



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Procedure Management and Committees Support Division

## Pharmacovigilance Risk Assessment Committee (PRAC) Draft agenda for the meeting on 30 August – 02 September 2016

Chair: June Raine – Vice-Chair: Almath Spooner

30 August 2016, 13:00 – 19:30, room 3/A

31 August 2016, 08:30 – 19:30, room 3/A

01 September 2016, 08:30 – 19:30, room 3/A

02 September 2016, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

15 September 2016, 09:00 – 12:00, room 7/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).

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<sup>1</sup> Indacaterol, glycopyrronium bromide - WS1005 – procedure scope corrected on page 36; Atazanavir sulfate - LEG 83 – procedure removed on page 67 as outcome due at a later stage; Pharmacovigilance programme and revised implementation - removed on page 98 as discussion due at a later stage



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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 30 August – 02 September 2016. See September 2016 PRAC minutes (to be published post October 2016 PRAC meeting).

### **1.2. Adoption of agenda of the meeting of 30 August–02 September 2016**

**Action:** For adoption

### **1.3. Adoption of the minutes of the previous meeting on 04-08 July 2016**

**Action:** For adoption

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

### **2.1. Newly triggered procedures**

None

### **2.2. Ongoing procedures**

None

### **2.3. Procedures for finalisation**

None

### **2.4. Planned public hearings**

None

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

#### 3.1. Newly triggered procedures

None

#### 3.2. Ongoing procedures

##### 3.2.1. Retinoids: acitretin (NAP); adapalene (NAP); alitretinoin - PANRETIN (CAP); bexarotene – TARGRETIN (CAP); isotretinoin (NAP); tazarotene (NAP); tretinoin (NAP) - EMEA/H/A-31/1446

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Applicant: Eisai Ltd (Panretin, Targretin), various

PRAC Rapporteur: Leonor Chambel; PRAC Co-rapporteur: Julie Williams

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

**Action:** For discussion of a request to revise the procedural timetable

#### 3.3. Procedures for finalisation

None

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

None

#### 3.5. Others

None

### 4. Signals assessment and prioritisation<sup>2</sup>

#### 4.1. New signals detected from EU spontaneous reporting systems

##### 4.1.1. Azacitidine – VIDAZA (CAP)

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Applicant: Celgene Europe Limited

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

PRAC Rapporteur: Sabine Straus

Scope: Signal of pericarditis and pericardial effusion

**Action:** For adoption of PRAC recommendation

EPITT 18733 – New signal

Lead Member State: NL

#### 4.1.2. Esomeprazole (CAP), NAP

---

Applicants: Pfizer Consumer Healthcare Ltd (Nexium Control), various

PRAC Rapporteur: To be appointed

Scope: Signal of gastric polyps

**Action:** For adoption of PRAC recommendation

EPITT 18725 – New signal

Lead Member States: LT, SE

#### 4.1.3. Lenalidomide – REVLIMID (CAP)

---

Applicant: Celgene Europe Limited

PRAC Rapporteur: Claire Ferard

Scope: Signal of hemophagocytic lymphohistiocytosis (HLH)

**Action:** For adoption of PRAC recommendation

EPITT 18689 – New signal

Lead Member State: FR

#### 4.1.4. Ritonavir – NORVIR (CAP)

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Applicant: AbbVie Ltd

PRAC Rapporteur: Menno van der Elst

Scope: Signal of retinal pigment epitheliopathy

**Action:** For adoption of PRAC recommendation

EPITT 18703 – New signal

Lead Member State: NL

## 4.2. New signals detected from other sources

#### 4.2.1. Darbepoetin alfa – ARANESP (CAP)

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Applicant: Amgen Europe B.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Signal of incorrect use of device associated with adverse reactions including underdose, drug dose omission, accidental exposure to product and injection site reactions

**Action:** For adoption of PRAC recommendation

EPITT 18718 – New signal

Lead Member State: DE

#### 4.2.2. Propofol (NAP); valproate (NAP)

---

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of pharmacokinetic drug interaction leading to an increased propofol exposure

**Action:** For adoption of PRAC recommendation

EPITT 18696 – New signal

Lead Member State: NO

#### 4.2.3. Proton pump inhibitors (PPIs): dexlansoprazole (NAP); esomeprazole – NEXIUM CONTROL (CAP), NAP; lansoprazole (NAP); omeprazole (NAP); pantoprazole – CONTROLOC CONTROL (CAP), PANTECTA CONTROL (CAP), PANTOLOC CONTROL (CAP), PANTOZOL CONTROL (CAP), SOMAC CONTROL (CAP), NAP; rabeprazole (NAP)

---

Applicants: Pfizer Consumer Healthcare Ltd (Nexium Control), Takeda GmbH (Controloc Control, Pantecta Control, Pantoloc Control, Pantozol Control, Somac Control), various

PRAC Rapporteur: To be appointed

Scope: Signal of incident chronic kidney disease (CKD) and progression to end stage renal disease (ESRD)

**Action:** For adoption of PRAC recommendation

EPITT 18698 – New signal

Lead Member State: UK

### 4.3. Signals follow-up and prioritisation

#### 4.3.1. Agomelatine - THYMANAX (CAP) - EMEA/H/C/000916/SDA/028; VALDOXAN (CAP) - EMEA/H/C/000915/SDA/028

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Applicant: Servier (Ireland) Industries Ltd, Les Laboratoires Servier

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: Signal of urinary retention

**Action:** For adoption of PRAC recommendation

EPITT 18637 – Follow-up to April 2016

#### 4.3.2. Agomelatine - THYMANAX (CAP) - EMEA/H/C/000916/SDA/029; VALDOXAN (CAP) - EMEA/H/C/000915/SDA/029

---

Applicant: Servier (Ireland) Industries Ltd, Les Laboratoires Servier

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: Signal of leukopenia

**Action:** For adoption of PRAC recommendation

EPITT 18638 – Follow-up to April 2016

#### 4.3.3. Boceprevir – VICTRELIS (CAP); daclatasvir – DAKLINZA (CAP); dasabuvir – EXVIERA (CAP); ledipasvir, sofosbuvir – HARVONI (CAP); ombitasvir, paritaprevir, ritonavir – VIEKIRAX (CAP); simeprevir - OLYSIO (CAP); sofosbuvir – SOVALDI (CAP)

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Applicants: AbbVie Ltd (Exviera, Viekirax), Bristol-Myers Squibb Pharma EEIG (Daklinza), Gilead Sciences International Ltd (Harvoni, Sovaldi), Janssen-Cilag International N.V. (Incivo, Olysio), Merck Sharp & Dohme Limited (Victrelis)

PRAC Rapporteur: Dolores Montero Corominas

Scope: Signal of drug interaction between direct-acting antivirals (DAAV) and vitamin K antagonists leading to a reduced international normalized ratio (INR)

**Action:** For adoption of PRAC recommendation

EPITT 18654 – Follow-up to June 2016

#### 4.3.4. Cobicistat-containing products: cobicistat – TYBOST (CAP); cobicistat, atazanavir sulfate – EVOTAZ (CAP); cobicistat, darunavir – REZOLSTA (CAP); cobicistat elvitegravir, emtricitabine, tenofovir alafenamide – GENVOYA (CAP); cobicistat elvitegravir, emtricitabine, tenofovir disoproxil fumarate – STRIBILD (CAP); NAP

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Applicants: Gilead Sciences International Ltd (Genvoya, Stribild, Tybost), Bristol-Myers Squibb Pharma EEIG (Evotaz), Janssen-Cilag International N.V. (Rezolsta)

PRAC Rapporteur: Rafe Suvarna

Scope: Signal of drug interaction with corticosteroids leading to adrenal suppression

**Action:** For adoption of PRAC recommendation

EPITT 18647 – Follow-up to April 2016

#### 4.3.5. Iomeprol (NAP)

---

Applicant: various

PRAC Rapporteur: Helga Haugom Olsen

Scope: Signal of haemolysis

**Action:** For adoption of PRAC recommendation

EPITT 18625 – Follow-up to April 2016

- 4.3.6. Selective serotonin reuptake inhibitors (SSRIs): citalopram (NAP); escitalopram (NAP); fluoxetine (NAP); fluvoxamine (NAP); mirtazapine (NAP); paroxetine (NAP); sertraline (NAP)  
Serotonin–noradrenaline reuptake inhibitors (SNRIs): duloxetine - ARICLAIM (CAP), DULOXETINE LILLY (CAP), CYMBALTA (CAP), XERISTAR (CAP), YENTREVE (CAP); sibutramine (NAP); venlafaxine (NAP)
- 

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

PRAC Rapporteur: Claire Ferard

Scope: Signal of risk of autistic spectrum disorders (ASD) after in utero exposure to selective serotonin reuptake inhibitors (SSRI)

**Action:** For adoption of PRAC recommendation

EPITT 14082 – Follow-up to May 2016

## 5. Risk management plans (RMPs)

### 5.1. Medicines in the pre-authorisation phase

#### 5.1.1. Aceneuramic acid - EMEA/H/C/004176, Orphan

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Applicant: Ultragenyx UK Limited

Scope: Treatment of hereditary inclusion body myopathy (HIBM)

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

#### 5.1.2. Adalimumab - EMEA/H/C/004212

---

Scope: Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn's disease, paediatric Crohn's disease and ulcerative colitis

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

#### 5.1.3. Adalimumab - EMEA/H/C/004373

---

Scope: Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn's disease, paediatric Crohn's disease and ulcerative colitis

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

#### 5.1.4. Alectinib - EMEA/H/C/004164

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Scope: Treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive

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

#### 5.1.5. Brodalumab - EMEA/H/C/003959

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Scope: Treatment of moderate to severe plaque psoriasis

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

#### 5.1.6. Chlormethine - EMEA/H/C/002826, Orphan

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Applicant: Actelion Registration Ltd

Scope: Treatment of mycosis fungoides-type cutaneous T-cell lymphoma (MF-type CTCL)

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

#### 5.1.7. Emtricitabine, tenofovir disoproxil – EMEA/H/C/004215

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

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

#### 5.1.8. Eryaspase - EMEA/H/C/004055, Orphan

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Applicant: Erytech Pharma S.A.

Scope: Treatment of leukaemia

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

#### 5.1.9. Insulin aspart - EMEA/H/C/004046

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Scope: Treatment of diabetes mellitus in adults

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

#### 5.1.10. Insulin glargine - EMEA/H/C/004101

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Scope: Treatment of diabetes mellitus

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

#### 5.1.11. Ivabradine - EMEA/H/C/004217

---

Scope: Treatment of angina pectoris

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

#### 5.1.12. Lonococog alfa - EMEA/H/C/004075

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Scope: Treatment of haemophilia A

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

#### 5.1.13. Lutetium (<sup>177</sup>Lu) dotatate - EMEA/H/C/004123, Orphan

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Applicant: Advanced Accelerator Applications

Scope (accelerated assessment): Treatment of gastro-entero-pancreatic neuroendocrine tumours

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

#### 5.1.14. Nonacog beta pegol - EMEA/H/C/004178, Orphan

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Applicant: Novo Nordisk A/S

Scope: Treatment of haemophilia B

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

#### 5.1.15. Parathyroid hormone - EMEA/H/C/003861, Orphan

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Applicant: NPS Pharma Holdings Limited

Scope: Treatment of hypoparathyroidism

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

#### 5.1.16. Sildenafil - EMEA/H/C/004289

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Scope: Treatment of patients with pulmonary arterial hypertension

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

#### 5.1.17. Tadalafil - EMEA/H/C/004297

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Scope: Treatment of pulmonary arterial hypertension (PAH)

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

#### 5.1.18. Tenofovir alafenamide - EMEA/H/C/004169

---

Scope: Treatment of chronic hepatitis B in adults

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

#### 5.1.19. Teriparatide - EMEA/H/C/004368; TERROSA (CAP MAA) – EMEA/H/C/003916

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Scope: Treatment of osteoporosis

**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. Abiraterone - ZYTIGA (CAP) - EMEA/H/C/002321/II/0045

---

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Eva Segovia

Scope: Update of the RMP to modify the planned dates for assessment in the risk minimisation measures for all important identified and potential risks as well as missing information

**Action:** For adoption of PRAC Assessment Report

### 5.2.2. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/II/0014

---

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Update of the RMP (version 2.0) to include progressive multifocal leukoencephalopathy (PML) as an important potential risk, to describe the pharmacovigilance activities associated to PML and to include a standardize case definition for the diagnosis of PML

**Action:** For adoption of PRAC Assessment Report

### 5.2.3. Aliskiren - RASILEZ (CAP) - EMEA/H/C/000780/WS0771/0104; aliskiren, hydrochlorothiazide - RASILEZ HCT (CAP) - EMEA/H/C/000964/WS0771/0075

---

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of the RMP with regard to identified risks, missing information, concomitant use of other medicines, drug-drug interactions, removal of safety issues attributed to the withdrawn aliskiren/amlodipine (Rasilamlo) and aliskiren/amlodipine/HCTZ (Rasitrio). The variation is supported by study report SPA100A: antihypertensive effects and long-term safety of aliskiren in elderly patients

**Action:** For adoption of PRAC Assessment Report

### 5.2.4. Antithrombin alfa - ATRYN (CAP) - EMEA/H/C/000587/II/0027

---

Applicant: GTC Biotherapeutics UK Limited

PRAC Rapporteur: Claire Ferard

Scope: Introduction of a RMP (version 1) as requested in the sixth annual re-assessment (EMEA/H/C/000587/S/0021) and second five-year renewal (EMEA/H/C/000587/R/0024)

**Action:** For adoption of PRAC Assessment Report

#### 5.2.5. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/II/0045

---

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP in order to reflect details of the category 3 study HGS1006-C1112/BEL115471: a phase 3/4, multicentre, double-blind, randomized, placebo-controlled, 52-week study to evaluate the efficacy and safety of belimumab in adult subjects of black race with systemic lupus erythematosus (SLE). The final due date of the study is amended accordingly

**Action:** For adoption of PRAC Assessment Report

#### 5.2.6. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/II/0020

---

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Update of the RMP in order to reflect the outcome of the recently finalised procedure under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA) including updates on renal impairment/renal failure; hypersensitivity and DKA. In addition, the MAH proposed to revise the dates for completion of clinical studies and included additional studies as requested in the Article 20 procedure

**Action:** For adoption of PRAC Assessment Report

#### 5.2.7. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/II/0016

---

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP in order to reflect the outcome of the recently finalised procedure under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA) including updates on renal impairment/renal failure; hypersensitivity and DKA. In addition, the MAH proposed to revise the dates for completion of clinical studies and included additional studies as requested in the Article 20 procedure

**Action:** For adoption of PRAC Assessment Report

#### 5.2.8. Catridecacog - NOVOTHIRTEEN (CAP) - EMEA/H/C/002284/II/0015

---

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Claire Ferard

Scope: Update of the RMP (version 13) in order to add final data from completed study F13CD-3720 (a multicentre, open-label, single-arm, and multiple dosing trial on safety of monthly replacement therapy with recombinant factor XIII (rFXIII) in patients with congenital factor XIII deficiency). The MAH took the opportunity to update the RMP to include other information based on the new data lock point of 31 March 2016

**Action:** For adoption of PRAC Assessment Report

5.2.9. [Dapagliflozin, metformin - EBYMECT \(CAP\) - EMEA/H/C/004162/WS0968/0012](#);  
[XIGDUO \(CAP\) - EMEA/H/C/002672/WS0968/0023](#)  
[Dapagliflozin - EDISTRIDE \(CAP\) - EMEA/H/C/004161/WS0968/0009](#); [FORXIGA \(CAP\) - EMEA/H/C/002322/WS0968/0028](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of the RMP in order to implement the outcome of the recently finalised procedure under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA) including the addition of atypical DKA as an important identified risk for all sodium-glucose cotransporter-2 (SGLT2) inhibitors, upgrade of a drug utilisation study (DUS) from category 4 to 3 as well as the addition of a description of an ongoing mechanistic study. Finally, the RMP is updated to add a description of a DKA epidemiological study assessing the incidence of DKA

**Action:** For adoption of PRAC Assessment Report

5.2.10. [Deferasirox - EXJADE \(CAP\) - EMEA/H/C/000670/II/0051](#)

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: Update of the RMP (version 13.0) in order to remove any reference to a new tradename to be implemented for the new film-coated tablets formulation (approved as part of X/43) as a new routine risk minimisation measure. The MAH took the opportunity to update the educational materials to reflect changes from recently approved procedures (II/45, R/47 and PSUSA/00000939/201510)

**Action:** For adoption of PRAC Assessment Report

5.2.11. [Dimethyl fumarate - TECFIDERA \(CAP\) - EMEA/H/C/002601/II/0026](#)

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Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: Update of the RMP (version 7) in order to include the outcome of the evaluation from WS/689 (PML added as an important identified risk). The draft PASS protocol for category 3 study 109MS419 (a retrospective, multicentre, observational study to assess the effect of Tecfidera delayed-release capsules on lymphocyte subsets in subjects with relapsing forms of multiple sclerosis) was also submitted. In addition, a discussion on the overall totality of the non-clinical and clinical work being undertaken to further understand lymphopenia associated with Tecfidera treatment is included

**Action:** For adoption of PRAC Assessment Report

5.2.12. [Dronedarone - MULTAQ \(CAP\) - EMEA/H/C/001043/II/0035](#)

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Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP to propose revised additional risk minimisation measures to facilitate healthcare professionals' (HCP) compliance and to modify the timelines for study EFFECT-AF: a historic-prospective cohort with dynamic exposure and stratified competitive recruitment with balanced comparison groups of dronedarone versus alternative antiarrhythmic drugs of interest (EFFECT-AF/OBS13687. Annex II.D ('conditions or restrictions with regard to the safe and effective use of the medicinal product') of the Marketing Authorisation is updated accordingly

**Action:** For adoption of PRAC Assessment Report

**5.2.13. [Empagliflozin - JARDIANCE \(CAP\) - EMEA/H/C/002677/WS0953/0019;](#)  
[Empagliflozin, metformin - SYNJARDY \(CAP\) - EMEA/H/C/003770/WS0953/0019](#)**

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Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of the RMP in order to reflect the outcome of the recently finalised procedure under Article 20 of Regulation (EC) No 726/2004 on diabetic ketoacidosis (DKA) including the addition of atypical DKA as an important identified risk for all sodium-glucose cotransporter-2 (SGLT2) inhibitors. In addition, ongoing and planned activities are being included in the RMP

**Action:** For adoption of PRAC Assessment Report

**5.2.14. [Human fibrinogen, human thrombin - EVICEL \(CAP\) - EMEA/H/C/000898/II/0039](#)**

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Applicant: Omrix Biopharmaceuticals N. V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of a revised RMP (version 14) including updates on data exposure, medication error cases and effectiveness of risk minimisations measures related to the potential risk of air/gas embolism associated with spray application

**Action:** For adoption of PRAC Assessment Report

**5.2.15. [Human protein C - CEPROTIN \(CAP\) - EMEA/H/C/000334/II/0093](#)**

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Applicant: Baxter AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of the RMP (version 1.0) following the completion of procedure PSUSA/00002563/201507 to add the following risks to the summary of safety concerns: bleeding episodes as an identified risk; hypersensitivity reactions as identified risk; injection site reactions as a potential risk; inhibitor development as a potential risk as well as heparin induced thrombocytopenia as a potential risk

**Action:** For adoption of PRAC Assessment Report

5.2.16. Ibandronic acid - BONDRONAT (CAP) - EMEA/H/C/000101/WS0942/0074; BONVIVA (CAP) - EMEA/H/C/000501/WS0942/0056

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Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Implementation of the PRAC recommendation to add patient reminder cards as an additional risk minimisation measure to the ibandronic acid risk management plan, following the PRAC recommendation adopted in February 2016 as part of the PSUSA/00001702/201506 procedure

**Action:** For adoption of PRAC Assessment Report

5.2.17. Influenza vaccine (split virion, inactivated) - IDFLU (CAP) - EMEA/H/C/000966/WS1012/0047; INTANZA (CAP) - EMEA/H/C/000957/WS1012/0050

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Applicant: Sanofi Pasteur

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of the RMP (version 11.0) to include information on the enhanced safety surveillance for the Northern hemisphere (NH) 2016-2017 influenza season

**Action:** For adoption of PRAC Assessment Report

5.2.18. Insulin degludec - TRESIBA (CAP) - EMEA/H/C/002498/II/0022

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Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of the RMP (version 6) in order to upgrade the risk of mix-up between basal and bolus insulin from a potential to an important identified risk; to include paediatric patients in the additional risk minimisation activities to mitigate the important potential risk of medication errors due to mix-up between different strengths of Tresiba as well as to remove the category 4 studies: EX1250-4080 (DEVOTE: trial comparing cardiovascular safety of insulin degludec versus insulin glargine in subjects with type 2 diabetes at high risk of cardiovascular events), NN1250 4129 (a multicentre, prospective, open-label, single-arm, non-interventional, post marketing surveillance (PMS) study of insulin degludec to evaluate long term safety and efficacy in patients with diabetes mellitus in routine clinical practice in India), NN1250-4061 (a multicentre, open label, observational, non-interventional, PMS to evaluate safety and effectiveness during long-term treatment with insulin degludec in patients with diabetes mellitus requiring insulin therapy under normal clinical practice conditions), NN1250-4110 (a multicentre, prospective, open-label, single-arm, non-interventional, regulatory PMS study of insulin degludec to evaluate safety and effectiveness in patients of all age groups excluding less than 12 months old infants with diabetes mellitus in routine clinical practice in Korea) and NN1250-4189 (a multicentre, prospective, non-interventional study of insulin degludec investigating the safety and effectiveness in a real world population with type 1 and 2 diabetes mellitus)

**Action:** For adoption of PRAC Assessment Report

### 5.2.19. [Naltrexone, bupropion - MYSIMBA \(CAP\) - EMEA/H/C/003687/II/0005/G](#)

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Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of amended study designs for both the renal impairment study (effect of renal impairment on the pharmacokinetics of naltrexone PR/ bupropion PR tablet (category 3 study)) and the hepatic impairment study (effect of hepatic impairment on the pharmacokinetics of naltrexone PR /bupropion PR tablet (category 3 study)) as outlined in the currently approved RMP (version 8)

**Action:** For adoption of PRAC Assessment Report

### 5.2.20. [Vardenafil - LEVITRA \(CAP\) - EMEA/H/C/000475/WS0973/0053; VIVANZA \(CAP\) - EMEA/H/C/000488/WS0973/0049](#)

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Applicant: Bayer Pharma AG

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of the RMP to include a safety concern (identified risk) already assessed and implemented in the Levitra/Vivanza product information (EMEA/H/C/xxxx/WS/0861) on the contraindication relating to the concomitant use of riociguat and phosphodiesterase type 5 (PDE5) inhibitors including vardenafil

**Action:** For adoption of PRAC Assessment Report

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

### 5.3.1. [Abiraterone - ZYTIGA \(CAP\) - EMEA/H/C/002321/X/0039](#)

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Eva Segovia

Scope: Line extension to introduce a new pharmaceutical form associated with a new strength (500 mg film-coated tablets)

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

### 5.3.2. [Amifampridine - FIRDAPSE \(CAP\) - EMEA/H/C/001032/II/0043](#)

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Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.4 and 5.3 of the SmPC in order to delete the statement that amifampridine has not been fully tested in carcinogenicity models and to provide the findings from the carcinogenicity reports required for the completion of SOB 004. The RMP (version 9) is updated accordingly. In addition, the MAH took the opportunity to request the removal in Annex II of the requirement to complete carcinogenicity testing in an appropriate model

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

### 5.3.3. [Ataluren - TRANSLARNA \(CAP\) - EMEA/H/C/002720/II/0026](#)

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Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.4 and 4.5 of the SmPC to remove the interaction with inhibitors of breast cancer resistant protein (BCRP) based on the results of a drug-drug interaction study of the co-administration of ataluren and inhibitors of BCRP

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

### 5.3.4. [Ataluren - TRANSLARNA \(CAP\) - EMEA/H/C/002720/II/0027](#)

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Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Update of section 4.8 of the SmPC to add that the safety profile of ataluren in non-ambulatory patients is similar to the safety profile in ambulatory patients following the results of a 48-week open label extension study in patients with nonsense mutation Duchenne muscular dystrophy (nmDMD)

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

### 5.3.5. [Belatacept - NULOJIX \(CAP\) - EMEA/H/C/002098/II/0038](#)

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Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.8 and 5.1 of the SmPC following the completion of the post-authorisation efficacy studies: IM103-008 (belatacept evaluation of nephroprotection and efficacy as first-line immunosuppression trial (BENEFIT) and IM103-027 (belatacept evaluation of nephro-protection and efficacy as first-line immunosuppression trial - extended criteria donors (BENEFIT-EXT)). The Package Leaflet and the RMP (version 12) are updated accordingly

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

### 5.3.6. [C1-esterase inhibitor, human - CINRYZE \(CAP\) - EMEA/H/C/001207/II/0045](#)

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Applicant: Shire Services BVBA

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include children with hereditary angioedema (HAE) in the treatment and pre-procedure prevention of angioedema attacks. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2, 6.5 and 6.5 of the SmPC are updated. The Package Leaflet and Labelling are updated accordingly. In addition, the MAH proposed to update regional information in module 3.2.R due to the proposed dose recommendation for children

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

### 5.3.7. Cabazitaxel - JEVTANA (CAP) - EMEA/H/C/002018/II/0034

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Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Claire Ferard

Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to add information from completed study EFC11785 (randomized, open-label multicentre study comparing cabazitaxel at 20 mg/m<sup>2</sup> and at 25 mg/m<sup>2</sup> every 3 weeks in combination with prednisone for the treatment of metastatic castration-resistant prostate cancer previously treated with a docetaxel-containing regimen). In addition, the MAH proposed to modify the wording in section 4.1 from 'hormone refractory' to 'castration resistant' prostate cancer to reflect the current terminology of the disease in the clinical practice. The RMP is updated accordingly and in accordance with the outcome of the latest PSUR procedure (PSUSA/000476/201506)

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

### 5.3.8. Canakinumab - ILARIS (CAP) - EMEA/H/C/001109/X/0045/G

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped application comprising a line extension covering an additional formulation (150 mg/ml solution for injection) and a type II variation to add a new indication based on the results of the pivotal phase 3 study CACZ885N2301 on the treatment of adults and children of 2 years of age and older with one of the following periodic fever syndromes: tumour necrosis factor receptor associated periodic syndrome (TRAPS); hyperimmunoglobulin D syndrome (HIDS), mevalonate kinase deficiency (MKD); familial Mediterranean fever (FMF) in patients in whom colchicine is contraindicated, is not tolerated, or does not provide an adequate response. 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 11) are updated accordingly. In addition, the annexes have been aligned with the latest QRD template (version 10)

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

### 5.3.9. Carfilzomib - KYPROLIS (CAP) - EMEA/H/C/003790/II/0007/G

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Applicant: Amgen Europe B.V.

PRAC Rapporteur: Marina Dimov Di Giusti

Scope: Update of sections 4.2 and 5.2 of the SmPC to revise the guidance on the use of carfilzomib in patients with renal and hepatic impairments further to the submission of completed studies relating to renal impairment (CFZ001: an open-label, single arm, phase 1 study of the pharmacokinetics and safety of carfilzomib in subjects with relapsed multiple myeloma and end-stage renal disease) and hepatic impairment (CFZ002: an open-label, single arm, phase 1 study of the pharmacokinetics and safety of carfilzomib in subjects with advanced malignancies and varying degrees of hepatic impairment). The RMP is updated accordingly. In addition, the MAH took the opportunity to implement some editorial changes to the Product Information

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

### 5.3.10. Ceritinib - ZYKADIA (CAP) - EMEA/H/C/003819/II/0008

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 5.1 of the SmPC to reflect the final study report from study A2201 (a phase 2, multicentre, single-arm study in adult patients with anaplastic lymphoma kinase (ALK)-activated non-small cell lung cancer (NSCLC) previously treated with chemotherapy and crizotinib) to confirm the efficacy of ceritinib in the treatment of patients previously treated with crizotinib

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

### 5.3.11. Conestat alfa - RUCONEST (CAP) - EMEA/H/C/001223/X/0034

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Applicant: Pharming Group N.V

PRAC Rapporteur: Rafe Suvarna

Scope: Addition of a new pharmaceutical form 'powder and solvent for solution for injection' with self-administration kit

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

### 5.3.12. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/II/0044

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Applicant: Pfizer Limited

PRAC Rapporteur: Claire Ferard

Scope: Update of section 5.2 of the SmPC in order to provide the results of the final overall survival analysis in study A8081007 (a phase 3, randomized, open-label study of the efficacy and safety of crizotinib vs standard of care chemotherapy (pemetrexed or docetaxel) in patients with advanced non-small cell lung cancer (NSCLC) harboring a translocation or inversion event involving the anaplastic lymphoma kinase (ALK) gene locus (SOB001)). The MAH took the opportunity to request the conversion of the conditional marketing authorisation into a full marketing authorisation. The RMP (version 7.2) is updated accordingly

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

### 5.3.13. Darunavir - PREZISTA (CAP) - EMEA/H/C/000707/WS0955/0081; Darunavir, cobicistat - REZOLSTA (CAP) - EMEA/H/C/002819/WS0955/0012

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final clinical study report (CSR) of category 3 study GS-US-236-0130: a phase 3b, open label, single-arm trial to evaluation the safety and efficacy of cobicistat-boosted darunavir (DRV) plus two fully active nucleoside reverse transcriptase inhibitors (NRTIs) in human immunodeficiency virus (HIV)-1 infected, antiretroviral therapy (ART)-naïve and experienced adults with no DRV-resistant associated mutations (RAMs). The RMPs (version 24.0 for Prezista, version 3.0 for Rezolsta) are updated accordingly, and

in accordance with changes previously requested by CHMP and PRAC

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

#### 5.3.14. [Dolutegravir - TIVICAY \(CAP\) - EMEA/H/C/002753/X/0018/G](#)

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Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Julie Williams

Scope: Grouped application comprising a line extension to add two new strengths (10 mg and 25 mg tablets) to support the extension of indication for the treatment of paediatric patients from 6 years of age infected with human immunodeficiency virus (HIV). Data from cohort I and II A of study ING112578 (a 48 week Phase 1/2 multicentre open-label non-comparative study to evaluate pharmacokinetic (PK), safety, tolerability and antiviral activity of dolutegravir in HIV-1 infected children and adolescents of 6 weeks to <18 years of age) are presented in support of the new therapeutic indication

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

#### 5.3.15. [Eculizumab - SOLIRIS \(CAP\) - EMEA/H/C/000791/II/0086/G](#)

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Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations including: 1) update of section 4.8 of the SmPC with the adverse drug reactions (ADR) frequencies to reflect overall exposure to eculizumab in clinical trials; 2) update of section 4.4 of the SmPC with warning and precautions on meningococcal vaccination timing as recommended by PRAC. The Package Leaflet, Annex II and the RMP (version 13) are updated accordingly. In addition, the RMP is updated in order to implement the previous PRAC recommendation to remove the off label use from missing information, to provide the exposure data from PSUR#13 and to update the epidemiology sections with more complete and recent scientific literature data. Moreover, the MAH took the opportunity to update the Product Information to add editorial changes and to bring it in line with the latest QRD template

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

#### 5.3.16. [Empagliflozin - JARDIANCE \(CAP\) - EMEA/H/C/002677/II/0014](#)

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Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Extension of indication to include the prevention of cardiovascular events, based on the final data of the cardiovascular safety clinical trial EMPA-REG OUTCOME (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). As a consequence, section 4.1 of the SmPC is updated in order to add safety information on this study. The Package Leaflet is updated accordingly

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

5.3.17. [Empagliflozin - JARDIANCE \(CAP\) - EMEA/H/C/002677/WS0971/0022;](#)  
[Empagliflozin, metformin - SYNJARDY \(CAP\) - EMEA/H/C/003770/WS0971/0021](#)

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Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of the final clinical report for study 1245.28 (4-year data) (a phase 3, randomised, double-blind, active controlled parallel group efficacy and safety study of empagliflozin compared to glimepiride administered orally during 104 weeks with a 104-week extension period in patients with type 2 diabetes mellitus and insufficient glycaemic control despite metformin treatment)

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

5.3.18. [Empagliflozin, metformin - SYNJARDY \(CAP\) - EMEA/H/C/003770/II/0015](#)

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Applicant: Boehringer Ingelheim GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Extension of indication to include the treatment with Synjardy as adjunct to standard care therapy in adult patients with type 2 diabetes mellitus and high cardiovascular risk when the treatment with empagliflozin and metformin is appropriate and empagliflozin is needed to reduce the risk of all-cause mortality by reducing cardiovascular death and cardiovascular death or hospitalization for heart failure. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated based on the final clinical study report of study EMPA-REG OUTCOME (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). The Package Leaflet and RMP (version 5.0) is updated accordingly

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

5.3.19. [Everolimus - VOTUBIA \(CAP\) - EMEA/H/C/002311/II/0041](#)

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include the adjunctive treatment of patients aged 2 years and older with refractory seizures associated with tuberous sclerosis complex (TSC) for Votubia 2 mg, 3 mg and 5 mg dispersible tablets. Sections 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated based on the results from the pivotal study. In addition, sections 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 are also updated for the 2.5 mg, 5 mg and 10 mg tablets to reflect data relevant to these formulations. The Package Leaflet is updated accordingly. Furthermore, the Product Information is brought in line with the latest QRD template (version 10)

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

### 5.3.20. Ferric maltol - FERACCRU (CAP) - EMEA/H/C/002733/II/0002/G

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Applicant: Shield TX (UK) Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of two final study reports for in vitro studies conducted as part of post-authorisation measures (MEA 001) drug-drug interaction study to investigate drug interactions with Feraccru; and (MEA 002): drug-drug interaction study to identify uridine diphosphate glucuronosyltransferase (UGT) isoenzyme(s) that are responsible for metabolism of ferric maltol. The RMP is updated accordingly

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

### 5.3.21. Florbetapir (<sup>18</sup>F) - AMYVID (CAP) - EMEA/H/C/002422/II/0022

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Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Update of sections 4.4 and 5.1 of the SmPC in order to introduce quantitative read as an adjunct to visual read of florbetapir (<sup>18</sup>F) positron emission tomography (PET) scans. The RMP (version 2.0) is updated accordingly. In addition, the MAH took the opportunity to bring the Product Information in line with the latest QRD template (version 10.0)

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

### 5.3.22. Glycopyrronium bromide - ENUREV BREEZHALER (CAP) - EMEA/H/C/002691/WS1001/0016; SEEBRI BREEZHALER (CAP) - EMEA/H/C/002430/WS1001/0016; TOVANOR BREEZHALER (CAP) - EMEA/H/C/002690/WS1001/0018

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Update of section 4.8 of the SmPC to include the adverse drug reaction (ADR) dysphonia. The Package Leaflet is updated accordingly

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

### 5.3.23. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0025

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Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Update of the SmPC section 4.4 to remove the warning and precaution regarding the effect of ibrutinib on the QT interval and section 5.1 to provide additional information regarding the pharmacodynamic effect of ibrutinib on QT/QTc intervals and cardiac electrophysiology

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

#### 5.3.24. [Idebenone - RAXONE \(CAP\) - EMEA/H/C/003834/II/0003](#)

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Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Carmela Macchiarulo

Scope: Extension of indication to include treatment of patients with Duchenne muscular dystrophy in whom respiratory function has started to decline and who are currently not taking concomitant glucocorticoids

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

#### 5.3.25. [Imiquimod - ALDARA \(CAP\) - EMEA/H/C/000179/II/0067](#)

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Applicant: Meda AB

PRAC Rapporteur: Rafe Suvarna

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to add data on the results of study X-03016-3284 (LEIDA 2, a phase IV randomised active controlled study: long-term effects of imiquimod 5% cream and diclofenac 3% gel in the treatment of actinic keratoses on the face or scalp with respect to the risk of progression to in-situ and invasive squamous cell carcinoma) and of a meta-analysis of studies X-03016-3271 (LEIDA, a phase IV randomized active controlled study: long-term effects of imiquimod 5% cream and diclofenac 3% gel in the treatment of actinic keratoses on the face or scalp) and X-03016-3284. The RMP is updated (version 3) accordingly

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

#### 5.3.26. [Indacaterol, glycopyrronium bromide - ULTIBRO BREEZHALER \(CAP\) - EMEA/H/C/002679/WS1005/0013; ULUNAR BREEZHALER \(CAP\) - EMEA/H/C/003875/WS1005/0013; XOTERNA BREEZHALER \(CAP\) - EMEA/H/C/003755/WS1005/0015](#)

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Update of section 4.8 of the SmPC to add dysphonia and revise the adverse drug reactions selection and frequencies based on the MAH's review of all safety data. As a consequence, section 4.4 of the SmPC is updated. The Package Leaflet and the RMP (version 2.0) are updated accordingly. Annex II is updated in line with the latest QRD template

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

#### 5.3.27. [Ivacaftor - KALYDECO \(CAP\) - EMEA/H/C/002494/II/0049](#)

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Applicant: Vertex Pharmaceuticals (Europe) Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of the final clinical study report (CSR) for study VX11-770-109 (a phase 3, 2-arm, open-label roll-over study from study VX11-770-108 (study 108) to evaluate the long-term safety and pharmacodynamics of ivacaftor treatment in paediatric subjects with

cystic fibrosis and a cystic fibrosis transmembrane conductance regulator (CFTR) gating mutation) to fulfil the RMP commitment to address the following safety concerns: hepatotoxicity, cataracts, cardiac arrhythmias, use in children between 2 to 5 years old, long-term safety. The RMP (version 5.1) is updated accordingly

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

#### 5.3.28. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/II/0089/G

Applicant: Celgene Europe Limited

PRAC Rapporteur: Claire Ferard

Scope: Extension of indication to add the treatment of adult patients with newly diagnosed multiple myeloma (NDMM) who have undergone autologous stem cell transplantation (ASCT). The sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated accordingly. In addition, the Package Leaflet and the RMP are updated accordingly. Furthermore, the MAH introduced 7-day pack sizes for the 10 mg and 15 mg strengths with subsequent changes to the Product Information

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

#### 5.3.29. Levetiracetam - LEVETIRACETAM HOSPIRA (CAP) - EMEA/H/C/002783/II/0012

Applicant: Hospira UK Limited

PRAC Rapporteur: Veerle Verlinden

Scope: Update the Product Information in line with the company core safety information (CSI) (version 1.0) to include rhabdomyolysis and blood creatine phosphokinase increased as adverse drug reactions (ADR)

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

#### 5.3.30. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/II/0011/G

Applicant: Vertex Pharmaceuticals (Europe) Ltd

PRAC Rapporteur: Almath Spooner

Scope: Grouped variation on the final results of two in-vitro studies evaluating the potential off target activity of M6-ivacaftor to address post-authorisation measure MEA005. The RMP is updated accordingly. In addition, the MAH took the opportunity to update administrative aspects of the RMP. The RMP (version 2.5) is updated accordingly

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

#### 5.3.31. Meningococcal group A, C, W135 and Y conjugate vaccine - NIMENRIX (CAP) - EMEA/H/C/002226/II/0049

Applicant: Pfizer Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Extension of indication to cover a wider paediatric population starting from 6 weeks

of age. As a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and the RMP are updated accordingly.

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

#### 5.3.32. [Meningococcal group B vaccine \(rDNA, component, adsorbed\) - BEXSERO \(CAP\) - EMEA/H/C/002333/II/0044/G](#)

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Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped variations to: 1) update of section 4.8 of the SmPC to include fever as an adverse reaction in adolescents from 11 years of age and adults, and to include hypotonic-hyporesponsive episode (HHE) as an adverse reaction in infants and children up to 10 years of age; 2) update of sections 4.4 and 5.1 of the SmPC to reflect safety and immunogenicity data from a clinical study involving the use of Bexsero in subjects 2 through 17 years of age with increased risk of meningococcal disease. The Package Leaflet is updated accordingly

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

#### 5.3.33. [Methylthioninium chloride - METHYLTHIONINIUM CHLORIDE PROVEBLUE \(CAP\) - EMEA/H/C/002108/II/0030/G](#)

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Applicant: Provepharm SAS

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of section 4.8 of the SmPC in order to include paresthesia, dysgeusia, syncope, presyncope, feeling of change in body temperature, chest discomfort, shoulder pain and limb discomfort based on data from two clinical studies. In addition, frequencies were added in the tabulated list of adverse reactions. The Package and the RMP (version 2.0) are updated accordingly

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

#### 5.3.34. [Natalizumab - TYSABRI \(CAP\) - EMEA/H/C/000603/II/0095](#)

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Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section sections 4.2, 4.3, 4.8, 5.1 and 5.2 of the SmPC based on the results of paediatric studies 101MS028 (meta-analysis of the safety and efficacy of natalizumab in paediatric patients with multiple sclerosis) and 101MS328 (a phase 1, multicentre, open-label, single-arm, multiple dose study to evaluate the the pharmacokinetics and pharmacodynamics of natalizumab in paediatric subjects with relapsing remitting multiple sclerosis (RMS)), in accordance with the paediatric investigation plan (EMEA-001095-PIP-12). The RMP (version 21) is updated accordingly

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

### 5.3.35. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/II/0097/G

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Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations to: 1) update of section 4.4 of the SmPC to include information about the use of plasmapheresis (PLEX) or intravenous immunoglobulin (IVIg) which can affect meaningful interpretation of serum anti- John Cunningham (JC) virus (V) antibody testing, 2) update of sections 4.4 and 4.8 of the SmPC upon request by PRAC following the assessment of procedure SDA/063 regarding a signal on necrotising retinitis. The Package Leaflet and the RMP (version 22.0) are updated accordingly

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

### 5.3.36. Nitisinone - ORFADIN (CAP) - EMEA/H/C/000555/II/0057

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Applicant: Swedish Orphan Biovitrum International AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to amend the dosing frequency further to the results of a clinical pharmacology study NTBC-003 ('an open-label, non-randomized, sequential, multicentre study to evaluate the pharmacokinetics, efficacy and safety of once daily dosing compared to twice daily dosing of Orfadin in patients diagnosed with hereditary tyrosinemia type 1'). The Package Leaflet is updated accordingly

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

### 5.3.37. Nitisinone - ORFADIN (CAP) - EMEA/H/C/000555/II/0058

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Applicant: Swedish Orphan Biovitrum International AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of section 5.3 of the SmPC in order to add a statement that carcinogenic potential was not shown in a 26-week carcinogenicity study

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

### 5.3.38. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0012

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Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the monotherapy treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL): - after autologous stem cell transplant (ASCT) and treatment with brentuximab vedotin, or - after at least two prior therapies in patients who are not candidates for ASCT. As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the proposed new indication, add a warning that patients with active autoimmune disease and symptomatic interstitial lung disease were excluded from clinical trials of cHL, and update the safety and pharmacodynamic information. The Package Leaflet and the RMP (version 5.0) are updated accordingly. Furthermore, the product information is brought in line with the latest QRD

template (version 10.0)

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

### 5.3.39. [Olaparib - LYNPARZA \(CAP\) - EMEA/H/C/003726/II/0008/G](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of sections 4.2 and 5.2 of the SmPC with recommendations for patients with renal impairment based on the results of study D0816C00006 (MEA 006) (an open-label, non-randomised, multicentre, comparative, phase 1 study of the pharmacokinetics, safety and tolerability of olaparib following a single oral 300 mg dose to patients with advanced solid tumours and normal renal function or renal impairment) that evaluated the influence of mild and moderate renal impairment on the pharmacokinetics of olaparib. The Package Leaflet and RMP are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, to bring the product information in line with the latest QRD template version and to introduce minor corrections in the product information. Furthermore, a grouping of two type IB variations is submitted to revise the study milestones dates for the category 3 study D0816C00005 (an open-label, non-randomised, multicentre, comparative, phase 1 study to determine the pharmacokinetics, safety and tolerability of olaparib following a single oral 300 mg dose to patients with advanced solid tumours and normal hepatic function or mild or moderate hepatic impairment) and category 1 study D0816C00002 (phase 3 randomised, double blind, placebo controlled study of olaparib maintenance monotherapy in platinum sensitive relapsed BRCA mutated ovarian cancer patients with a complete or partial response following platinum based chemotherapy) in the RMP. Annex II is amended accordingly

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

### 5.3.40. [Olaparib - LYNPARZA \(CAP\) - EMEA/H/C/003726/II/0009/G](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of sections 4.2 and 5.2 of the SmPC to include information related to hepatic impairment based on the results of study D0816C00005 (MEA 005) (an open-label, non-randomised, multicentre, comparative, phase 1 study to determine the pharmacokinetics, safety and tolerability of olaparib following a single oral 300 mg dose to patients with advanced solid tumours and normal hepatic function or mild or moderate hepatic impairment). In addition, sections 4.4 and 4.5 are updated to include information related to moderate cytochrome P450, family 3, subfamily A (CYP3A) inducers based on the addendum to the Simcyp modelling report. The Package Leaflet and RMP are updated accordingly

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

### 5.3.41. [Oritavancin - ORBACTIV \(CAP\) - EMEA/H/C/003785/II/0012/G](#)

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Applicant: The Medicines Company UK Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Grouped variations to: 1) update sections 4.4 and 4.5 of the SmPC in order to delete the warning related to the interaction with warfarin and include the results of the interaction study (MDCO-ORI-14-02: an open-label study to assess the drug-drug interaction potential of a single 1200 mg intravenous (IV) dose of oritavancin co-administered with warfarin in healthy subjects) respectively. The Package Leaflet and RMP (version 2.2) are updated accordingly; 2) update of the RMP (version 2.2) to delete the category 3 study MDCO-ORI-14-03 (an open-label study to evaluate the safety of a single 1200 mg IV dose of oritavancin in subjects on concomitant chronic warfarin therapy being treated for acute bacterial skin and skin structure infection (ABSSSI))

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

#### 5.3.42. [Osimertinib - TAGRISSO \(CAP\) - EMEA/H/C/004124/II/0004](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Sabine Straus

Scope: Update of section 5.2 of the SmPC to reflect the results of study 20 performed to assess the absolute bioavailability and to evaluate the pharmacokinetic (PK) parameters of osimertinib in plasma following a single oral dose and a radio-labelled intravenous (IV) microdose of [<sup>14</sup>C] Tagrisso in healthy male subjects. In addition, the MAH took the opportunity to make a minor correction in SmPC section 6.5 and the Package Leaflet, where blister strips have been amended to blisters. The RMP (version 5.0) is updated accordingly

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

#### 5.3.43. [Pertuzumab - PERJETA \(CAP\) - EMEA/H/C/002547/II/0026](#)

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Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Submission of study MO22324 (PHEREXA), a multicentre randomized phase III study to compare the combination of trastuzumab and capecitabine, with or without pertuzumab, in patients with human epidermal growth factor-2 (HER2)-positive metastatic breast cancer that have progressed after one line of trastuzumab-based therapy in the metastatic setting. Annex II is updated to reflect the fulfilment of the condition of the Marketing Authorisation. The RMP (version 7.0) is updated accordingly. In addition, the MAH took the opportunity to include in the RMP a minor amendment to the BERENICE protocol (a multicentre, multinational, phase 2 study to evaluate pertuzumab in combination with trastuzumab and standard neoadjuvant anthracycline-based chemotherapy in patients with human epidermal growth factor (HER2)-positive, locally advanced, inflammatory, or early-stage breast cancer)

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

#### 5.3.44. [Pirfenidone - ESBRIET\(CAP\) - EMEA/H/C/002154/X/0035/G](#)

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Applicant: Roche Registration Limited

PRAC Rapporteur: Julie Williams

Scope: Line extension to introduce a new pharmaceutical form associated with 3 new strengths (267mg, 534mg and 801mg film-coated tablets). In addition, manufacturing sites are also introduced for the currently approved 267mg hard capsules presentations (EU/1/11/667/001-003): F. Hoffmann-La Roche Ltd, Basel, Switzerland as an alternative site responsible for quality control of the active substance; Synlab Umweltinstitut GmbH, Linz, Austria, as an alternative site responsible for quality control of the active substance

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

#### 5.3.45. [Pneumococcal polysaccharide conjugate vaccine \(adsorbed\) - SYNFLORIX \(CAP\) - EMEA/H/C/000973/II/0108](#)

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Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of sections 4.2 4.4, 4.8 and 5.1 of the SmPC in order to add information obtained from two clinical studies in subjects at risk for pneumococcal infections (study 10PN-PD-DIT-034 (open label, controlled study in South Africa to evaluate the immunogenicity, safety and reactogenicity of Synflorix administered as a 3-dose primary immunisation course in human immunodeficiency virus (HIV) infected infants, HIV exposed uninfected infants and HIV unexposed uninfected infants) and study 10PN-PD-DIT-064 (open, controlled study to evaluate immunogenicity, safety and reactogenicity of Synflorix administered intramuscularly to sickle cell disease subjects from 8 weeks to less than 2 years of age, as compared to age-matched healthy subjects). In addition, the MAH took the opportunity to introduce consequential changes to the RMP and to change the final due date of a post-marketing surveillance study

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

#### 5.3.46. [Rivaroxaban - XARELTO \(CAP\) - EMEA/H/C/000944/II/0042/G](#)

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Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of section 5.1 of the SmPC following the submission of a prospective, single-arm, non-interventional, open-label cohort study conducted to investigate the safety and effectiveness in a real-world setting, study XANTUS (SN 15914) in order to fulfil MEA 025. In addition, update of section 5.1 of the SmPC following the submission of a prospective, non-interventional, open-label cohort study that was conducted in patients with acute deep vein thrombosis (DVT) to investigate the safety and effectiveness in a real-world setting, study XALIA (SN 15915) in order to fulfil MEA 027. The RMP (version 9.0) is updated accordingly. Additionally the final clinical study reports for studies X-TRA (SN 16320, phase IIIb) and VENTURE-AF (SN 15694, phase IIIb) were also included in the RMP. Finally, the MAH took the opportunity to introduce a minor editorial change in the list of representatives in the package leaflets of all strengths

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

#### 5.3.47. [Rufinamide - INOVELON \(CAP\) - EMEA/H/C/000660/II/0037](#)

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Applicant: Eisai Ltd

PRAC Rapporteur: Claire Ferard

Scope: Extension of indication to include the treatment of seizures associated with Lennox-Gastaut syndrome in paediatric patients of 1 year of age and older, based on the results of study E2080-G000-303 (study 303): a randomized, controlled, open-label study to evaluate the cognitive development effects and safety, and pharmacokinetics of adjunctive rufinamide treatment in paediatric subjects 1 to less than 4 years of age with inadequately controlled Lennox-Gastaut syndrome. This study was conducted to fulfil the long-term (2 years) safety and efficacy objectives required as part of the paediatric investigation plan (PIP) EMEA-000709-PIP01-09. 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 9.0) are updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the annexes, to implement changes in line with the latest QRD template and to combine the SmPCs, labelling and Package Leaflets for the three authorised strengths of the tablet formulation in line with the current version of the QRD template

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

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5.3.48. [Sevelamer - RENVELA \(CAP\) - EMEA/H/C/000993/WS0965/0035; SEVELAMER CARBONATE ZENTIVA \(CAP\) - EMEA/H/C/003971/WS0965/0007](#)

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Applicant: Genzyme Europe BV

PRAC Rapporteur: Veerle Verlinden

Scope: Extension of indication to include the control of hyperphosphataemia in paediatric patients (>6 years of age and a body surface area (BSA) of >0.75 m<sup>2</sup>) with chronic kidney disease. As a consequence, section 4.2 of the SmPC is updated to detail the posology in the paediatric patients. The Package Leaflet is updated accordingly

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

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5.3.49. [Tadalafil - ADCIRCA \(CAP\) - EMEA/H/C/001021/WS0993/0025, CIALIS \(CAP\) - EMEA/H/C/000436/WS0993/0085](#)

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Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of section 4.4 of the SmPC in order to add a new warning on the risk of non-arteritic anterior ischemic optic neuropathy (NAION) based on the final results of study H6D-MC- LVHQ (category 3 study). In addition, the RMP (version 8.0) is updated accordingly

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

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5.3.50. [Ustekinumab - STELARA \(CAP\) - EMEA/H/C/000958/X/0049/G](#)

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: Line extension to add a new pharmaceutical form (concentrate for solution for infusion), a new strength (130 mg) and a new route of administration (intravenous use) as well as an extension of indication to add as a new indication the treatment of Crohn's

disease

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

### 5.3.51. Vismodegib - ERIVEDGE (CAP) - EMEA/H/C/002602/II/0025/G

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Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.4, 4.6, 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information in the product information after finalisation of study MO25616 (specific obligation (SOB) 013) (a single arm, open-label, Phase 2, multicentre study to assess the safety of vismodegib in patient with locally advanced or metastatic basal cell carcinoma (BCC)). Considering the fulfilment of the SOB, the MAH also proposed the switch of the conditional marketing authorisation (MA) to a full MA not subject to specific obligations. Data from the same study also fulfilled the analysis required in MEA 005 regarding evaluation of the time for washout of vismodegib after treatment discontinuation and in MEA 008 regarding reporting of adverse events. The Package Leaflet and the RMP are updated accordingly. Furthermore, the MAH took the opportunity to update the RMP with regard to the results from non-clinical studies subject to variation II/21 and to propose the deletion of hyponatremia as an important potential risk in the RMP and as an adverse drug reaction in the product information as per the outcome of the latest PSUR procedure (PSUSA/00010140/201407)

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

### 5.3.52. Vismodegib - ERIVEDGE (CAP) - EMEA/H/C/002602/II/0029

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Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC with additional information to describe the risk of epiphyses premature fusion in paediatric patients. The Package Leaflet and RMP (version 9.2) are updated accordingly. In addition, the MAH took the opportunity to include some editorial changes in the product information

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

## 6. Periodic safety update reports (PSURs)

### 6.1. PSUR procedures including centrally authorised products (CAPs) only

#### 6.1.1. Aclidinium bromide - BRETARIS GENUAIR (CAP); EKLIRA GENUAIR (CAP) - PSUSA/00009005/201601

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Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.2. Agomelatine - THYMANAX (CAP); VALDOXAN (CAP) - PSUSA/00000071/201602

Applicant: Les Laboratoires Servier (Valdoxan), Servier (Ireland) Industries Ltd (Thymanax)

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.3. Asfotase alfa - STRENSIQ (CAP) - PSUSA/00010421/201601

Applicant: Alexion Europe SAS

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.4. Ataluren - TRANSLARNA (CAP) - PSUSA/00010274/201601

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.5. Atazanavir, cobicistat - EVOTAZ (CAP) - PSUSA/00010404/201601

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.6. Axitinib - INLYTA (CAP) - PSUSA/00010022/201601

Applicant: Pfizer Limited

PRAC Rapporteur: Helga Haugom Olsen

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.7. Besilesomab - SCINTIMUN (CAP) - PSUSA/00000385/201601 (with RMP)

Applicant: Cis Bio International

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

#### 6.1.8. Bevacizumab - AVASTIN (CAP) - PSUSA/00000403/201602

Applicant: Roche Registration Limited  
PRAC Rapporteur: Doris Stenver  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

#### 6.1.9. Brentuximab vedotin - ADCETRIS (CAP) - PSUSA/00010039/201602

Applicant: Takeda Pharma A/S  
PRAC Rapporteur: Sabine Straus  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

#### 6.1.10. Brimonidine<sup>3</sup> - MIRVASO (CAP) - PSUSA/00010093/201602 (with RMP)

Applicant: Galderma International  
PRAC Rapporteur: Rafe Suvarna  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

#### 6.1.11. Carfilzomib - KYPROLIS (CAP) - PSUSA/00010448/201601

Applicant: Amgen Europe B.V.  
PRAC Rapporteur: Marina Dimov Di Giusti  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

#### 6.1.12. Cobimetinib - COTELLIC (CAP) - PSUSA/00010450/201602

Applicant: Roche Registration Limited  
PRAC Rapporteur: Sabine Straus  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

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<sup>3</sup> centrally authorised product only

6.1.13. Colistimethate sodium (dry inhalation powder) - COLOBREATHE (CAP) - PSUSA/00009112/201602

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Applicant: Forest Laboratories UK Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.14. Copper (<sup>64</sup>Cu) chloride - CUPRYMINA (CAP) - PSUSA/00010040/201602

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Applicant: Sparkle S.r.l.

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.15. Daclatasvir - DAKLINZA (CAP) - PSUSA/00010295/201601

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Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Margarida Guimarães

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.16. Dapagliflozin, metformin - EBYMECT (CAP); XIGDUO (CAP) - PSUSA/00010294/201601

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Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.17. Degarelix - FIRMAGON (CAP) - PSUSA/00000944/201602 (with RMP)

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Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.18. Dexamethasone (indicated in uveitis and macular oedema) - OZURDEX (CAP) - PSUSA/00000985/201601

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Applicant: Allergan Pharmaceuticals Ireland

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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#### 6.1.19. [Dinutuximab - UNITUXIN \(CAP\) - PSUSA/00010420/201602](#)

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Applicant: United Therapeutics Europe Ltd

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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#### 6.1.20. [Dolutegravir - TIVICAY \(CAP\); dolutegravir, abacavir, lamivudine - TRIUMEQ \(CAP\) - PSUSA/00010075/201601](#)

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Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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#### 6.1.21. [Eliglustat - CERDELGA \(CAP\) - PSUSA/00010351/201601](#)

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Applicant: Genzyme Europe BV

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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#### 6.1.22. [Elosulfase alfa - VIMIZIM \(CAP\) - PSUSA/00010218/201602](#)

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Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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#### 6.1.23. [Entacapone - COMTAN \(CAP\); COMTESS \(CAP\); ENTACAPONE ORION \(CAP\) - PSUSA/00001223/201601](#)

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Applicant: Novartis Europharm Ltd (Comtan), Orion Corporation (Comtess, Entacapone Orion)

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.24. Etanercept - ENBREL (CAP) - PSUSA/00001295/201602

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Applicant: Pfizer Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.25. Evolocumab - REPATHA (CAP) - PSUSA/00010405/201601

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Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.26. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - PSUSA/00010352/201602

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Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.27. Fampridine - FAMPYRA (CAP) - PSUSA/00001352/201601

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Applicant: Biogen Idec Ltd

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.28. Fenofibrate, simvastatin - CHOLIB (CAP) - PSUSA/00010096/201602 (with RMP)

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Applicant: BGP Products Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.29. Florbetaben (<sup>18</sup>F) - NEURACEQ (CAP) - PSUSA/00010094/201602

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Applicant: Piramal Imaging Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

**6.1.30. Gadoversetamide - OPTIMARK (CAP) - PSUSA/00001508/201601**

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Applicant: Mallinckrodt Deutschland GmbH

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

**6.1.31. Gimeracil, oteracil monopotassium, tegafur - TEYSUNO (CAP) - PSUSA/00002875/201601**

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Applicant: Nordic Group B.V.

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

**6.1.32. Hepatitis B (rDNA) vaccine (adjuvanted, adsorbed) - FENDRIX (CAP) - PSUSA/00001598/201602**

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Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

**6.1.33. Human alpha 1-proteinase inhibitor - RESPREEZA (CAP) - PSUSA/00010410/201602**

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Applicant: CSL Behring GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

**6.1.34. Human coagulation factor VIII, human von Willebrand factor<sup>4</sup> - VONCENTO (CAP) - PSUSA/00010102/201602**

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Applicant: CSL Behring GmbH

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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<sup>4</sup> Centrally authorised product only

#### 6.1.35. Idelalisib - ZYDELIG (CAP) - PSUSA/00010303/201601

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Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.36. Infliximab<sup>5</sup> - INFLECTRA (CAP); REMSIMA (CAP) - PSUSA/00010106/201601

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Applicant: Celltrion Healthcare Hungary Kft. (Remsima), Hospira UK Limited (Inflectra)

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.37. Ingenol mebutate - PICATO (CAP) - PSUSA/00010035/201601

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Applicant: Leo Pharma A/S

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.38. Insulin glargine - ABASAGLAR (CAP); LANTUS (CAP); TOUJEO (CAP) - PSUSA/00001751/201602

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Applicant: Eli Lilly Regional Operations GmbH (Abasaglar), Sanofi-aventis Deutschland GmbH (Lantus, Toujeo)

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.39. Ivacaftor - KALYDECO (CAP) - PSUSA/00009204/201601 (with RMP)

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Applicant: Vertex Pharmaceuticals (Europe) Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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<sup>5</sup> Biosimilars only

6.1.40. Lamivudine<sup>6</sup> - EPIVIR (CAP); lamivudine, zidovudine - COMBIVIR (CAP) - PSUSA/00009207/201511

---

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.41. Lenvatinib - LENVIMA (CAP) - PSUSA/00010380/201602

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Applicant: Eisai Europe Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.42. Lipegfilgrastim - LONQUEX (CAP) - PSUSA/00010111/201601

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Applicant: Sicor Biotech UAB

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.43. Lixisenatide - LYXUMIA (CAP) - PSUSA/00010017/201601

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Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.44. Lomitapide - LOJUXTA (CAP) - PSUSA/00010112/201601 (with RMP)

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Applicant: Aegerion Pharmaceuticals Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.45. Meningococcal group-B vaccine (rDNA, component, adsorbed) - BEXSERO (CAP) - PSUSA/00010043/201601

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Applicant: GSK Vaccines S.r.l.

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<sup>6</sup> Indicated in human immunodeficiency virus infections

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

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6.1.46. [Modified vaccinia Ankara virus - IMVANEX \(CAP\) - PSUSA/00010119/201601](#)

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Applicant: Bavarian Nordic A/S  
PRAC Rapporteur: Rafe Suvarna  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

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6.1.47. [Nalmefene - SELINCRO \(CAP\) - PSUSA/00010120/201602](#)

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Applicant: H. Lundbeck A/S  
PRAC Rapporteur: Martin Huber  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

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6.1.48. [Nilotinib - TASIGNA \(CAP\) - PSUSA/00002162/201601](#)

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Applicant: Novartis Europharm Ltd  
PRAC Rapporteur: Doris Stenver  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

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6.1.49. [Nitisinone - ORFADIN \(CAP\) - PSUSA/00002169/201602](#)

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Applicant: Swedish Orphan Biovitrum International AB  
PRAC Rapporteur: Carmela Macchiarulo  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

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6.1.50. [Nivolumab - OPDIVO \(CAP\) - PSUSA/00010379/201601](#)

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Applicant: Bristol-Myers Squibb Pharma EEIG  
PRAC Rapporteur: Brigitte Keller-Stanislawski  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

#### 6.1.51. Paclitaxel albumin - ABRAXANE (CAP) - PSUSA/00010123/201601

Applicant: Celgene Europe Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.52. Panobinostat - FARYDAK (CAP) - PSUSA/00010409/201602

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.53. Pegfilgrastim - NEULASTA (CAP); RISTEMPA (CAP) - PSUSA/00002326/201601

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.54. Peginterferon beta-1A - PLEGRIDY (CAP) - PSUSA/00010275/201601 (with RMP)

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.55. Pegloticase - KRYSTEXXA<sup>7</sup> - PSUSA/00010046/201601

Applicant: Crealta Pharmaceuticals Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

**Action:** For information

#### 6.1.56. Perampanel - FYCOMPA (CAP) - PSUSA/00009255/201601

Applicant: Eisai Europe Ltd

PRAC Rapporteur: Julie Williams

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<sup>7</sup> EC decision on the MA withdrawal of Krystexxa dated 30 June 2016

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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6.1.57. [Perflutren - LUMINITY \(CAP\); OPTISON \(CAP\) - PSUSA/00002350/201512](#)

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Applicant: GE Healthcare AS (Optison), Lantheus MI UK Ltd (Luminity)

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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6.1.58. [Phenylephrine, ketorolac - OMIDRIA \(CAP\) - PSUSA/00010419/201601](#)

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Applicant: Omeros London Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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6.1.59. [Pneumococcal polysaccharide conjugate vaccine \(13-valent, adsorbed\) - PREVENAR 13 \(CAP\) - PSUSA/00009263/201601](#)

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Applicant: Pfizer Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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6.1.60. [Pomalidomide - IMNOVID \(CAP\) - PSUSA/00010127/201602 \(with RMP\)](#)

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Applicant: Celgene Europe Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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6.1.61. [Prasugrel - EFIENT \(CAP\) - PSUSA/00002499/201602](#)

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Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.62. Pregabalin - LYRICA (CAP); PREGABALIN PFIZER (CAP) - PSUSA/00002511/201601

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.63. Pyronaridine, artesunate - PYRAMAX (Art 58<sup>8</sup>) – EMEA/H/W/002319/PSUV/0013

Applicant: Shin Poong Pharmaceutical Co., Ltd

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.64. Rasagiline - AZILECT (CAP); RASAGILINE RATIOPHARM (CAP) - PSUSA/00002612/201601

Applicant: Teva B.V.

PRAC Rapporteur: Leonor Chambel

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.65. Roflumilast - DALIRESP (CAP); DAXAS (CAP); LIBERTEK (CAP) - PSUSA/00002658/201601 (with RMP)

Applicant: Takeda GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.66. Rufinamide - INOVELON (CAP) - PSUSA/00002671/201601

Applicant: Eisai Ltd

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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<sup>8</sup> Article 58 of Regulation (EC) No 726/2004 allows the Agency's Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO), on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)

#### 6.1.67. Ruxolitinib - JAKAVI (CAP) - PSUSA/00010015/201602

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.68. Sacubitril, valsartan - ENTRESTO (CAP) - PSUSA/00010438/201601

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.69. Safinamide - XADAGO (CAP) - PSUSA/00010356/201602

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Applicant: Zambon SpA

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.70. Samarium (<sup>153</sup>Sm) lexidronam - QUADRAMET (CAP) - PSUSA/00002682/201602

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Applicant: Cis Bio International

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.71. Silodosin - SILODYX (CAP); UROREC (CAP) - PSUSA/00002701/201601

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Applicant: Recordati Ireland Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.72. Simoctocog alfa - NUWIQ (CAP) - PSUSA/00010276/201601

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Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.73. [Sodium phenylbutyrate - AMMONAPS \(CAP\); PHEBURANE \(CAP\) - PSUSA/00002758/201512](#)

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Applicant: Lucane Pharma (Pheburane), Swedish Orphan Biovitrum International AB (Ammonaps)

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.74. [Sugammadex - BRIDION \(CAP\) - PSUSA/00002799/201601](#)

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Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.75. [Tasimelteon - HETLIOZ \(CAP\) - PSUSA/00010394/201601](#)

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Applicant: Vanda Pharmaceuticals Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.76. [Trastuzumab emtansine - KADCYLA \(CAP\) - PSUSA/00010136/201602](#)

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Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

6.1.77. [Ulipristal acetate<sup>9</sup> - ESMYA \(CAP\) - PSUSA/00009325/201602](#)

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Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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<sup>9</sup> For the treatment of moderate to severe symptoms of uterine fibroids

#### 6.1.78. Velaglucerase alfa - VPRIV (CAP) - PSUSA/00003103/201602

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Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.79. Vismodegib - ERIVEDGE (CAP) - PSUSA/00010140/201601

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Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.1.80. Vorapaxar - ZONTIVITY (CAP) - PSUSA/00010357/201601

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Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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

#### 6.2.1. Alendronic acid, colecalciferol - ADROVANCE (CAP); FOSAVANCE (CAP); VANTAVO (CAP); NAP - PSUSA/00000079/201601

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Applicant: Merck Sharp & Dohme Limited (Adrovanche, Fosavance, Vantavo), various

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.2.2. Alitretinoin - PANRETIN (CAP); NAP - PSUSA/00000090/201601

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Applicant: Eisai Ltd (Panretin), various

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.2.3. [Levetiracetam - KEPBRA \(CAP\), NAP - PSUSA/00001846/201511](#)

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Applicant: UCB Pharma S.A., various

PRAC Rapporteur: Veerle Verlinden

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.2.4. [Orlistat - ALLI \(CAP\); XENICAL \(CAP\); NAP - PSUSA/00002220/201602](#)

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Applicant: Glaxo Group Ltd (Alli), Roche Registration Limited (Xenical), various

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.2.5. [Riluzole - RILUTEK \(CAP\); RILUZOLE ZENTIVA \(CAP\); NAP - PSUSA/00002645/201512](#)

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Applicant: Aventis Pharma S.A. (Rilutek, Riluzole Zentiva), various

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.2.6. [Rivastigmine - EXELON \(CAP\); PROMETAX \(CAP\); RIVASTIGMINE 1A PHARMA \(CAP\); RIVASTIGMINE HEXAL \(CAP\); RIVASTIGMINE SANDOZ \(CAP\); NAP - PSUSA/00002654/201601](#)

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Applicant: Novartis Europharm Ltd (Exelon, Prometax), 1 A Pharma GmbH (Rivastigmine 1A Pharma), Hexal AG (Rivastigmine Hexal), Sandoz GmbH (Rivastigmine Sandoz), various

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.2.7. [Sufentanil - ZALVISO \(CAP\); NAP - PSUSA/00002798/201511](#)

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Applicant: Grunenthal GmbH (Zalviso), various

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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

#### 6.3.1. Acipimox (NAP) - PSUSA/00000050/201512

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Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.2. Alanine, arginine, aspartic acid, cysteine, glucose anhydrous, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, olive oil refined, ornithine, phenylalanine, proline, serine, sodium chloride, sodium glycerophosphate hydrated, soya bean oil refined, taurine, threonine, tryptophan, tyrosine, valine, potassium acetate, calcium chloride dihydrate, magnesium acetate tetrahydrate (NAP) - PSUSA/00010190/201512

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Applicant: various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.3. Alendronate (NAP) - PSUSA/00000078/201601

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Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.4. Alizapride (NAP) - PSUSA/00000091/201601

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Applicant: various

PRAC Lead: Veerle Verlinden

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.5. Allopurinol (NAP) - PSUSA/00000095/201512

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Applicant: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

### 6.3.6. Antithrombin III (NAP) - PUSA/00003159/201512

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Applicant: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

### 6.3.7. Bendamustine hydrochloride (NAP) - PSUSA/00003162/201601

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Applicant: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

### 6.3.8. Bisoprolol, hydrochlorothiazide (NAP) - PSUSA/00000420/201511

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Applicant: various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

### 6.3.9. Botulinum neurotoxin type A (150 kD) free from complexing proteins (NAP) - PSUSA/00009084/201512

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Applicant: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

### 6.3.10. Botulinum toxin A (NAP) - PSUSA/00000426/201512

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Applicant: various

PRAC Lead: Almath Spooner

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

### 6.3.11. Botulinum toxin A-haemagglutinin complex (NAP) - PSUSA/00000427/201512

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Applicant: various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.12. Bupropion (NAP) - PSUSA/00000461/201512

Applicant: various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.13. Caffeine, ergotamine (NAP) - PSUSA/00000485/201511

Applicant: various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.14. Carboprost (NAP) - PSUSA/00000560/201601

Applicant: various

PRAC Lead: Jana Mlada

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.15. Cefoperazone (NAP) - PSUSA/00000597/201601

Applicant: various

PRAC Lead: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.16. Cefoperazone, sulbactam (NAP) - PSUSA/00000598/201601

Applicant: various

PRAC Lead: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.17. Cefotaxime (NAP) - PSUSA/00000599/201512

Applicant: various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.18. Ciclosporin (systemic use) (NAP) - PSUSA/00000745/201512

Applicant: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.19. Doxazosin (NAP) - PSUSA/00001169/201512

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.20. Exemestane (NAP) - PSUSA/00001345/201512

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.21. Flumazenil (NAP) - PSUSA/00001413/201512

Applicant: various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.22. Flunitrazepam (NAP) - PSUSA/00001418/201601

Applicant: various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### 6.3.23. Gaxilose (NAP) - PSUSA/00010283/201601

Applicant: various

PRAC Lead: Dolores Montero Corominas  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

#### 6.3.24. [Hydromorphone \(NAP\) - PSUSA/00001686/201511](#)

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Applicant: various  
PRAC Lead: Gabriela Jazbec  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

#### 6.3.25. [Ketamine \(NAP\) - PSUSA/00001804/201512](#)

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Applicant: various  
PRAC Lead: Veerle Verlinden  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

#### 6.3.26. [Lidocaine hydrochloride, phenylephrine hydrochloride, tropicamide \(NAP\) - PSUSA/00010390/201601](#)

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Applicant: various  
PRAC Lead: Doris Stenver  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

#### 6.3.27. [Lubiprostone \(NAP\) - PSUSA/00010290/201601](#)

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Applicant: various  
PRAC Lead: Julie Williams  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

#### 6.3.28. [Magnesium sulphate, sodium sulphate, potassium sulphate \(NAP\) - PSUSA/00010239/201602](#)

---

Applicant: various  
PRAC Lead: Eva Jirsova  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

### 6.3.29. Niflumic acid (NAP) - PSUSA/00002157/201512

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Applicant: various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

### 6.3.30. Paclitaxel (NAP) - PSUSA/00002264/201512

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Applicant: various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

### 6.3.31. Rupatadine (NAP) - PSUSA/00002673/20151

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Applicant: various

PRAC Lead: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

### 6.3.32. Sertindole (NAP) - PSUSA/00002695/201601

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Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

### 6.3.33. Testosterone (all formulations apart from transdermal application and testosterone undecanoate injection) (NAP) - PSUSA/00002907/201512

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Applicant: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

### 6.3.34. Testosterone (transdermal application) (NAP) - PSUSA/00002908/201512

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Applicant: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### **6.3.35. Testosterone undecanoate (injection) (NAP) - PSUSA/00010161/201512**

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Applicant: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### **6.3.36. Valaciclovir (NAP) - PSUSA/00003086/201512**

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Applicant: various

PRAC Lead: Jana Mlada

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

#### **6.3.37. Zafirlukast (NAP) - PSUSA/00003138/201512**

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Applicant: various

PRAC Lead: Almath Spooner

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CMDh

### **6.4. Follow-up to PSUR/PSUSA procedures**

#### **6.4.1. Basiliximab - SIMULECT (CAP) - EMEA/H/C/000207/LEG 043**

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of a detailed analysis and review of cases of certain types of adverse drug reactions (ADRs) including 'new onset diabetes after transplantation (NODAT)', 'polyomavirus infections' and 'hepatotoxicity' and the exclusion criteria applied to cases with confounders, e.g. time to onset (TTO)>40 days, sepsis or unknown information on TTO or indication as requested in the conclusions of PSUSA/00000301/201504 [PSUR#17 on three yearly frequency] adopted by PRAC and CHMP in December 2015

**Action:** For adoption of advice to CHMP

#### **6.4.2. Bortezomib - VELCADE (CAP) - EMEA/H/C/000539/LEG 053.1**

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: MAH's response to the request for supplementary information (RSI) dated April 2016 of LEG 053 on the evaluation of a cumulative review of cases reporting progressive multifocal leukoencephalopathy (PML) with the use of bortezomib submitted by the MAH as requested in the conclusions of PSUSA/00000424/201504 procedure adopted by PRAC and CHMP in November 2015

**Action:** For adoption of advice to CHMP

#### 6.4.3. Brimonidine - MIRVASO (CAP) - EMEA/H/C/002642/LEG 006

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Applicant: Galderma International

PRAC Rapporteur: Rafe Suvarna

Scope: Submission of a detailed review on evidence-based summary of the risk-benefit balance including the proportion of patients who benefit from Mirvaso, the magnitude and persistence of the improvement (i.e. clinical relevance) taking into account data from clinical trials (including pre-authorisation randomised clinical trials and more recent data, such as from the MIRACLE study – including information on drop-outs from these studies), post-marketing usage and survey data. In addition, the MAH submitted further data on risk minimisation measures relating to test dose, possible change of excipients and other risk minimisation strategies as requested in the conclusions of PSUSA/00010093/201508 adopted by PRAC and CHMP in March 2016

**Action:** For adoption of advice to CHMP

#### 6.4.4. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/LEG 010

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Submission of the CIOMS<sup>10</sup> forms for all cases of pancreatitis and additionally the 11 reports for which multiple patients were reported as requested in the conclusions of PSUSA/00010077/201509 adopted by PRAC and CHMP in April 2016

**Action:** For adoption of advice to CHMP

#### 6.4.5. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/LEG 009

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the CIOMS<sup>11</sup> forms for all cases of pancreatitis and additionally the 11 reports for which multiple patients were reported as requested in the conclusions of PSUSA/00010077/201509 adopted by PRAC and CHMP in April 2016

**Action:** For adoption of advice to CHMP

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<sup>10</sup> Council for International Organisations of Medical Sciences

<sup>11</sup> Council for International Organisations of Medical Sciences

#### 6.4.6. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/LEG 004

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Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of a detailed review on hypersensitivity as requested in the conclusions of PSUSA/00010029/201510 procedure adopted by PRAC and CHMP in April 2016

**Action:** For adoption of advice to CHMP

#### 6.4.7. Dapagliflozin - FORXIGA (CAP) - EMEA/H/C/002322/LEG 021

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Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of a detailed review on hypersensitivity as requested in the conclusions of PSUSA/00010029/201510 procedure adopted by PRAC and CHMP in April 2016

**Action:** For adoption of advice to CHMP

#### 6.4.8. Gefitinib - IRESSA (CAP) - EMEA/H/C/001016/LEG 021

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Applicant: AstraZeneca AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a detailed literature review on resistance mechanism to gefitinib by transformation of non-small cell lung cancer (NSCLC) and lung adenocarcinoma to small cell carcinoma as requested in the conclusions of PSUSA/00001518/201507 procedure adopted by PRAC and CHMP in January 2016

**Action:** For adoption of advice to CHMP

#### 6.4.9. Gefitinib - IRESSA (CAP) - EMEA/H/C/001016/LEG 022

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Applicant: AstraZeneca AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a detailed analysis on a safety meta-analysis reporting a higher frequency of gefitinib-related hepatotoxicity of grade  $\geq 3$  in Asians compared to non-Asians (Takeda et al, Lung Cancer. 2015, Apr;88(1):74-9) as requested in the conclusions of PSUSA/00001518/201507 procedure adopted by PRAC and CHMP in January 2016

**Action:** For adoption of advice to CHMP

#### 6.4.10. Vemurafenib - ZELBORAF (CAP) - EMEA/H/C/002409/LEG 032

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Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a detailed review on hypersensitivity reactions and dermatologic reactions (including myositis and rhabdomyolysis) as requested in the conclusions of

PSUSA/00009329/201508/0027 procedure adopted by PRAC and CHMP in March 2016

**Action:** For adoption of advice to CHMP

## 7. Post-authorisation safety studies (PASS)

### 7.1. Protocols of PASS imposed in the marketing authorisation(s)<sup>12</sup>

#### 7.1.1. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/PSP/0041.1

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Applicant: Amgen Europe B.V.

PRAC Rapporteur: Jana Mladá

Scope: MAH's response to a request for supplementary information (RSI) as per the outcome of PSP/0041 [protocol for study 20150136: an observational study measuring the safety and effectiveness of blinatumomab as well as utilisation and treatment practices] adopted by PRAC in April 2016

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

#### 7.1.2. Ethinylestradiol (NAP); ethinylestradiol, levonorgestrel (NAP) - EMEA/H/N/PSP/0037.1

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Applicant: Teva Pharma B.V. (Seasonique)

PRAC Rapporteur: Claire Ferard

Scope: Submission of a revised protocol as per the outcome of PSP/0037 adopted by PRAC in March 2016 for a post-authorisation safety study to assess the risk of venous thromboembolic events (VTE) in women exposed to Seasonique: a retrospective longitudinal cohort study assessing the safety of short and long-term use of Seasonique

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

#### 7.1.3. Ketoconazole - KETOCONAZOLE HRA (CAP) - EMEA/H/C/PSP/0040.1

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Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Željana Margan Koletić

Scope: Submission of a revised protocol as per the outcome of PSP/0040 adopted by PRAC in March 2016 for a post-authorisation safety study: a multi-country, observational registry to collect clinical information on patients with Cushing syndrome patients exposed to ketoconazole (preferably using the existing European Registry on Cushing's syndrome (ERCUSYN) registry), to assess drug utilisation patterns and to document the safety and effectiveness of ketoconazole

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

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<sup>12</sup> In accordance with Article 107n of Directive 2001/83/EC

#### 7.1.4. [Lenalidomide - REVLIMID \(CAP\) - EMEA/H/C/PSP/0020.3](#)

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Applicant: Celgene Europe Limited

PRAC Rapporteur: Claire Ferard

Scope: Submission of a revised PASS protocol for study CC-5013-MM-034: a prospective non-interventional PASS: product registry of previously untreated adult multiple myeloma patients who are 'transplant non-eligible' (TNE) (Revlimid TNE NDMM Registry)

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

#### 7.1.5. [Lesinurad - ZURAMPIC \(CAP\) - EMEA/H/C/PSP/0050](#)

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Applicant: Astra Zeneca AB

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of a PASS protocol for an observational post-authorisation study of lesinurad patients (SATURATES), to investigate the cardiovascular risk in association with lesinurad exposure, mainly in patients with a history of cardiovascular disorders

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

#### 7.1.6. [Pitolisant - WAKIX \(CAP\) - EMEA/H/C/PSP/0039.1](#)

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Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Submission of a revised protocol for a multicentre, observational PASS to document the drug utilisation of Wakix and to collect information on the safety of Wakix when used in routine medical practice

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

#### 7.1.7. [Poly \(o-2-hydroxyethyl\) starch \(NAP\) - EMEA/H/N/PSP/j/0008](#)

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Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of a revised protocol for a retrospective drug utilisation study to investigate the routine use of hydroxyethyl starch (HES)-containing infusion solutions in hospitals

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

#### 7.1.8. [Thiocolchicoside \(NAP\) - EMEA/H/N/PSP/j/0030.2](#)

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Applicant: Sanofi-Aventis Recherche & Développement, other companies involved in the consortium

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of a revised protocol for a drug utilisation study to characterise

prescribing practices for the medicinal products during typical clinical use in representative groups of prescribers and to assess main reasons for prescription

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

## 7.2. Protocols of PASS non-imposed in the marketing authorisation(s)<sup>13</sup>

### 7.2.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 006.1

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Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Submission of a revised protocol for a pregnancy registry study OBS13436: an international Lemtrada pregnancy exposure cohort in multiple sclerosis

**Action:** For adoption of advice to CHMP

### 7.2.2. Clopidogrel - CLOPIDOGREL ZENTIVA (CAP) - EMEA/H/C/000975/LEG 013

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Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Leonor Chambel

Scope: Submission of a protocol for study OBS014770, a non-interventional PASS: a cross-sectional drug utilisation study (DUS) using databases assessing the off-label use of clopidogrel and fixed dose combination (FDC) of clopidogrel/acetylsalicylic acid (ASA) for primary prevention of cardio-vascular (CV) events in five European countries as requested in the conclusions of PSUSA/0000820/201311 adopted by PRAC and CHMP in July 2014

**Action:** For adoption of advice to CHMP

### 7.2.3. Clopidogrel - ISCOVER (CAP) - EMEA/H/C/000175/LEG 034

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Applicant: sanofi-aventis groupe

PRAC Rapporteur: Leonor Chambel

Scope: Submission of a protocol for study OBS014770, a non-interventional PASS: a cross-sectional drug utilisation study (DUS) using databases assessing the off-label use of clopidogrel and fixed dose combination (FDC) of clopidogrel/acetylsalicylic acid (ASA) for primary prevention of cardio-vascular (CV) events in five European countries as requested in the conclusions of PSUSA/0000820/201311 adopted by PRAC and CHMP in July 2014

**Action:** For adoption of advice to CHMP

### 7.2.4. Clopidogrel - PLAVIX (CAP) - EMEA/H/C/000174/LEG 031

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Applicant: Sanofi Clir SNC

PRAC Rapporteur: Leonor Chambel

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<sup>13</sup> In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004

Scope: Submission of a protocol for study OBS014770, a non-interventional PASS: a cross-sectional drug utilisation study (DUS) using databases assessing the off-label use of clopidogrel and fixed dose combination (FDC) of clopidogrel/acetylsalicylic acid (ASA) for primary prevention of cardio-vascular (CV) events in five European countries as requested in the conclusions of PSUSA/0000820/201311 adopted by PRAC and CHMP in July 2014

**Action:** For adoption of advice to CHMP

#### 7.2.5. Clopidogrel, acetylsalicylic acid - CLOPIDOGREL/ACETYLSALICYLIC ACID ZENTIVA (CAP) - EMEA/H/C/001144/LEG 008

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Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Leonor Chambel

Scope: Submission of a protocol for study OBS014770, a non-interventional PASS: a cross-sectional drug utilisation study (DUS) using databases assessing the off-label use of clopidogrel and fixed dose combination (FDC) of clopidogrel/acetylsalicylic acid (ASA) for primary prevention of cardio-vascular (CV) events in five European countries as requested in the conclusions of PSUSA/0000820/201311 adopted by PRAC and CHMP in July 2014

**Action:** For adoption of advice to CHMP

#### 7.2.6. Clopidogrel, acetylsalicylic acid - DUOPLAVIN (CAP) - EMEA/H/C/001143/LEG 011

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Applicant: Sanofi Clir SNC

PRAC Rapporteur: Leonor Chambel

Scope: Submission of a protocol for study OBS014770, a non-interventional PASS: a cross-sectional drug utilisation study (DUS) using databases assessing the off-label use of clopidogrel and fixed dose combination (FDC) of clopidogrel/acetylsalicylic acid (ASA) for primary prevention of cardio-vascular (CV) events in five European countries as requested in the conclusions of PSUSA/0000820/201311 adopted by PRAC and CHMP in July 2014

**Action:** For adoption of advice to CHMP

#### 7.2.7. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/MEA 003; FORXIGA (CAP) - EMEA/H/C/002322/MEA 020

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Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of a PASS protocol to evaluate the incidence of diabetic ketoacidosis (DKA) in SGLT-2-inhibitors as an outcome of the recently completed Article 20 referral on sodium-dependent glucose cotransporters (SGLT)-2 inhibitors (EMEA/H/A-20/1419)

**Action:** For adoption of advice to CHMP

#### 7.2.8. Dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/MEA 003; XIGDUO (CAP) - EMEA/H/C/002672/MEA 006

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Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Submission of a PASS protocol to evaluate the incidence of diabetic ketoacidosis (DKA) in SGLT-2-inhibitors as an outcome of the recently completed Article 20 referral on sodium-dependent glucose cotransporters (SGLT)-2 inhibitors (EMA/H/A-20/1419)

**Action:** For adoption of advice to CHMP

#### 7.2.9. Eculizumab - SOLIRIS (CAP) - EMA/H/C/000791/MEA 053

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Submission of an amended PASS protocol M07-001: a prospective registry for an observational, multicentre, multinational study of patients with paroxysmal nocturnal haemoglobinuria (PNH), to update the list of targeted AEs for safety reporting, collect all SAEs irrespective of eculizumab treatment status, changes in language for data collection and administrative changes

**Action:** For adoption of advice to CHMP

#### 7.2.10. Edoxaban - LIXIANA (CAP) - EMA/H/C/002629/MEA 005.2

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: Submission of a revised PASS protocol for study DSE-EDO-01-14-EU: a drug utilisation study (DUS) for exploring edoxaban prescription patterns in Europe: a retrospective drug utilisation chart review study

**Action:** For adoption of advice to CHMP

#### 7.2.11. Edoxaban - LIXIANA (CAP) - EMA/H/C/002629/MEA 006.2

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: submission of a revised PASS protocol for study DSE-EDO-04-14-EU: a non-interventional study on edoxaban treatment in routine clinical practice for patients with non valvular atrial fibrillation

**Action:** For adoption of advice to CHMP

#### 7.2.12. Edoxaban - LIXIANA (CAP) - EMA/H/C/002629/MEA 007.2

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: Submission of a revised PASS protocol for study DSE-EDO-05-14-EU: a non-interventional study on edoxaban treatment in routine clinical practice in patients with venous thromboembolism in Europe

**Action:** For adoption of advice to CHMP

#### 7.2.13. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 004.2

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's response to MEA-004.1 [PASS study 1245.97 to assess the risk of urinary tract malignancies in relation to empagliflozin exposure in patients with type 2 mellitus diabetes: a multi-database European study, preceded by feasibility assessment] as per request for supplementary information (RSI) adopted in May 2016

**Action:** For adoption of advice to CHMP

#### 7.2.14. Fenofibrate, simvastatin - CHOLIB (CAP) - EMEA/H/C/002559/MEA 002.3

Applicant: BGP Products Ltd

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA-002.2 [revised PASS protocol for study ABT285.E.001: a drug utilisation research (DUR) study on the use of fenofibrate and simvastatin fixed combination: a European multinational study using secondary health records databases] as per the request for supplementary information (RSI) adopted in February 2016

**Action:** For adoption of advice to CHMP

#### 7.2.15. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/MEA 016

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Submission of a PASS protocol for a study PCI-1103-CA: open-label, extension trial in subjects with B-cell lymphoma and chronic lymphocytic leukaemia (CLL) to determine the long-term safety of ibrutinib

**Action:** For adoption of advice to CHMP

#### 7.2.16. Panobinostat - FARYDAK (CAP) - EMEA/H/C/003725/MEA 002.2

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA-002.1 [PASS study LBH589D2408 on panobinostat use in relapsed or relapsed/refractory multiple myeloma patients who have received at least two prior regimens including bortezomib and an immunomodulatory agent in a real-world setting according to the current EU prescribing information and document adherence to dosing regimen (including the dosing card, blister pack) by describing clinical characteristics, frequency and severity of the medication error events] as per request for supplementary information (RSI) adopted in May 2016

**Action:** For adoption of advice to CHMP

#### 7.2.17. Safinamide - XADAGO (CAP) - EMEA/H/C/002396/MEA 004.1

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Applicant: Zambon SpA

PRAC Rapporteur: Almath Spooner

Scope: MAH's response to MEA 004 [protocol for study Z7219N02: a drug utilisation study (DUS): observational European multicentre retrospective-prospective cohort study to observe Safinamide safety profile and pattern of use in clinical practice during the first post-commercialisation phase] as per request for supplementary information (RSI) adopted in January 2016

**Action:** For adoption of advice to CHMP

#### 7.2.18. Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/MEA 021.2

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Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: MAH's responses to MEA 021.1 [protocol for study GS-EU-337-2030: an observational, cross-sectional post-authorisation safety study to assess healthcare providers awareness of risks related to sofosbuvir and ledipasvir/sofosbuvir (LDV/SOF)] as per request for supplementary information adopted as adopted in June 2016

**Action:** For adoption of advice to CHMP

#### 7.2.19. Sofosbuvir, ledipasvir - HARVONI (CAP) - EMEA/H/C/003850/MEA 014.2

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Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Margarida Guimarães

Scope: MAH's responses to MEA 014.1 [protocol for study GS-EU-337-2030: an observational, cross-sectional PASS to assess healthcare providers awareness of risks related to sofosbuvir and ledipasvir/sofosbuvir (LDV/SOF)] as per request for supplementary information as adopted as adopted in June 2016

**Action:** For adoption of advice to CHMP

#### 7.2.20. Telavancin - VIBATIV (CAP) - EMEA/H/C/001240/ANX 007.4

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Applicant: Clinigen Healthcare Ltd

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to a request for supplementary information (RSI) as per the outcome of ANX/007.3 on pregnancy exposure registry (9809-CL-1409) as adopted in June 2015

**Action:** For adoption of advice to CHMP

#### 7.2.21. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 044.1

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA-044 [draft protocol for an adolescent registry: an observational PASS of ustekinumab in the treatment of pediatric patients aged 12 years and older with moderate to severe plaque psoriasis] as per the request for supplementary information (RSI) adopted in March 2016

**Action:** For adoption of advice to CHMP

#### 7.2.22. Vernakalant - BRINAVESS (CAP) - EMEA/H/C/001215/MEA 026.3

Applicant: Cardiome UK Limited

PRAC Rapporteur: Menno van der Elst

Scope: MAH's responses to MEA 026.2 [revised PASS protocol for vernakalant intravenous (IV) sterile concentrate prospective safety registry study: a prospective observational registry study to characterise normal conditions of use, dosing and safety following administration of vernakalant intravenous (IV) sterile concentrate (study 6621 049-00)] as per request for supplementary information (RSI) adopted by PRAC in July 2016

**Action:** For adoption of advice to CHMP

### **7.3. Results of PASS imposed in the marketing authorisation(s)<sup>14</sup>**

#### 7.3.1. Cyproterone, ethinylestradiol (NAP) - EMEA/H/N/PSR/J/0003

Applicant: Bayer Pharma AG, various

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final study results on the drug utilisation study (DUS) (database) designed to characterize the prescribing behaviours for cyproterone acetate/ethinylestradiol (CPA/EE) in three European countries: Netherlands, United Kingdom and Italy

**Action:** For adoption of a recommendation to CMDh

#### 7.3.2. Cyproterone, ethinylestradiol (NAP) - EMEA/H/N/PSR/J/0005

Applicant: Bayer Pharma AG, various

PRAC Rapporteur: Menno van der Elst

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

**Action:** For adoption of a recommendation to CMDh

#### 7.3.3. Cyproterone, ethinylestradiol (NAP) - EMEA/H/N/PSR/J/0006

Applicant: Bayer Pharma AG, various

<sup>14</sup> In accordance with Article 107p-q of Directive 2001/83/EC

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final study results on the PASS to evaluate the effectiveness of the risk minimisation activities with the objective to measure physicians' knowledge of safety and safe use information for cyproterone acetate/ethinylestradiol (CPA/EE) in five European countries: Austria, the Czech Republic, France, the Netherlands, and Spain

**Action:** For adoption of a recommendation to CMDh

## 7.4. Results of PASS non-imposed in the marketing authorisation(s)<sup>15</sup>

### 7.4.1. Aliskiren – RASILEZ (CAP) - EMEA/H/C/000780/WS0890/0107; aliskiren, hydrochlorothiazide - RASILEZ HCT (CAP) - EMEA/H/C/000964/WS0890/0077

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Submission of the final results of study SPP100A2417: a multi-database cohort study to assess the incidence rates of colorectal hyperplasia among hypertensive patients

**Action:** For adoption of PRAC Assessment Report

### 7.4.2. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/II/0037/G

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Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations: final study reports of two drug utilisation studies (DUS) examining the utilisation pattern of apixaban in Sweden (study B0661017) and in the Netherlands (study B0661018) to fulfil post-approval measures listed in RMP. The RMP is updated to reflect the data from the two completed DUS, to reflect the proposed DUS in Denmark (study B0661073) following the difficulty to use the data from the Netherlands due to the limited number of patients, to reflect changes approved in the SmPC with regard to the administration as a crushed tablet (II/030) and to the prothrombin complex concentrates (II/029), as well as to include minor updates to various post-marketing commitment studies

**Action:** For adoption of PRAC Assessment Report

### 7.4.3. Betaine anhydrous - CYSTADANE (CAP) - EMEA/H/C/000678/II/0025

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

PRAC Rapporteur: Valerie Strassmann

Scope: Submission of the final report of Cystadane surveillance registry (in collaboration with the European network and registry for homocystinurias and methylation defects (E-HOD)): long-term clinical and safety information in patients with cystathionine betasynthase (CBS), 5, 10-methylenetetrahydrofolate reductase (MTHFR) or cobalamin cofactor

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<sup>15</sup> 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

metabolism (Cbl) treated with Cystadane

**Action:** For adoption of PRAC Assessment Report

#### [7.4.4. Boceprevir - VICTRELIS \(CAP\) - EMEA/H/C/002332/II/0039](#)

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Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Claire Ferard

Scope: Submission of the final report for the category 3 observational PASS (study P08518) of Victrelis among chronic hepatitis C patients (observational prospective follow-up study to assess the utilisation of boceprevir and the management of pre-specified health outcomes of interest (HOIs) under conditions of routine clinical care). The RMP (version 10.0) is updated accordingly

**Action:** For adoption of PRAC Assessment Report

#### [7.4.5. Dabigatran etexilate - PRADAXA \(CAP\) - EMEA/H/C/000829/II/0093](#)

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Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: Submission of the final clinical study report for PASS 1160.149: observational study to evaluate the effectiveness of the risk minimisation activities in the treatment of stroke prevention in atrial fibrillation (SPAF) in order to address part of follow-up measure MEA 026. The RMP (version 31.6) is updated accordingly

**Action:** For adoption of PRAC Assessment Report

#### [7.4.6. Etanercept - ENBREL \(CAP\) - EMEA/H/C/000262/II/0198](#)

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Applicant: Pfizer Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Submission of the final clinical study report (CSR) for the British Society for Paediatric and Adolescent Rheumatology (BSPAR) etanercept registry, a cohort study (category 3 study)

**Action:** For adoption of PRAC Assessment Report

#### [7.4.7. Glycopyrronium bromide - ENUREV BREEZHALER \(CAP\) - EMEA/H/C/002691/WS1002/0017; SEEBRI BREEZHALER \(CAP\) - EMEA/H/C/002430/WS1002/0017; TOVANOR BREEZHALER \(CAP\) - EMEA/H/C/002690/WS1002/0019](#)

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Submission of the final study report (CSR) of study CNVA237A2401T: a multinational, multi-database drug utilisation study of inhaled NVA237 in Europe to estimate the subpopulation with cardio- and cerebrovascular co-morbidity and to identify patient groups with missing information as per the RMP. The RMP (version 6.0) is updated

accordingly

**Action:** For adoption of PRAC Assessment Report

#### 7.4.8. [Imatinib - GLIVEC \(CAP\) - EMEA/H/C/000406/II/0100](#)

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Eva Segovia

Scope: Submission of the final clinical study report (CSR) for study CSTI571A2403: 'a global Gleevec/Glivec and Tasigna pregnancy exposure registry' (category 3 study)

**Action:** For adoption of PRAC Assessment Report

#### 7.4.9. [Influenza vaccine \(live attenuated, nasal\) - FLUENZ TETRA \(CAP\) - EMEA/H/C/002617/II/0055](#)

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Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final clinical study report (CSR) for PASS study MA-VA-MEDI3250-1115: a post-marketing cohort study of the safety of Fluenz Tetra in subjects from 2 to 49 years of age

**Action:** For adoption of PRAC Assessment Report

#### 7.4.10. [Influenza vaccine \(live attenuated, nasal\) - FLUENZ TETRA \(CAP\) - EMEA/H/C/002617/II/0057](#)

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Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final study report for PASS D2660R00002: a non-interventional study of live attenuated influenza vaccine (LAIV) utilisation to identify and characterize medication errors due to expired vaccine use in individuals 2-17 years of age in the clinical practice research datalink (CPRD)

**Action:** For adoption of PRAC Assessment Report

#### 7.4.11. [Insulin glargine - LANTUS \(CAP\) - EMEA/H/C/000284/II/0105](#)

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Applicant: Sanofi-aventis Deutschland GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final clinical study report for a PASS: UK SoloStar differentiation study: a study in patients with type 1 or type 2 diabetes in the UK, to evaluate the ease of differentiating between SoloStar pens containing different types of insulin with the current and new labels. This submission addresses MEA 037

**Action:** For adoption of PRAC Assessment Report

#### 7.4.12. Insulin glulisine – APIDRA (CAP) - EMEA/H/C/000557/II/0066

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Applicant: Sanofi-aventis Deutschland GmbH

PRAC Rapporteur: Julie Williams

Scope: Submission of the final clinical study report for a PASS: UK SoloStar differentiation study, a study in patients with type 1 or type 2 diabetes in the UK, to evaluate the ease of differentiating between SoloStar pens containing different types of insulin with the current and new labels. This submission addresses MEA 037

**Action:** For adoption of PRAC Assessment Report

#### 7.4.13. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/II/0038

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Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Submission of the final study report for study CA184242: a risk minimisation tool effectiveness evaluation survey. The RMP (version 12) is updated accordingly

**Action:** For adoption of PRAC Assessment Report

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

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Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final results from the study and sub-study on breast cancer: 'liraglutide safety and surveillance programme using the Optum research database' (category 3 study)

**Action:** For adoption of PRAC Assessment Report

#### 7.4.15. Romiplostim - NPLATE (CAP) - EMEA/H/C/000942/II/0057

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Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva A. Segovia

Scope: Submission of the final clinical study report (CSR) for study 20120269: a study assessing the proportion of subjects with chronic idiopathic thrombocytopenic purpura (ITP) and their caregivers who administer romiplostim correctly after receipt of the home administration training (HAT) materials

**Action:** For adoption of PRAC Assessment Report

#### 7.4.16. Saxagliptin - ONGLYZA (CAP) - EMEA/H/C/001039/WS0960/0040/G; saxagliptin, metformin hydrochloride - KOMBOGLYZE (CAP) - EMEA/H/C/002059/WS0960/0033/G

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Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations consisting of the final results of five epidemiological study for: 1) study D1680R00011 (comparison of risk of major cardiovascular events between patients with type 2 diabetes initiating saxagliptin and those initiating other oral anti-diabetic treatments), 2) study D1680R00012 (comparison of risk of hospitalisation with acute liver failure between patients with type 2 diabetes initiating saxagliptin and those initiating other oral anti-diabetic treatments), 3) study D1680R00013 (comparison of risk of hospitalisation for infection between patients with type 2 diabetes initiating saxagliptin and those initiating other oral anti-diabetic treatment), 4) study D1680R00014 (comparison of risk of hospitalisation for severe hypersensitivity (including severe cutaneous) reactions between patients with type 2 diabetes initiating saxagliptin and those initiating other oral anti-diabetic treatment), 5) study D1680R00015 (comparison of risk of hospitalisation for acute kidney injury between patients with type 2 diabetes initiating saxagliptin and those initiating other oral anti-diabetic treatment). The RMP (version 11) is updated accordingly and include further routine changes. In addition, a safety review based on literature is included to investigate acute kidney injury associated with saxagliptin and saxagliptin/metformin following a previous PRAC request

**Action:** For adoption of PRAC Assessment Report

#### 7.4.17. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/II/0041

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final results of study PGL10-014 (PREMYA): a prospective multicentre non-interventional study of women treated with Esmya (ulipristal acetate) as preoperative treatment of moderate to severe symptoms of uterine fibroids. The RMP is updated accordingly

**Action:** For adoption of PRAC Assessment Report

#### 7.4.18. Voriconazole - VFEND (CAP) - EMEA/H/C/000387/II/0121

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Submission of the results of study A1501102: a non-interventional post authorisation safety study (PASS), evaluating the effectiveness of additional risk minimisation measure that aim to reduce the risks of phototoxicity, squamous cell carcinoma (SCC) of the skin and hepatic toxicity in patients receiving voriconazole in the European Union (EU). As a consequence, the RMP (version 5) is updated accordingly

**Action:** For adoption of PRAC Assessment Report

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

### 7.5.1. Elosulfase alfa - VIMIZIM (CAP) - EMEA/H/C/002779/MEA 005.1

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Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Second annual report for the multicentre, multinational, observational study: Morquio A registry study (MARS)

**Action:** For adoption of advice to CHMP

### 7.5.2. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 002.3

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Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Annual interim report for study 1245.96: an observational cohort study using existing data including diabetic ketoacidosis (DKA) as a safety topic of interest assessing a number of risks in patients treated with empagliflozin compared with patients treated with other sodium-glucose cotransporter-2 (SGLT2) inhibitors or with dipeptidyl peptidase-4 (DPP-4) inhibitors

**Action:** For adoption of advice to CHMP

### 7.5.3. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 003

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Applicant: Boehringer Ingelheim GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Annual interim report for study 1245.96: an observational cohort study using existing data including diabetic ketoacidosis (DKA) as a safety topic of interest assessing a number of risks in patients treated with empagliflozin compared with patients treated with other sodium-glucose cotransporter-2 (SGLT2) inhibitors or with dipeptidyl peptidase-4 (DPP-4) inhibitors

**Action:** For adoption of advice to CHMP

### 7.5.4. Etanercept - BENEPALI (CAP) - EMEA/H/C/004007/II/0008

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Applicant: Samsung Bioepis UK Limited (SBUK)

PRAC Rapporteur: Rafe Suvarna

Scope: Submission of the final clinical study report (CSR) for the 100 weeks open-label extension phase of study SB4-G31-RA (a phase III study, as safety follow-up to evaluate the long-term safety, tolerability, immunogenicity and efficacy of Benepali in subjects with rheumatoid arthritis (RA) treated previously with Benepali or Enbrel (category 3 study listed in the RMP)) to fulfil MEA 001. In addition, the MAH took the opportunity to update the RMP to reflect the changes introduced to Annex II of the Product Information during the initial

Marketing Authorisation (MA)

**Action:** For adoption of advice to CHMP

7.5.5. [Indacaterol, glycopyrronium bromide - ULTIBRO BREEZHALER \(CAP\) - EMEA/H/C/002679/ANX 002.3; ULUNAR BREEZHALER \(CAP\) - EMEA/H/C/003875/ANX 003.2; XOTERNA BREEZHALER \(CAP\) - EMEA/H/C/003755/ANX 002.3](#)

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Second interim report for study CQVA149A2402: a multinational database cohort study to assess RMP specified safety outcomes in association with indacaterol/glycopyrronium bromide in Europe

**Action:** For adoption of advice to CHMP

7.5.6. [Indacaterol, glycopyrronium bromide - ULTIBRO BREEZHALER \(CAP\) - EMEA/H/C/002679/MEA 003.4; ULUNAR BREEZHALER \(CAP\) - EMEA/H/C/003875/MEA 004.3; XOTERNA BREEZHALER \(CAP\) - EMEA/H/C/003755/MEA 003.4](#)

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Second interim report for a drug utilisation study (DUS) CQVA 149A2401: multinational, multi-database drug utilisation study of indacaterol/glycopyrronium bromide in Europe

**Action:** For adoption of advice to CHMP

7.5.7. [Infliximab - INFLECTRA \(CAP\) - EMEA/H/C/002778/MEA 007.1](#)

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Applicant: Hospira UK Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of the MAH's response to MEA-007: annual safety and efficacy interim analysis for registry CT-P13 4.2: an observational, prospective cohort study to evaluate safety and efficacy of Inflectra in patients with rheumatoid arthritis (EU and Korea) as per the request for supplementary information (RSI) adopted in September 2015

**Action:** For adoption of advice to CHMP

7.5.8. [Infliximab - INFLECTRA \(CAP\) - EMEA/H/C/002778/MEA 010.1](#)

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Applicant: Hospira UK Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of the MAH's response to MEA-010: annual safety and efficacy interim analysis for registry CT-P13 4.3: an observational, prospective cohort study to evaluate the safety and efficacy of Inflectra in patients with Crohn's disease (CD), and ulcerative colitis

(UC) (EU and Korea) as per the request for supplementary information (RSI) adopted in September 2015

**Action:** For adoption of advice to CHMP

#### **7.5.9. [Infliximab - REMSIMA \(CAP\) - EMEA/H/C/002576/MEA 007.1](#)**

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Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of the MAH's response to MEA-007: annual safety and efficacy interim analysis for registry CT-P13 4.2: an observational, prospective cohort study to evaluate safety and efficacy of Inflectra in patients with rheumatoid arthritis (EU and Korea) as per the request for supplementary information (RSI) adopted in September 2015

**Action:** For adoption of advice to CHMP

#### **7.5.10. [Infliximab - REMSIMA \(CAP\) - EMEA/H/C/002576/MEA 010.1](#)**

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Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of the MAH's response to MEA-010: annual safety and efficacy interim analysis for registry CT-P13 4.3: an observational, prospective cohort study to evaluate the safety and efficacy of Inflectra in patients with Crohn's disease (CD), and ulcerative colitis (UC) (EU and Korea) as per the request for supplementary information (RSI) adopted in September 2015

**Action:** For adoption of advice to CHMP

#### **7.5.11. [Influenza vaccine \(live attenuated, nasal\) - FLUENZ TETRA \(CAP\) - EMEA/H/C/002617/MEA 004.6](#)**

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Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of the MAH's response to MEA-004.5 [interim results of the enhanced safety surveillance study D2560C00008: a postmarketing non-interventional cohort study of the safety of live attenuated influenza vaccine (LAIV) in subjects 2 through 17 years of age] per the request for supplementary information (RSI) adopted in June 2016

**Action:** For adoption of advice to CHMP

#### **7.5.12. [Insulin lispro - HUMALOG \(CAP\) - EMEA/H/C/000088/MEA 028.3](#)**

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Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Interim results of a category 3 PASS study: post-approval safety surveillance to assess the changes in frequency of hypersensitivity and immunogenicity events with the new manufacturing process (sKPB) of Humalog and Liprolog

**Action:** For adoption of advice to CHMP

#### 7.5.13. [Insulin lispro - LIPROLOG \(CAP\) - EMEA/H/C/000393/MEA 021.3](#)

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Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Interim results of a category 3 PASS study: post-approval safety surveillance to assess the changes in frequency of hypersensitivity and immunogenicity events with the new manufacturing process (sKPB) of Humalog and Liprolog

**Action:** For adoption of advice to CHMP

#### 7.5.14. [Meningococcal group B vaccine \(rDNA, component, adsorbed\) - BEXSERO \(CAP\) - EMEA/H/C/002333/MEA 017.1](#)

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Applicant: GSK Vaccines S.r.l.

PRAC Rapporteur: Qun-Ying Yue

Scope: Interim progress report for study V72\_36OB: an observational safety study after meningococcal B vaccine Bexsero vaccination in routine UK care settings

**Action:** For adoption of advice to CHMP

#### 7.5.15. [Ospemifene - SENSHIO \(CAP\) - EMEA/H/C/PSP/0023.3](#)

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Applicant: Shionogi Limited

PRAC Rapporteur: Julie Williams

Scope: Annual interim report for an observational retrospective cohort study utilising existing databases in Germany, Italy, Spain, and the United States. (category 1) to evaluate the incidence of venous thromboembolism and other adverse events, as agreed in the RMP, in vulvar and vaginal atrophy (VVA) patients treated with ospemifene as compared to: 1) patients newly prescribed selective oestrogen receptor modulators (SERMs) for oestrogen-deficiency conditions or breast cancer prevention; 2) the incidence in untreated VVA patients

**Action:** For adoption of advice to CHMP

#### 7.5.16. [Perampanel - FYCOMPA \(CAP\) - EMEA/H/C/002434/MEA 004.4](#)

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Applicant: Eisai Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Annual progress report for a post-marketing observational safety study to evaluate the long-term safety and tolerability of Fycompa as add-on therapy in epilepsy patients (PASS Study E2007-G000-402)

**Action:** For adoption of advice to CHMP

#### 7.5.17. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/MEA 256.8

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Claire Ferard

Scope: Interim results for study GS-EU-174-0224: a drug utilisation study (DUS) in human immunodeficiency virus (HIV)-1 and hepatitis B virus (HBV)-infected paediatric patients to follow-up the effectiveness of the risk minimisation measures

**Action:** For adoption of advice to CHMP

#### 7.5.18. Trastuzumab emtansine - KADCYLA (CAP) - EMEA/H/C/002389/MEA 011.2

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Third annual interim report for study H4621g (MoTHER pregnancy register): an observational study of pregnancy and pregnancy outcomes in women with breast cancer treated with Herceptin, Perjeta in combination with Herceptin, or Kadcyla during pregnancy or within 7 months prior to conception

**Action:** For adoption of advice to CHMP

#### 7.5.19. Turoctocog alfa - NOVOEIGHT (CAP) - EMEA/H/C/002719/MEA 004

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Progress report for study NN7008-3553: a multicentre non-interventional study of safety and efficacy of turoctocog alfa (recombinant factor VIII (rFVIII)) during long-term treatment of severe and moderately severe haemophilia A (FVIII  $\leq$ 2%)

**Action:** For adoption of advice to CHMP

#### 7.5.20. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 023.8

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: Sixth interval safety registry report for study CNTO1275PSO4005: Nordic database initiative for exposure to ustekinumab: a review and analysis of adverse events from the Swedish national registry system

**Action:** For adoption of advice to CHMP

#### 7.5.21. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 024.8

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: Sixth annual interim report for study CNTO1275PSO4007: pregnancy research

initiative (C0743T); exposure to ustekinumab during pregnancy in patients with psoriasis: a review and analysis of birth outcomes from the Swedish, Danish, and Finnish medical birth registers

**Action:** For adoption of advice to CHMP

## 7.6. Others

### 7.6.1. Vernakalant - BRINAVESS (CAP) - EMEA/H/C/001215/LEG 028

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Applicant: Cardiome UK Limited

PRAC Rapporteur: Menno van der Elst

Scope: Submission of a detailed analysis of a case of hypotension (AR-C14004-16-00020) including the CIOMS<sup>16</sup> form, causality assessment report

**Action:** For adoption of advice to CHMP

### 7.6.2. Vernakalant - BRINAVESS (CAP) - EMEA/H/C/001215/LEG 029

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Applicant: Cardiome UK Limited

PRAC Rapporteur: Menno van der Elst

Scope: Submission of a detailed analysis of a case of hypotension (ES-C14004-16-00035) including the CIOMS<sup>17</sup> form, causality assessment report

**Action:** For adoption of advice to CHMP

### 7.6.3. Vernakalant - BRINAVESS (CAP) - EMEA/H/C/001215/LEG 030

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Applicant: Cardiome UK Limited

PRAC Rapporteur: Menno van der Elst

Scope: Submission of a detailed analysis of a case of hypotension (AT-C14004-16-00066) including the CIOMS<sup>18</sup> form, causality assessment report

**Action:** For adoption of advice to CHMP

## 7.7. New Scientific Advice

None

## 7.8. Ongoing Scientific Advice

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

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<sup>16</sup> Council for International Organisations of Medical Sciences

<sup>17</sup> Council for International Organisations of Medical Sciences

<sup>18</sup> Council for International Organisations of Medical Sciences

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

None

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

### 8.1. Annual reassessments of the marketing authorisation

None

### 8.2. Conditional renewals of the marketing authorisation

None

### 8.3. Renewals of the marketing authorisation

#### 8.3.1. 5-aminolevulinic acid - AMELUZ (CAP) - EMEA/H/C/002204/R/0023 (without RMP)

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Applicant: Biofrontera Bioscience GmbH

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

#### 8.3.2. Azilsartan medoxomil - EDARBI (CAP) - EMEA/H/C/002293/R/0018 (without RMP)

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Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

#### 8.3.3. Betaine anhydrous - CYSTADANE (CAP) - EMEA/H/C/000678/R/0024 (with RMP)

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

PRAC Rapporteur: Valerie Strassmann

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

#### 8.3.4. Desloratadine - DESLORATADINE ACTAVIS (CAP) - EMEA/H/C/002435/R/0008 (without RMP)

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Applicant: Actavis Group PTC ehf

PRAC Rapporteur: Jean-Michel Dogné

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

#### 8.3.5. [Levetiracetam - LEVETIRACETAM SUN \(CAP\) - EMEA/H/C/002051/R/0013 \(without RMP\)](#)

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Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Veerle Verlinden

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

#### 8.3.6. [Mercaptopurine - XALUPRINE \(CAP\) - EMEA/H/C/002022/R/0012 \(without RMP\)](#)

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Applicant: Nova Laboratories Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

#### 8.3.7. [Pasireotide - SIGNIFOR \(CAP\) - EMEA/H/C/002052/R/0028 \(without RMP\)](#)

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

#### 8.3.8. [Pioglitazone - GLIDIPION \(CAP\) - EMEA/H/C/002558/R/0009 \(without RMP\)](#)

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Applicant: Actavis Group PTC ehf

PRAC Rapporteur: Almath Spooner

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

#### 8.3.9. [Pioglitazone - PIOGLITAZONE ACTAVIS \(CAP\) - EMEA/H/C/002324/R/0009 \(without RMP\)](#)

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Applicant: Actavis Group PTC ehf

PRAC Rapporteur: Almath Spooner

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

### 8.3.10. Ranibizumab - LUCENTIS (CAP) - EMEA/H/C/000715/R/0062 (without RMP)

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Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

### 8.3.11. Sunitinib - SUTENT (CAP) - EMEA/H/C/000687/R/0062 (with RMP)

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Applicant: Pfizer Limited

PRAC Rapporteur: Carmela Macchiarulo

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

### 8.3.12. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/R/0040 (with RMP)

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Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

## 9. Product related pharmacovigilance inspections

### 9.1. List of planned pharmacovigilance inspections

None

### 9.2. Ongoing or concluded pharmacovigilance inspections

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

### 9.3. Others

None

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

### 10.1. Safety related variations of the marketing authorisation

#### 10.1.1. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/II/0086/G

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Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: PRAC consultation on grouped variations including: 1) update of section 4.8 of the SmPC with the adverse drug reactions (ADR) frequencies to reflect overall exposure to eculizumab in clinical trials; 2) update of section 4.4 of the SmPC with warning and precautions on meningococcal vaccination timing as recommended by PRAC. The Package Leaflet, Annex II and the RMP (version 13) are updated accordingly. In addition, the RMP is updated in order to implement the previous PRAC recommendation to remove the off label use from missing information, to provide the exposure data from PSUR#13 and to update the epidemiology sections with more complete and recent scientific literature data.

Moreover, the MAH took the opportunity to update the Product Information to add editorial changes and to bring it in line with the latest QRD template

**Action:** For adoption of advice to CHMP

See also 5.3.15.

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

None

### 10.3. Other requests

#### 10.3.1. Edoxaban – LIXIANA (CAP); lixisenatide – LYXUMIA (CAP)

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Applicant: Daiichi Sankyo Europe GmbH (Lixiana), Sanofi-Aventis Groupe (Lyxumia)

PRAC Rapporteur: Julie Williams (Lixiana); Qun-Ying Yue (Lyxumia)

Scope: PRAC consultation on a case of potential for name-related confusion with Lixiana (edoxaban), Lyxumia (lixisenatide) and Lysanxia (prazepam) identified in the post-authorisation phase

**Action:** For adoption of advice to CHMP

### 10.4. Scientific Advice

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

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

### 11.1. Safety related variations of the marketing authorisation

#### 11.1.1. Glibenclamide (NAP)

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Applicant: Sanofi (Daonil), various

PRAC Rapporteur: Veerle Verlinden

Scope: PRAC consultation on a variation procedure for Daonil (glibenclamide) NAT/H/1134/01/II/126 relating to the risk of cardiovascular mortality

**Action:** For adoption of advice to Member States

### 11.2. Other requests

#### 11.2.1. Chlormadinone, ethinyl estradiol (NAP) - EMEA/H/N/PSP/j/0012.3

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Applicant: Gedeon Richter, various

PRAC Rapporteur: Valerie Strassmann

Scope: PRAC consultation on the statistical analysis plan for an imposed PASS comparing the risk of venous thromboembolism with chlormadinone/ethinyloestradiol versus levonorgestrel/ethinyloestradiol following the PRAC endorsement in January 2016 of its protocol, as per the conclusions of the Article 31 referral on combined hormonal contraceptive (EMA/607314/2013)

**Action:** For adoption of advice to Member States

## 12. Organisational, regulatory and methodological matters

### 12.1. Mandate and organisation of the PRAC

None

### 12.2. Coordination with EMA Scientific Committees or CMDh-v

#### 12.2.1. Joint Paediatric Committee (PDCO)-PRAC Working Group - guideline on conduct of pharmacovigilance for medicines used by the paediatric population – draft GVP chapter for special populations

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**Action:** For discussion

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

12.3.1. Scientific Advice Working Party (SAWP) – Pilot phase on involving the PRAC in non-imposed PASS protocols

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**Action:** For discussion

### **12.4. Cooperation within the EU regulatory network**

12.4.1. Seasonal influenza vaccines enhanced safety surveillance systems - EMA review

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**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**

None

### **12.9. Pharmacovigilance audits and inspections**

12.9.1. Pharmacovigilance systems and their quality systems

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None

12.9.2. Pharmacovigilance inspections

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None

12.9.3. Pharmacovigilance audits

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None

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

### 12.10.1. Periodic safety update reports

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None

### 12.10.2. Granularity and Periodicity Advisory Group (GPAG)

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PRAC lead: Menno van der Elst, Margarida Guimarães

**Action:** For discussion

### 12.10.3. PSURs repository

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None

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

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**Action:** For adoption

## 12.11. Signal management

### 12.11.1. Guideline on 'Electronic reaction monitoring reports (eRMR) user manual'

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PRAC lead: Sabine Straus

**Action:** For discussion

### 12.11.2. Guideline on 'Screening for adverse drug reactions in EudraVigilance'

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PRAC lead: Sabine Straus

**Action:** For discussion

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

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PRAC lead: Sabine Straus

**Action:** For discussion

### 12.11.4. Signal management – List of substances subject to worksharing

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**Action:** For discussion

## **12.12. Adverse drug reactions reporting and additional reporting**

### **12.12.1. Management and reporting of adverse reactions to medicinal products**

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None

### **12.12.2. Additional monitoring**

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None

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

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**Action:** For adoption

## **12.13. EudraVigilance database**

### **12.13.1. Activities related to the confirmation of full functionality**

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None

## **12.14. Risk management plans and effectiveness of risk minimisations**

### **12.14.1. Risk management systems**

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None

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

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None

## **12.15. Post-authorisation safety studies (PASS)**

### **12.15.1. Post-authorisation Safety Studies – imposed PASS**

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None

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

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None

## **12.16. Community procedures**

### **12.16.1. Referral procedures for safety reasons**

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None

## **12.17. Renewals, conditional renewals, annual reassessments**

None

## **12.18. Risk communication and transparency**

### **12.18.1. Public hearings - Dry-run outcome**

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**Action:** For discussion

### **12.18.2. Safety communication**

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None

## **12.19. Continuous pharmacovigilance**

### **12.19.1. Incident management**

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None

## **12.20. Others**

None

### **12.20.1. EMA Scientific Committees support – organisational adjustments**

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**Action:** For discussion

### **12.20.2. Good Pharmacovigilance Practices (GVP) – adoption of revised GVP modules in 2016-2017**

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**Action:** For discussion

### **12.20.3. Initial marketing authorisation application (MAA) procedures: early background summaries – review of experience**

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**Action:** For discussion

12.20.4. Strategy on measuring the impact of pharmacovigilance - draft reflection paper on PRAC criteria to prioritise collaborative impact research

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PRAC lead: Marieke De Bruin

**Action:** For adoption

12.20.5. Strategy on measuring the impact of pharmacovigilance - PRAC Interest Group impact proposal for prioritised topics

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PRAC lead: Marieke De Bruin

**Action:** For discussion

12.20.6. Effects tables in selected important benefit/risk reviews - Pilot phase

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PRAC lead: Rafe Suvarna

**Action:** For discussion

## 13. Any other business

## 14. Explanatory notes

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

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

(Items 2 and 3 of the PRAC agenda)

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

[http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general\\_content\\_000150.jsp&mid=WC0b01ac05800240d0](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000150.jsp&mid=WC0b01ac05800240d0)

### **Signals assessment and prioritisation**

(Item 4 of the PRAC agenda)

A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine and that warrants further investigation. Signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. The evaluation of safety signals is a routine part of pharmacovigilance and is essential to ensuring that regulatory authorities have a comprehensive knowledge of a medicine's benefits and risks.

The presence of a safety signal does not mean that a medicine has caused the reported adverse event. The adverse event could be a symptom of another illness or caused by another medicine taken by the patient. The evaluation of safety signals is required to establish whether or not there is a causal relationship between the medicine and the reported adverse event.

The evaluation of safety signals may not necessarily conclude that the medicine caused the adverse event in question. In cases where a causal relationship is confirmed or considered likely, regulatory action may be necessary and this usually takes the form of an update of the summary of product characteristics and the package leaflet.

### **Risk Management Plans (RMPs)**

(Item 5 of the PRAC agenda)

The RMP describes what is known and not known about the side effects of a medicine and states how these risks will be prevented or minimised in patients. It also includes plans for studies and other activities to gain more knowledge about the safety of the medicine and risk factors for developing side effects.

RMPs are continually modified and updated throughout the lifetime of the medicine as new information becomes available.

### **Assessment of Periodic Safety Update Reports (PSURs)**

(Item 6 of the PRAC agenda)

A PSUR is a report providing an evaluation of the benefit-risk balance of a medicine, which is submitted by marketing authorisation holders at defined time points following a medicine's authorisation.

PSURs summarises data on the benefits and risks of a medicine and includes the results of all studies carried out with this medicine (in the authorised and unauthorised indications).

### **Post-authorisation Safety Studies (PASS)**

(Item 7 of the PRAC agenda)

A PASS is a study of an authorised medicinal product carried out to obtain further information on its safety, or to measure the effectiveness of risk management measures. The results of a PASS help regulatory agencies to evaluate the safety and benefit-risk profile of a medicine.

### **Product related pharmacovigilance inspections**

(Item 9 of the PRAC agenda)

Inspections carried out by regulatory agencies to ensure that marketing authorisation holders comply with their pharmacovigilance obligations.

More detailed information on the above terms can be found on the EMA website: [www.ema.europa.eu/](http://www.ema.europa.eu/)