutathera (lutetium (¹⁷⁷Lu) oxodotreotide) for unresectable or metastatic, somatostatin receptor positive gastroenteropancreatic neuroendocrine tumours (GEP-NET) [final report expected in December 2025] (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.2.21. Lutetium (¹⁷⁷Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/MEA 001.1

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response complementing MEA 001 [PASS protocol A-LUT-T-E02-402 (SALUS study, listed as a category 3 study in the RMP): an international post-authorisation safety registry to assess the long-term safety of Lutathera for unresectable or metastatic, somatostatin receptor positive gastroenteropancreatic neuroendocrine tumours (GEP-NETs)]

Action: For adoption of advice to CHMP

7.2.22. [Mirabegron - BETMIGA \(CAP\) - EMEA/H/C/002388/MEA 009.2](#)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's response to MEA 009.1 [Protocol for PASS study 178-PV-002: a drug utilisation study (DUS) of Betmiga (mirabegron) using real-world healthcare databases from the Netherlands, Spain, United Kingdom and Finland] as per the request for supplementary information (RSI) adopted in January 2018

Action: For adoption of advice to CHMP

7.2.23. [Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA \(CAP\) - EMEA/H/C/003687/MEA 003.4](#)

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 003.3 [protocol synopsis for an observational retrospective database study based on secondary data analysis using existing databases, as suitable] as per the request for supplementary information (RSI) adopted at the November 2017 PRAC meeting

Action: For adoption of advice to CHMP

7.2.24. [Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA \(CAP\) - EMEA/H/C/003687/MEA 004.5](#)

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's responses to MEA 004.4 [PASS protocol for study NB-452: a cross-sectional survey to evaluate the effectiveness of the physician prescribing checklist (PPC) among physicians in the EU] as per the request for supplementary information (RSI) adopted in January 2018

Action: For adoption of advice to CHMP

7.2.25. [Tofacitinib - XELJANZ \(CAP\) - EMEA/H/C/004214/MEA 007](#)

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Protocol for a non-interventional PASS study A3921298 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 (listed as a category 3 study in the RMP)

Action: For adoption of advice to CHMP

7.2.26. Vernakalant - BRINAVESS (CAP) - EMEA/H/C/001215/MEA 026.4

Applicant: Cardiome UK Limited

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 026.3 [protocol for study 6621 049-00 (SPECTRUM): a prospective observational registry study to characterise normal conditions of use, dosing and safety following administration of vernakalant intravenous (IV) sterile concentrate]

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)²⁸

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)²⁹

7.4.1. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/II/0039

Applicant: Bayer AG

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of the final report for PASS study 16526 (listed as a category 3 study in the RMP): an observational study to evaluate the physician and patient knowledge of safety and safe use information for aflibercept in Europe as stated in the EU educational material of Eylea (aflibercept)

Action: For adoption of PRAC Assessment Report

7.4.2. Azilsartan medoxomil - EDARBI (CAP) - EMEA/H/C/002293/II/0021

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from a drug utilisation study (DUS) (listed as a category 3 study in the RMP): a retrospective non-interventional cohort study using a patient level electronic medical records database in Germany aimed to describe the prescription of Edarbi (azilsartan medoxomil) in patients with essential hypertension and those prescribed Edarbi (azilsartan medoxomil) for other reasons. The RMP (version 5.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.3. Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/II/0047/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

²⁸ In accordance with Article 107p-q of Directive 2001/83/EC

²⁹ In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

Scope: Grouped variations consisting of: 1) submission of the final report for study IM103061 (listed as a category 3 study in the RMP): an epidemiological study on pregnancy outcome among belatacept users in the US; 2) submission of the final report for study IM103089 (listed as a category 3 study in the RMP): evaluation of retrospective data to assess the association between belatacept and the risk of post-transplant lymphoproliferative disorder (PTDL) in renal transplant recipients in Europe. The RMP (version 15) is updated accordingly

Action: For adoption of PRAC Assessment Report

[7.4.4. Dronedarone - MULTAQ \(CAP\) - EMEA/H/C/001043/II/0039/G](#)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations consisting of: 1) submission of the final report from study DRONE_C_05917 (listed as a category 3 study in the RMP): a non-interventional epidemiological study aimed for the surveillance of serious liver injuries/diseases (SLD) with the use of dronedarone using multiple databases in the US, including the addendum on surveillance of interstitial lung disease (ILD); 2) submission of the final report from study DRONE_C_05911 (listed as a category 3 study in the RMP): a non-interventional epidemiological study aimed at studying the concomitant use of dronedarone and digoxin (or statins) and the risk of digitalis intoxication (or rhabdomyolysis and myopathy). The RMP (version 11.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

[7.4.5. Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil - STRIBILD \(CAP\) - EMEA/H/C/002574/II/0087](#)

Applicant: Gilead Sciences International Limited

PRAC Rapporteur: Julie Williams

Scope: Submission of the final report for study GS-EU-236-0141 (listed as a category 3 study in the RMP, in fulfilment of a MEA 006): an observational drug utilisation study (DUS) of Stribild (elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil) in adults with human immunodeficiency virus 1 (HIV-1) infection

Action: For adoption of PRAC Assessment Report

[7.4.6. Fluticasone furoate, vilanterol - RELVAR ELLIPTA \(CAP\) - EMEA/H/C/002673/WS1283/0035; REVINTY ELLIPTA \(CAP\) - EMEA/H/C/002745/WS1283/0031](#)

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of the final report for study 205052 (PRJ2214): a drug utilisation study (DUS) to identify the extent of any off-label prescribing fluticasone furoate/vilanterol (FF/VI) in any dose in children less than 12 years of age; and prescribing of FF/VI 200/25 mcg in patients with a diagnosis of chronic obstructive pulmonary disease (COPD) considering the

presence of a concurrent diagnosis of asthma. The RMP (version 9.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.7. [Glycopyrronium bromide - ENUREV BREEZHALER \(CAP\) - EMEA/H/C/002691/WS1299/0025; SEEBRI BREEZHALER \(CAP\) - EMEA/H/C/002430/WS1299/0025; TOVANOR BREEZHALER \(CAP\) - EMEA/H/C/002690/WS1299/0028](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Doris Stenver

Scope: Submission of the final study report for study CNVA237A2402T (a category 1 study in the RMP and marketing authorisations): a multinational, multi-database cohort study to assess adverse cardiovascular and cerebrovascular outcomes and mortality in association with inhaled glycopyrronium bromide (NVA237) in Europe. As a consequence, Annex II is updated. In addition, the additional monitoring list is to be updated by removing Enurev Breezhaler, Seebri Breezhaler, Tovanor Breezhaler (glycopyrronium bromide). As a consequence, Annex I and IIIB are updated. The MAH also took this opportunity to update the local representatives. The RMP (version 8) is also updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.8. [Indacaterol, glycopyrronium - ULTIBRO BREEZHALER \(CAP\) - EMEA/H/C/002679/WS1340/0022; ULUNAR BREEZHALER \(CAP\) - EMEA/H/C/003875/WS1340/0022; XOTERNA BREEZHALER \(CAP\) - EMEA/H/C/003755/WS1340/0025](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Doris Stenver

Scope: Submission of the final report for study CQVA149A2401: a multinational, multi-database drug utilisation study (DUS) of indacaterol/glycopyrronium bromide (QVA149) in Europe with the objective to estimate the use of QVA149 off-label and in the subpopulations with missing information mentioned in the RMP

Action: For adoption of PRAC Assessment Report

7.4.9. [Mannitol - BRONCHITOL \(CAP\) - EMEA/H/C/001252/II/0031, Orphan](#)

Applicant: Pharmaxis Pharmaceuticals Limited

PRAC Rapporteur: Julie Williams

Scope: Submission of the final report of a survey on healthcare professionals (listed as a category 3 study in the RMP): a final survey aimed at measuring the effectiveness of the educational materials at 6 months post-launch and 6 months post-redistribution of the revised healthcare professional leaflet. The RMP (version 7.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.10. Micafungin - MYCAMINE (CAP) - EMEA/H/C/000734/II/0035

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report for the online survey for EU PAS register number EUPAS13634 measuring the effectiveness of the Mycamine prescriber checklist in the EU. The RMP (version 18.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.11. Prucalopride - RESOLOR (CAP) - EMEA/H/C/001012/II/0042

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Patrick Batty

Scope: Submission of the final clinical study report (CSR) for the post-authorisation drug utilisation study (DUS) SHP555-804 (in fulfilment of MEA 006.11): a DUS to examine characteristics of patients prescribed Resolor (prucalopride) and a pharmacoepidemiological study of the occurrence of major cardiovascular events, pregnancy, and pregnancy outcomes in the UK clinical practice research datalink (CPRD) database. The RMP (version 14.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.12. Radium (²²³Ra) dichloride - XOFIGO (CAP) - EMEA/H/C/002653/II/0031

Applicant: Bayer AG

PRAC Rapporteur: Patrick Batty

Scope: Submission of the final clinical study report (CSR) for study 17399 (listed as category 4 study in the RMP): an observational PASS to evaluate the use of radium-223 dichloride in patients in Sweden with a diagnosis of castration-resistant prostate cancer (CRPC) with bone metastases (mCRPC) and patients in whom radium-223 dichloride may have been potentially used off-label

Action: For adoption of PRAC Assessment Report

7.4.13. Ranibizumab - LUCENTIS (CAP) - EMEA/H/C/000715/II/0070/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) submission of the final report from the LUMINOUS study (CRFB002A2406): an observational, multicentre study to assess the long term safety and effectiveness of ranibizumab in routine clinical practice, in fulfilment of the post-authorisation measures MEA 036, MEA 048 and MEA 054; The RMP is updated accordingly; 2) submission of an updated RMP (version 17.0) to include changes not consequential to LUMINOUS study. In addition, the MAH is proposing the removal of the use of educational materials and targeted follow-up checklists listed in Annex II-D of the product information

Action: For adoption of PRAC Assessment Report

7.4.14. Somatropin - NUTROPINAQ (CAP) - EMEA/H/C/000315/II/0069/G

Applicant: Ipsen Pharma

PRAC Rapporteur: Doris Stenver

Scope: Grouped variations consisting of: 1) submission of the final report from the international cooperative growth study (iNCGS) Post marketing surveillance programme for NutropinAq (somatropin): a study collecting long-term safety and effectiveness data on NutropinAq during treatment of paediatric growth disorders for which growth hormone is indicated; 2) submission of an updated RMP (version 3.0) in order to include updates from the PASS iNCGS post marketing surveillance programme for NutropinAq. In addition, the RMP has been formatted in accordance with the new RMP template

Action: For adoption of PRAC Assessment Report

7.4.15. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0009

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Submission of the final clinical study report (CSR) for study A3921024 (listed as a category 3 study in the RMP (MEA 003)): a long term, non-interventional, open label follow-up study to evaluate the long-term safety of patients on 5 mg twice a day (BID) of Xeljanz (tofacitinib) with a secondary objective of evaluating sustained efficacy in patients with rheumatoid arthritis

Action: For adoption of PRAC Assessment Report

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

7.5.1. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 024.8

Applicant: Genzyme Europe BV

PRAC Rapporteur: Caroline Laborde

Scope: Annual report for the Pompe registry: a global, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease. The registry aims at detecting adverse events and/or lack of efficacy in patients, and at collecting immunological data, and follow-up growth disturbances in children

Action: For adoption of advice to CHMP

7.5.2. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 025.9

Applicant: Genzyme Europe BV

PRAC Rapporteur: Caroline Laborde

Scope: Annual report 2017 for the Pompe registry: a global, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease, focussing on data on patients with renal or hepatic insufficiency

Action: For adoption of advice to CHMP

7.5.3. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/MEA 017.2

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: First interim report for study ALIROC07997: a PASS using healthcare databases, in order to monitor the safety of Praluent (alirocumab) in patients affected with the human immunodeficiency virus (HIV) (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.5.4. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 002.1

Applicant: Samsung Bioepis UK Limited

PRAC Rapporteur: Patrick Batty

Scope: Second annual interim report from an established nationwide register (British Society for Rheumatology Rheumatoid Arthritis Register (BSRBR-RA)) for patients with rheumatological disorders treated with biologic agents, designed as a national prospective study whose primary purpose is to assess long-term toxicity from the use of these agents in routine practice

Action: For adoption of advice to CHMP

7.5.5. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 003.1

Applicant: Samsung Bioepis UK Limited

PRAC Rapporteur: Patrick Batty

Scope: Second annual interim report for study from RABBIT-RA (Rheumatoide Arthritis: Beobachtung der Biologika-Therapie): a prospective, observational cohort study evaluating the long-term effectiveness, safety, and costs associated with tumour necrosis factor (TNF)-inhibitor therapies in the treatment of rheumatoid arthritis (RA) and comparing it to a cohort of RA patients treated with non-biologic disease-modifying anti-rheumatic drugs (DMARDs)

Action: For adoption of advice to CHMP

7.5.6. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 004.1

Applicant: Samsung Bioepis UK Limited

PRAC Rapporteur: Patrick Batty

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

Action: For adoption of advice to CHMP

7.5.7. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/MEA 005.1

Applicant: Samsung Bioepis UK Limited

PRAC Rapporteur: Patrick Batty

Scope: Second annual interim report for study from BADBIR (British Association of Dermatologists Biologic Interventions Register): a nationwide registry assessing the long-term safety of biologic treatments for psoriasis

Action: For adoption of advice to CHMP

7.5.8. Florbetaben (¹⁸F) - NEURACEQ (CAP) - EMEA/H/C/002553/MEA 001.5

Applicant: Piramal Imaging Limited

PRAC Rapporteur: Patrick Batty

Scope: Interim report for study FBB-01-03-13 (PASS2): a non-interventional prospective observational multicentre, multinational registry to observe usage pattern, safety and tolerability of NeuraCeq (florbetaben (¹⁸F)) in clinical practice, including off-label use [final clinical study report: Q2 2020]

Action: For adoption of advice to CHMP

7.5.9. Insulin detemir - LEVEMIR (CAP) - EMEA/H/C/000528/MEA 045.8

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Doris Stenver

Scope: Fourth annual progress report for diabetes pregnancy registry (NN304-4016): an international non-interventional prospective cohort study to evaluate the safety of treatment with insulin detemir in pregnancy women with diabetes mellitus

Action: For adoption of advice to CHMP

7.5.10. Ivabradine - CORLENTOR (CAP) - EMEA/H/C/000598/ANX 027.2

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study CLE-16257-107: a multinational, retrospective, drug utilisation study (DUS) in select European countries aimed at describing the characteristics of ivabradine users, as well as describing the patterns of use of ivabradine, and the effectiveness of risk minimisation measures (RMM) as required in the conclusions of the safety referral procedure under Article 20 of Regulation (EC) No 726/2004

(EMA/H/A20/1404) finalised in 2014 and agreed protocol (EMA/H/C/PSP/j/0019.1.A.1) dated May 2016

Action: For adoption of advice to CHMP

[7.5.11. Ivabradine - IVABRADINE ANPHARM \(CAP\) - EMEA/H/C/004187/ANX 002.1](#)

Applicant: Anpharm Przedsiębiorstwo Farmaceutyczne S.A.

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study CLE-16257-107: a multinational, retrospective, drug utilisation study (DUS) in select European countries aimed at describing the characteristics of ivabradine users, as well as describing the patterns of use of ivabradine, and the effectiveness of risk minimisation measures (RMM) as required in the conclusions of the safety referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMA/H/A20/1404) finalised in 2014 and agreed protocol (EMA/H/C/PSP/j/0019.1.A.1) dated May 2016

Action: For adoption of advice to CHMP

[7.5.12. Ivabradine - PROCORALAN \(CAP\) - EMEA/H/C/000597/ANX 027.2](#)

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study CLE-16257-107: a multinational, retrospective, drug utilisation study (DUS) in select European countries aimed at describing the characteristics of ivabradine users, as well as describing the patterns of use of ivabradine, and the effectiveness of risk minimisation measures (RMM) as required in the conclusions of the safety referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMA/H/A20/1404) finalised in 2014 and agreed protocol (EMA/H/C/PSP/j/0019.1.A.1) dated May 2016

Action: For adoption of advice to CHMP

[7.5.13. Meningococcal group B vaccine \(rDNA, component, adsorbed\) - BEXSERO \(CAP\) - EMEA/H/C/002333/MEA 017.5](#)

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Qun-Ying Yue

Scope: First interim report for study V72_36OB: a post-licensure observational safety study after Bexsero (meningococcal B vaccine 4CMenB) vaccination in routine UK care [final report due date: 31/12/2019]

Action: For adoption of advice to CHMP

[7.5.14. Naloxegol - MOVENTIG \(CAP\) - EMEA/H/C/002810/MEA 006.4](#)

Applicant: Kyowa Kirin Limited

PRAC Rapporteur: Almath Spooner

Scope: Progress report for study D3820R00009 (EVM-17123): an observational PASS of Moventig (naloxegol) conducted amongst patients aged 18 years and older treated with opioids chronically for non-cancer and cancer pain (from initial opinion/MA)

Action: For adoption of advice to CHMP

7.5.15. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 009.1

Applicant: Kyowa Kirin Limited

PRAC Rapporteur: Almath Spooner

Scope: Annual progress study report for study D3820R00008: a US post-marketing, comparative, observational study in order to evaluate the cardiovascular safety of naloxegol in patients with non-cancer pain in comparison to other treatments for opioid induced constipation [final study report: December 2023]

Action: For adoption of advice to CHMP

7.5.16. Octocog alfa - HELIXATE NEXGEN (CAP) - EMEA/H/C/000276/MEA 085.6

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Eighth annual report for the European Haemophilia Safety Surveillance (EUHASS) registry in order to evaluate cases with adverse events (AEs) of special interest

Action: For adoption of advice to CHMP

7.5.17. Octocog alfa - KOGENATE BAYER (CAP) - EMEA/H/C/000275/MEA 086.6

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Eighth annual report for the European Haemophilia Safety Surveillance (EUHASS) registry in order to evaluate cases with adverse events (AEs) of special interest

Action: For adoption of advice to CHMP

7.5.18. Octocog alfa - KOVALTRY (CAP) - EMEA/H/C/003825/MEA 004

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Eighth annual report for epidemiological study 14149 conducted within the European Haemophilia Safety Surveillance (EUHASS) registry in order to evaluate cases with adverse events (AEs) of special interest

Action: For adoption of advice to CHMP

7.5.19. Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/MEA 004.2

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 004.1 [Annual progress report for study GENA-99: a prospective, multinational, non-interventional post-authorisation study to document the long-term immunogenicity, safety, and efficacy of simoctocog alfa in patients with haemophilia A treated in routine clinical practice [final report due date: 2020]] as per the request for supplementary information (RSI) adopted at the December 2017 PRAC meeting

Action: For adoption of advice to CHMP

7.5.20. Simoctocog alfa - VIHUMA (CAP) - EMEA/H/C/004459/MEA 004.1

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 004 [Annual progress report for study GENA-99: a prospective, multinational, non-interventional post-authorisation study to document the long-term immunogenicity, safety, and efficacy of simoctocog alfa in patients with haemophilia A treated in routine clinical practice [final report due date: 2020]] as per the request for supplementary information (RSI) adopted at the December 2017 PRAC meeting

Action: For adoption of advice to CHMP

7.5.21. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 022.13

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Patrick Batty

Scope: Annual report for study C0168Z03 (PSOLAR: PSoriasis Longitudinal Assessment and Registry): an international prospective cohort study/registry programme designed to collect data on psoriasis (PSO) patients that are eligible to receive systemic therapies, including generalised phototherapy and biologics

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 011.1

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's response to MEA 011 [revised statistical analysis plan (SAP) and submission of protocol (version 1.0) for a meta-analysis of three clinical trials: 1) study 1245.25: a phase 3, multicentre, international, randomised, parallel group, double-blind cardiovascular safety study of empagliflozin (10 mg and 25 mg administered orally once daily) compared to usual care in type 2 diabetes mellitus patients with increased cardiovascular risk (EMPA

REG); 2) study 1245.110: a phase 3 randomised, double-blind trial to evaluate efficacy and safety of once daily empagliflozin 10 mg compared to placebo, in patients with chronic heart failure with preserved ejection fraction (HFpEF) (EMPEROR-Preserved) and 3) study 1245.121: a randomised study on efficacy and safety of empagliflozin compared to placebo in patients with heart failure with reduced ejection fraction (EMPEROR-Reduced), including a graph of the cumulative incidence of amputation events and relevant preceding adverse events of special interest (AESI including gangrene, osteomyelitis) over time, to further characterise the important potential risk of lower limb amputation, as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMA/H/A-20/1442)] as per the request for supplementary information (RSI) adopted at the September 2017 PRAC meeting

Action: For adoption of advice to CHMP

7.6.2. Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMA/H/C/003833/MEA 003.1

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 003 [revised statistical analysis plan (SAP) and submission of protocol (version 1.0) for a meta-analysis of three clinical trials: 1) study 1245.25: a phase 3, multicentre, international, randomised, parallel group, double-blind cardiovascular safety study of empagliflozin (10 mg and 25 mg administered orally once daily) compared to usual care in type 2 diabetes mellitus patients with increased cardiovascular risk (EMPA REG); 2) study 1245.110: a phase 3 randomised, double-blind trial to evaluate efficacy and safety of once daily empagliflozin 10 mg compared to placebo, in patients with chronic heart failure with preserved ejection fraction (HFpEF) (EMPEROR-Preserved) and 3) study 1245.121: a randomised study on efficacy and safety of empagliflozin compared to placebo in patients with heart failure with reduced ejection fraction (EMPEROR-Reduced), including a graph of the cumulative incidence of amputation events and relevant preceding adverse events of special interest (AESI including gangrene, osteomyelitis) over time, to further characterise the important potential risk of lower limb amputation, as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMA/H/A-20/1442)] as per the request for supplementary information (RSI) adopted at the September 2017 PRAC meeting

Action: For adoption of advice to CHMP

7.6.3. Empagliflozin, metformin - SYNJARDY (CAP) - EMA/H/C/003770/MEA 007.1

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's response to MEA 007 [revised statistical analysis plan (SAP) and submission of protocol (version 1.0) for a meta-analysis of three clinical trials: 1) study 1245.25: a phase 3, multicentre, international, randomised, parallel group, double-blind cardiovascular safety study of empagliflozin (10 mg and 25 mg administered orally once daily) compared to usual care in type 2 diabetes mellitus patients with increased cardiovascular risk (EMPA

REG); 2) study 1245.110: a phase 3 randomised, double-blind trial to evaluate efficacy and safety of once daily empagliflozin 10 mg compared to placebo, in patients with chronic heart failure with preserved ejection fraction (HFpEF) (EMPEROR-Preserved) and 3) study 1245.121: a randomised study on efficacy and safety of empagliflozin compared to placebo in patients with heart failure with reduced ejection fraction (EMPEROR-Reduced), including a graph of the cumulative incidence of amputation events and relevant preceding adverse events of special interest (AESI including gangrene, osteomyelitis) over time, to further characterise the important potential risk of lower limb amputation, as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMA/H/A-20/1442)] as per the request for supplementary information (RSI) adopted at the September 2017 PRAC meeting

Action: For adoption of advice to CHMP

7.6.4. Trastuzumab - HERCEPTIN (CAP) - EMA/H/C/000278/LEG 100

Applicant: Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Assessment (drug safety report (DSR) 1083135) of cardiac monitoring practices in patients treated with Herceptin (trastuzumab) in order to assess the effectiveness of risk minimisation measures following the distribution of a direct healthcare professional communication (DHPC) as requested in the conclusions of variation EMA/H/C/000278/II/135 adopted at the October 2017 PRAC and CHMP

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

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

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/S/0019 (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. Anagrelide - XAGRID (CAP) - EMEA/H/C/000480/S/0081 (without RMP)

Applicant: Shire Pharmaceutical Contracts Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (Δ LNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - ZALMOXIS (CAP) - EMEA/H/C/002801/R/0010 (without RMP)

Applicant: MolMed SpA, ATMP³⁰

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/0041 (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

³⁰ Advanced therapy medicinal product

8.3. Renewals of the marketing authorisation

8.3.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/R/0020 (with RMP)

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Anette Stark

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/R/0032 (without RMP)

Applicant: Gentium S.r.l.

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Esomeprazole - NEXIUM CONTROL (CAP) - EMEA/H/C/002618/R/0021 (without RMP)

Applicant: Pfizer Consumer Healthcare Limited

PRAC Rapporteur: Simona Kudeliene

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Human fibrinogen, human thrombin - EVICEL (CAP) - EMEA/H/C/000898/R/0054 (without RMP)

Applicant: Omrix Biopharmaceuticals N. V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Infliximab - INFLECTRA (CAP) - EMEA/H/C/002778/R/0056 (without RMP)

Applicant: Hospira UK Limited

PRAC Rapporteur: Patrick Batty

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. [Infliximab - REMSIMA \(CAP\) - EMEA/H/C/002576/R/0047 \(without RMP\)](#)

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Patrick Batty

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. [Levodopa, carbidopa, entacapone - CORBILTA \(CAP\) - EMEA/H/C/002785/R/0015 \(with RMP\)](#)

Applicant: Orion Corporation

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. [Pomalidomide - IMNOVID \(CAP\) - EMEA/H/C/002682/R/0028 \(without RMP\)](#)

Applicant: Celgene Europe Limited

PRAC Rapporteur: Patrick Batty

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. [Radium \(²²³Ra\) dichloride - XOFIGO \(CAP\) - EMEA/H/C/002653/R/0030 \(without RMP\)](#)

Applicant: Bayer AG

PRAC Rapporteur: Patrick Batty

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

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

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

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh-v

12.2.1. EMA Scientific Committees – Timing for chair elections

Action: For discussion

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

12.3.1. Working Party with Healthcare Professionals' Organisations (HCPWP) - work plan 2018-2019

Action: For adoption

12.3.2. Working Party with Patients' and Consumers' Organisations (PCWP) – work plan 2018-2019

Action: For adoption

12.3.3. Blood Products Working Party - Haemophilia registries – workshop

Action: For discussion

12.4. Cooperation within the EU regulatory network

12.4.1. Brexit: preparedness of the regulatory network and capacity increase

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system – quarterly workload measures and performance indicators – Q1 2018 and predictions

Action: For discussion

12.8.2. PRAC workload statistics – Q1 2018

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Good Pharmacovigilance Practices (GVP) module I on 'Pharmacovigilance systems and their quality systems' - revision

Action: For discussion

12.9.2. Pharmacovigilance systems and their quality systems

None

12.9.3. Pharmacovigilance inspections- Template for sharing assessor's information – launch of pilot phase

Action: For discussion

12.9.4. Pharmacovigilance inspections - Union procedure on follow-up of pharmacovigilance inspections

Action: For adoption

12.9.5. Pharmacovigilance audits

None

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

- 12.10.1. Periodic safety update reports single assessment (PSUSA) – update on follow-up procedures (PSUFU) for nationally approved products (NAPs) and CMDh table on other considerations
-

PRAC lead: Menno van der Elst

Action: For discussion

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

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

12.15.2. Post-authorisation Safety Studies – non-imposed PASS

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. EMA relocation - update

Action: For discussion

12.20.2. Guideline on Good Pharmacovigilance Practices (GVP) – Product- or population-specific considerations IV: ‘Paediatric pharmacovigilance’

Action: For adoption

13. Any other business

Next meeting on: 14-17 May 2018

14. Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

EU Referral procedures for safety reasons: Urgent EU procedures and Other EU referral procedures

(Items 2 and 3 of the PRAC agenda)

A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the European Union (EU). For further detailed information on safety related referrals please see:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000150.jsp&mid=WCOb01ac05800240d0

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/