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SCIENCE MEDICINES HEALTH

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Inspections, Human Medicines Pharmacovigilance and Committees Division

## Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 03-06 September 2018

Chair: Sabine Straus – Vice-Chair: vacant

03 September 2018, 13:00 – 19:30, room 3/A

04 September 2018, 08:30 – 19:30, room 3/A

05 September 2018, 08:30 – 19:30, room 3/A

06 September 2018, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

20 September 2018, 09:00-12:00, room 9/B, via teleconference

### Health and safety information

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

### Disclaimers

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

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

### Note on access to documents

Some documents mentioned in the agenda cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents ([EMA/127362/2006, Rev. 1](http://www.ema.europa.eu/127362/2006_Rev_1)).



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## 1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 03-06 September 2018. See September 2018 PRAC minutes (to be published after the October 2018 PRAC meeting).

### 1.2. Agenda of the meeting on 03-06 September 2018

**Action:** For adoption

### 1.3. Minutes of the previous meeting on 09-12 July 2018

**Action:** For adoption

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

### 2.1. Newly triggered procedures

None

### 2.2. Ongoing procedures

None

### 2.3. Procedures for finalisation

None

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

### 3.1. Newly triggered procedures

None

### 3.2. Ongoing procedures

None

### 3.3. Procedures for finalisation

None



### 3.4. Re-examination procedures<sup>1</sup>

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. Apixaban – ELIQUIS (CAP)

---

Applicant(s): Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Signal of pancreatitis

**Action:** For adoption of PRAC recommendation

EPITT 19265 – New signal

Lead Member State(s): NL

Lead Member State(s): BE, DE, ES, FR, NL, SE, UK

#### 4.1.2. Gabapentin (NAP)

---

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of dysphagia

**Action:** For adoption of PRAC recommendation

EPITT 19296 – New signal

Lead Member State(s): DE

#### 4.1.3. Vorinconazole – VFEND (CAP)

---

Applicant(s): Pfizer Limited

PRAC Rapporteur: Menno van der Elst

Scope: Signal of drug reaction with eosinophilia and systemic symptoms (DRESS)

**Action:** For adoption of PRAC recommendation

EPITT 19276 – New signal

Lead Member State(s): NL

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

<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

## 4.2. New signals detected from other sources

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

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

PRAC Rapporteur: To be appointed

Scope: Signal of persistent sexual dysfunction after drug withdrawal

**Action:** For adoption of PRAC recommendation

EPITT 19277 – New signal

### 4.2.2. Denosumab – PROLIA (CAP)

---

Applicant(s): Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of alopecia

**Action:** For adoption of PRAC recommendation

EPITT 18332 – New signal

Lead Member State(s): SE

### 4.2.3. Fingolimod – GILENYA (CAP)

---

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Signal of autoimmune haemolytic anaemia

**Action:** For adoption of PRAC recommendation

EPITT 19260 – New signal

Lead Member State(s): FR

### 4.2.4. Nivolumab – OPDIVO (CAP)

---

Applicant(s): Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of scleroderma

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<sup>3</sup> Indicated in the treatment of major depressive disorder (MDD)

<sup>4</sup> Indicated in the treatment of major depressive disorder (MDD)

**Action:** For adoption of PRAC recommendation

EPITT 19282 – New signal

Lead Member State(s): DE

#### 4.2.5. Pazopanib – VOTRIENT (CAP)

---

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Doris Stenver

Scope: Signal of rhabdomyolysis

**Action:** For adoption of PRAC recommendation

EPITT 19281 – New signal

Lead Member State(s): DK

#### 4.2.6. Pemetrexed – ALIMTA (CAP); NAP

---

Applicant(s): Eli Lilly Nederland B.V. (Alimta), various

PRAC Rapporteur: To be appointed

Scope: Signal of syncope

**Action:** For adoption of PRAC recommendation

EPITT 19289 – New signal

Lead Member State(s): FR

#### 4.2.7. Rivaroxaban – XARELTO (CAP)

---

Applicant(s): Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of premature ending of the GALILEO<sup>5</sup> study in patients who have received an artificial heart valve through a transcatheter aortic valve replacement (TAVR)

**Action:** For adoption of PRAC recommendation

EPITT 19294 – New signal

Lead Member State(s): SE

#### 4.2.8. Sunitinib – SUTENT (CAP)

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Applicant(s): Pfizer Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Signal of aortic dissection

**Action:** For adoption of PRAC recommendation

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<sup>5</sup> A global multicentre, open-label, randomised, event-driven, active-controlled study comparing a rivaroxaban-based antithrombotic strategy to an antiplatelet-based strategy after transcatheter aortic valve replacement (TAVR) to optimize clinical outcomes

EPITT 19283 – New signal

Lead Member State(s): IT

#### 4.2.9. [Tocilizumab – ROACTEMRA \(CAP\)](#)

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Applicant(s): Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of psoriasis

**Action:** For adoption of PRAC recommendation

EPITT 19273 – New signal

Lead Member State(s): DE

### 4.3. [Signals follow-up and prioritisation](#)

#### 4.3.1. [Alemtuzumab – LEMTRADA \(CAP\) - EMEA/H/C/003718/SDA/008](#)

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Applicant(s): Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of cytomegalovirus (CMV) infection

EPITT 19193 – Follow-up to April 2018

#### 4.3.2. [Dimethyl fumarate – TECFIDERA \(CAP\) - EMEA/H/C/002601/SDA/019](#)

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Applicant(s): Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: Signal of immune thrombocytopenic purpura and thrombocytopenia

EPITT 19192 – Follow-up to April 2018

#### 4.3.3. [Duloxetine – ARICLAIM \(CAP\) – EMEA/H/C/000552/SDA/043, CYMBALTA \(CAP\) - EMEA/H/C/000572/SDA/047, DULOXETINE LILLY \(CAP\) - EMEA/H/C/004000/SDA/004, DULOXETINE MYLAN \(CAP\), DULOXETINE ZENTIVA \(CAP\), XERISTAR \(CAP\) - EMEA/H/C/000573/SDA/048, YENTREVE \(CAP\) - EMEA/H/C/000545/SDA/043; NAP](#)

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

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Signal of interstitial lung disease (ILD)

EPITT 19175 – Follow-up to April 2018

4.3.4. Fluoroquinolones:  
Ciprofloxacin (NAP); flumequine (NAP); levofloxacin – QUINSAIR (CAP), NAP;  
lomefloxacin (NAP); moxifloxacin (NAP); norfloxacin (NAP); ofloxacin (NAP);  
pefloxacin (NAP); prulifloxacin (NAP); rufloxacin (NAP)

---

Applicant(s): Raptor Pharmaceuticals Europe BV (Quinsair), various

PRAC Rapporteur: Martin Huber

Scope: Signal of aortic aneurysm and dissection

**Action:** For adoption of PRAC recommendation

EPITT 18651 – Follow-up to July 2018

4.3.5. Hydrochlorothiazide (NAP);  
Aliskiren, hydrochlorothiazide – RASILEZ HCT (CAP); amlodipine, valsartan,  
hydrochlorothiazide – COPALIA HCT (CAP); amlodipine besylate, valsartan,  
hydrochlorothiazide – DAFIRO HCT (CAP), EXFORGE HCT (CAP); irbesartan,  
hydrochlorothiazide – COAPROVEL (CAP), IFIRMACOMBI (CAP), IRBESARTAN  
HYDROCHLOROTHIAZIDE ZENTIVA (CAP), IRBESARTAN/HYDROCHLOROTHIAZIDE  
TEVA (CAP), KARVEZIDE (CAP); telmisartan, hydrochlorothiazide - ACTELSAR HCT  
(CAP), KINZALKOMB (CAP), MICARDISPLUS (CAP), PRITORPLUS (CAP), TOLUCOMBI  
(CAP)

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Applicant(s): Actavis Group PTC ehf (Actelsar HCT), Bayer Pharma AG (Kinzalkomb,  
PritorPlus), Boehringer Ingelheim International (MicardisPlus), Krka, d.d. (Ifirmacombi,  
Tolucombi), Noden Pharma DAC (Rasilez HCT), Novartis Europharm Limited (Copalia HCT,  
Dafiro HCT), Sanofi-aventis groupe (Irbesartan Hydrochlorothiazide Zentiva, Karvezide),  
Sanofi Clir SNC (CoAprovel), Teva B.V. (Irbesartan/Hydrochlorothiazide Teva), various

PRAC Rapporteur: Kirsti Villikka

Scope: Signal of skin cancer

**Action:** For adoption of PRAC recommendation

EPITT 19138 – Follow-up to July 2018

4.3.6. Ipilimumab – YERVOY (CAP)

---

Applicant(s): Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Signal of cytomegalovirus gastrointestinal infection

EPITT 19207 – Follow-up to May 2018

4.3.7. Olanzapine – ZALASTA (CAP) - EMEA/H/C/000792/SDA/006, ZYPADHERA (CAP) -  
EMEA/H/C/000890/SDA/028, ZYPREXA (CAP) - EMEA/H/C/000115/SDA/049,  
ZYPREXA VELOTAB (CAP) - EMEA/H/C/000287/SDA/042; NAP

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

PRAC Rapporteur: Kimmo Jaakkola

Scope: Signal of somnambulism

EPITT 19202 – Follow-up to April 2018

4.3.8. Sildenafil - GRANPIDAM (CAP), MYSILDECARD (CAP), REVATIO (CAP) – EMEA/H/C/000638/SDA/050, SILDENAFIL ACTAVIS (CAP), SILDENAFIL RATIOPHARM (CAP), SILDENAFIL TEVA (CAP), VIAGRA (CAP), VIZARSIN (CAP); NAP

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Applicant(s): Pfizer Limited (Revatio, Viagra), Accord Healthcare (Granpidam), Mylan S.A.S (Mysildecard), Actavis Group PTC (Sildenafil Actavis), Ratiopharm GmbH (Sildenafil Ratiopharm), Teva B.V. (Sildenafil Teva), Krka, d.d., Novo mesto (Vizarsin); various

PRAC Rapporteur: Menno van der Elst

Scope: Signal of pulmonary hypertension and fatal cases associated with use in an off-label indication, early-onset intrauterine growth restriction

**Action:** For adoption of PRAC recommendation

EPITT 19287 – Follow-up to July 2018

4.3.9. Sitagliptin – JANUVIA (CAP) - EMEA/H/C/000722/SDA/037, RISTABEN (CAP) - EMEA/H/C/001234/SDA/015, TESAVEL (CAP) - EMEA/H/C/000910/SDA/031, XELEVIA (CAP) - EMEA/H/C/000762/SDA/036; sitagliptin, metformin hydrochloride – JANUMET (CAP) - EMEA/H/C/000861/SDA/019, EFFICIB (CAP) - EMEA/H/C/000896/SDA/019, RISTFOR (CAP) - EMEA/H/C/001235/SDA/015, VELMETIA (CAP) - EMEA/H/C/000862/SDA/019  
Angiotensin-converting-enzyme (ACE)-inhibitors: benazepril (NAP); captopril (NAP); cilazapril (NAP); delapril (NAP); enalapril (NAP); fosinopril (NAP); imidapril (NAP); lisinopril (NAP); moexipril (NAP); perindopril (NAP); quinapril (NAP); ramipril (NAP); spirapril (NAP); trandolapril (NAP); zofenopril (NAP); zofenopril, hydrochlorothiazide (NAP)

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Applicant(s): Merck Sharp & Dohme B.V., various

PRAC Rapporteur: Menno van der Elst

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

Action: For adoption of PRAC recommendation

EPITT 17608 – Follow-up to April 2018

## 5. Risk management plans (RMPs)

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

#### 5.1.1. Apalutamide - EMEA/H/C/004452

---

Scope: Treatment of non-metastatic castration resistant prostate cancer (NM CRPC)

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

#### 5.1.2. Fexinidazole - EMEA/H/W/002320

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Scope: Treatment of human African trypanosomiasis (HAT)



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

#### 5.1.3. [Macimorelin - EMEA/H/C/004660](#)

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Scope: Diagnosis of adult growth hormone deficiency (AGHD)

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

#### 5.1.4. [Pegfilgrastim - EMEA/H/C/004915](#)

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Scope: Treatment of neutropenia

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

#### 5.1.5. [Romosozumab - EMEA/H/C/004465](#)

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Scope: Treatment of osteoporosis

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

#### 5.1.6. [Trastuzumab - EMEA/H/C/004916](#)

---

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

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

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

#### 5.2.1. [Aclidinium - BRETARIS GENUAIR \(CAP\) - EMEA/H/C/002706/WS1402/0038;](#) [EKLIRA GENUAIR \(CAP\) - EMEA/H/C/002211/WS1402/0038](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Update of the RMP (version 7.0) in order to reflect changes in categorisation of safety concerns and missing information in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template)

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

#### 5.2.2. [Aclidinium, formoterol fumarate dihydrate - BRIMICA GENUAIR \(CAP\) - EMEA/H/C/003969/WS1403/0023;](#) [DUAKLIR GENUAIR \(CAP\) - EMEA/H/C/003745/WS1403/0023](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Update of the RMP (version 4.0) in order to reflect changes in categorisation of safety concerns and missing information in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template)

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

#### 5.2.3. [Adalimumab - HUMIRA \(CAP\) - EMEA/H/C/000481/II/0182](#)

---

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

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

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

#### 5.2.4. [Cangrelor - KENGREXAL \(CAP\) - EMEA/H/C/003773/II/0015](#)

---

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Amelia Cupelli

Scope: Update of the RMP (version 2.0) in order to update the requirements for a planned study (listed as a category 3 in the RMP): a multicentre, observational, non-interventional European study of patients undergoing percutaneous coronary intervention (PCI) who receive cangrelor and transition to either clopidogrel, prasugrel or ticagrelor. In addition, the MAH took the opportunity to bring the RMP in line with revision 2 of the guidance on the format of RMP in the EU (template)

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

#### 5.2.5. [Capecitabine - XELODA \(CAP\) - EMEA/H/C/000316/II/0077](#)

---

Applicant: Roche Registration GmbH

PRAC Rapporteur: Martin Huber

Scope: Update of the RMP (version 9.1) in line with the product information changes recently approved within variation II/0074 concluded in March 2018. These include an update of the post-authorisation exposure, an update of the important identified risk 'dihydropyrimidine dehydrogenase deficiency (DPD)' and updates related to section 4.4 of the EU SmPC for DPD. In addition, the MAH took the opportunity to bring the RMP in line with revision 2 of the guidance on the format of RMP in the EU (template)

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

#### 5.2.6. [Delamanid - DELTYBA \(CAP\) - EMEA/H/C/002552/II/0030, Orphan](#)

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Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Julie Williams

Scope: Update of the RMP (version 2.10) in order to revise the risk re-categorisation justifications and lay language wording, as well as to add clarifications to the described additional pharmacovigilance activities to assess the effectiveness of risk minimisation measures and set up date of EU network of laboratories, as requested by PRAC following the assessment of the annual renewal procedure completed in February 2018

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

#### 5.2.7. Dexamethasone - NEOFORDEX (CAP) - EMEA/H/C/004071/II/0008

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Applicant: Laboratoires CTRS

PRAC Rapporteur: Ghania Chamouni

Scope: Update of the RMP (version 4.0) in order to propose the 'removal of the score line for subdivision of the 40mg tablet and consequent deletion of the 20mg posology' as a category 3 activity. In addition, the MAH updated the other category 3 activity: 'development of a 20mg oral dosage form'. In addition, the MAH took the opportunity to bring the RMP in line with revision 2 of the guidance on the format of RMP in the EU (template)

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

#### 5.2.8. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/II/0084

---

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 18.0) in order to remove the educational programme for prescribing healthcare professionals as an additional risk minimisation measure based on the outcome of the PSUSA procedure (PSUSA/00001560/201704) concluded at the December 2017 PRAC meeting

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

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

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Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

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

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

#### 5.2.10. Peginterferon alfa-2a - PEGASYS (CAP) - EMEA/H/C/000395/II/0101

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 9.0) in order to remove NV25361 study (listed as a category 3 study in the RMP): a phase 3b, randomized, open-label study of pegylated interferon alfa-2a in combination with lamivudine or entecavir compared with untreated control group in children with hepatitis B envelope antigen (HBeAg)-positive chronic hepatitis B (CHB) in the immune-tolerant phase. In addition, YV25718 study: a phase 3b parallel group, open label study of pegylated interferon alfa-2a monotherapy (PEG-IFN, Ro 25-8310) compared to untreated control in children with HBeAg positive chronic hepatitis B (study to establish the efficacy and safety of PEG-IFN monotherapy in children from 3 to less than 18 years of age with chronic hepatitis B) long term follow up milestone is amended from Q3 2020 to Q4 2021. In addition, the MAH took the opportunity to reflect

changes in categorisation of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' including updates in the epidemiology section

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

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

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Updated RMP (version 9.1) in order to remove 'theoretic carcinogenic potential' currently classified as missing information from the list of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of RMP in the EU (template)

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

- 5.2.12. [Teduglutide - REVESTIVE \(CAP\) - EMEA/H/C/002345/II/0045, Orphan](#)
- 

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of the RMP (version 8) in order to include the safety information from the final clinical study report (CSR) of study TED-C14-006 (listed as a category 3 study): a 24-week double-blind, safety, efficacy, and pharmacodynamic study investigating two doses of teduglutide in paediatric subjects aged 1 year through 17 years with short bowel syndrome who are dependent on parenteral support following the ongoing assessment by CHMP of variation II/0043

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

- 5.2.13. [Tenofovir disoproxil - VIREAD \(CAP\) - EMEA/H/C/000419/II/0190](#)
- 

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Adrien Inoubli

Scope: Update of the RMP (version 22.1) in line with revision 2 of GVP module V on 'Risk management systems' to propose the removal of additional risk minimisation activities on renal safety associated with human immunodeficiency virus (HIV) and hepatitis B virus (HBV) affected adults

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

#### 5.2.14. Zoledronic acid - ZOLEDRONIC ACID MYLAN (CAP) - EMEA/H/C/002482/WS1370/0015

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Applicant: Mylan S.A.S

PRAC Rapporteur: Doris Stenver

Scope: Update of the RMP (version 7.0) to implement the latest RMP template and to include 'and other anatomical sites' in addition to 'osteonecrosis of the jaw' as an important identified risk, to be aligned with the conclusions of the PSUSA procedure for zoledronic acid (PSUSA/00003149/201608) concluded by PRAC/CHMP in April 2017

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

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

#### 5.3.1. Adalimumab - CYLTEZO (CAP) - EMEA/H/C/004319/II/0004

---

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study 1297.3 (listed as a category 3 study in the RMP): an interventional trial to generate long-term safety, efficacy, and immunogenicity data for the administration of Cyltezo (adalimumab, biosimilar) in patients with moderate to severe rheumatoid arthritis (RA). The RMP (version 2.0) is updated accordingly

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

#### 5.3.2. Arsenic trioxide - TRISENOX (CAP) - EMEA/H/C/000388/X/0068

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Applicant: Teva B.V.

PRAC Rapporteur: Ghania Chamouni

Scope: Extension application to add a new strength of 2 mg/mL (concentrate for solution for solution for infusion) in vials. The RMP (version 2.0) is updated accordingly

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

#### 5.3.3. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0007/G

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Grouped variations consisting of: 1) extension of indication to include in combination with bevacizumab, paclitaxel and carboplatin the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC), based on the interim results of study GO29436: a phase 3, open-label, randomized study of atezolizumab in combination with carboplatin+paclitaxel with or without bevacizumab compared with carboplatin+paclitaxel+bevacizumab in chemotherapy-naïve patients with stage IV NSCLC (IMpower 150). As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated; 2) update of section 4.8 of the SmPC in order to update the monotherapy safety data and reflect the largest pooled monotherapy population available (including data from study IMvigor211: a phase 3, open-label, multicentre, randomized study to investigate the

efficacy and safety of atezolizumab compared with chemotherapy in patients with locally advanced or metastatic urothelial bladder cancer after failure with platinum-containing chemotherapy, and study PCD4989g: a phase 1, open-label, dose-escalation study of the safety and pharmacokinetics of atezolizumab administered intravenously as a single agent to patients with locally advanced or metastatic solid tumours or hematologic malignancies). The package leaflet and the RMP (version 4.0) are updated accordingly. In addition, the MAH took the opportunity to introduce small corrections and formatting changes throughout the SmPC

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

#### 5.3.4. [Beclometasone dipropionate, formoterol fumarate dihydrate, glycopyrronium - TRIMBOW \(CAP\) - EMEA/H/C/004257/II/0002](#)

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Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication to include all adult patients with moderate or severe chronic obstructive pulmonary disease (COPD). As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated in order to add the results of two phase 3 studies, namely: 1) study Triple 7 (CCD-05993AA1-07): a multinational, multicentre, randomised, open-label, active-controlled, 26-week, 2-arm, parallel group study to evaluate the non-inferiority of fixed combination of beclomethasone dipropionate plus formoterol fumarate plus glycopyrronium bromide administered via pressurised metered dose inhaler (pMDI) (CHF 5993) vs fixed combination of fluticasone furoate plus vilanterol administered via dry powder inhaler (DPI) (Relvar) plus tiotropium bromide (Spiriva) for the treatment of patients with COPD; 2) study Triple 8 (CCD-05993AA1-08): a 52-week, double blind, double dummy, randomized, multinational, multicentre, 2-arm parallel group, active controlled clinical trial of fixed combination of beclomethasone dipropionate plus formoterol fumarate plus glycopyrronium bromide administered via pMDI (CHF 5993) versus indacaterol/glycopyrronium (Ultibro) via DPI in patients with COPD (TRIBUTE). The package leaflet and the RMP (version 5.0) are updated accordingly

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

#### 5.3.5. [Cabozantinib - CABOMETYX \(CAP\) - EMEA/H/C/004163/II/0005](#)

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Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include the treatment of advanced hepatocellular carcinoma in adults following prior systemic therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC are updated with safety and efficacy information. The package leaflet and the RMP (version 4.0) are updated accordingly

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

#### 5.3.6. [Ceritinib - ZYKADIA \(CAP\) - EMEA/H/C/003819/X/0025](#)

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga



Scope: Extension application to introduce a new pharmaceutical form (film-coated tablets). The RMP (version 12) is updated accordingly

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

#### 5.3.7. [Choriogonadotropin alfa - OVITRELLE \(CAP\) - EMEA/H/C/000320/II/0073/G](#)

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Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations consisting of: 1) update of section 4.8 of the SmPC in order to indicate that thromboembolism can also occur without the presence of ovarian hyperstimulation syndrome (OHSS). The package leaflet and the RMP (version 5.1) are updated accordingly; 2) update of the RMP to extend the important potential risk of 'misuse' to 'weight loss and anabolic growth promoting effect'. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet, to make editorial changes in the product information and in Annex A (list of authorised presentations). The MAH also took the opportunity to make some minor revisions in the RMP

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

#### 5.3.8. [Dasatinib - SPRYCEL \(CAP\) - EMEA/H/C/000709/II/0059](#)

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Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Doris Stenver

Scope: Extension of indication to include Philadelphia chromosome positive (Ph+) acute lymphoblastic leukaemia for the treatment of paediatric patients. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 16.0) are updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes to the product information

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

#### 5.3.9. [Eluxadoline - TRUBERZI \(CAP\) - EMEA/H/C/004098/II/0005/G](#)

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Applicant: Allergan Pharmaceuticals International Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Grouped variations consisting of: 1) submission of the final report for study ELX-PH-08 (listed as a category 3 study in the RMP). This is an in vitro evaluation study aimed to investigate the effects on treating primary cultures of cryopreserved human hepatocytes with eluxadoline on the expression of cytochrome P450 (CYP) enzymes; 2) submission of the final report for study 3030-102-002 (listed as a category 3 study in the RMP). This is a randomised, open label study aimed to evaluate the effect of eluxadoline as a potential time dependent inhibitor of CYP3A4<sup>6</sup> with the substrate midazolam. The RMP (version 2.0) is updated to refine the important identified risk of 'sphincter of Oddi (SO) spasm' to 'SO spasm (sphincter of Oddi dysfunction, SOD)' and to include pancreatitis as an important identified risk as agreed in the conclusions of PSUSA/00010528/201703 finalised at PRAC/CHMP in October 2017

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<sup>6</sup> Cytochrome P 450 3A4

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

#### 5.3.10. [Enzalutamide - XTANDI \(CAP\) - EMEA/H/C/002639/II/0039/G](#)

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Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations consisting of: 1) update of sections 4.4, 4.7, 4.8 and 5.2 of the SmPC in order to amend the warning on possible association with seizure, to amend the effects on driving or operating machines, to amend the identified adverse reactions and to amend the 'race' subsection regarding pharmacokinetic properties based on the results from the completed studies PROSPER: a phase 3 randomized controlled study, designed to investigate the safety and efficacy of enzalutamide in patients with non-metastatic castration-resistant prostate cancer; and Asian PREVAIL: a multinational phase 3, randomized, double-blind, placebo-controlled efficacy and safety study of oral enzalutamide in chemotherapy-naive subjects with progressive metastatic prostate cancer who have failed androgen deprivation therapy; and the updated integrated clinical safety database. The package leaflet is updated accordingly; 2) extension of indication to include patients with non-metastatic castration-resistant prostate cancer (CRPC). As a consequence, sections 4.1 and 5.1 of the SmPC are updated, based on the supportive clinical study results of study MDV3100-14 (PROSPER): a phase 3 randomized controlled study, designed to investigate the safety and efficacy of enzalutamide in patients with non-metastatic castration-resistant prostate cancer; study MDV3100-09 (STRIVE): a multicentre phase 2 study to investigate the safety and efficacy of enzalutamide versus bicalutamide in men with non-metastatic or metastatic castration-resistant prostate cancer; and based on supportive non-clinical data from 7 new reports. The package leaflet and the RMP (version 12.1) are updated accordingly

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

#### 5.3.11. [Fingolimod - GILENYA \(CAP\) - EMEA/H/C/002202/X/0044/G](#)

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Grouped applications consisting of: 1) extension application to introduce a new strength of hard capsules (0.25 mg) to the currently approved presentations; 2) extension of indication to add a new indication for the treatment of paediatric patients of 10 years of age and above with relapsing multiple sclerosis (RMS). As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 5.3, 6 and 8 of the SmPC are updated. The package leaflet, labelling and the RMP (version 13.0) are updated accordingly. In addition, Annex II is updated to be 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

#### 5.3.12. [Exenatide - BYDUREON \(CAP\) - EMEA/H/C/002020/II/0050](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.1, 4.2, 4.4 and 5.1 of the SmPC based on the final clinical

study report (CSR) of study EXSCEL (EXenatide Study of Cardiovascular Event Lowering): 'a randomized, placebo controlled clinical trial to evaluate cardiovascular outcomes after treatment with exenatide once weekly in patients with type 2 diabetes mellitus' in fulfilment of PAM (LEG 009). The package leaflet and the RMP (version 31) are updated accordingly

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

#### 5.3.13. [Fluticasone furoate, umeclidinium, vilanterol - ELEBRATO ELLIPTA \(CAP\) - EMEA/H/C/004781/WS1369/0001; TRELEGY ELLIPTA \(CAP\) - EMEA/H/C/004363/WS1369/0001](#)

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Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to modify the current approved chronic obstructive pulmonary disease (COPD) therapeutic indication to 'maintenance treatment in adult patients with moderate to severe COPD'. As a consequence, sections 4.1, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 02) are updated accordingly. This is based on the results of study CTT116855: a phase 3, 52 week, randomized, double-blind, 3-arm parallel group study, comparing the efficacy, safety and tolerability of the fixed dose triple combination fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) with the fixed dose dual combinations of FF/VI and UMEC/VI, all administered once-daily in the morning via a dry powder inhaler in subjects with COPD; as well as study 200812: a phase 3B, 24-week randomised, double-blind study to compare 'closed' triple therapy (FF/UMEC/VI) with 'open' triple therapy (FF/VI + UMEC) in subjects with COPD; and the population pharmacokinetics (PK) report 208059

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

#### 5.3.14. [Glecaprevir, pibrentasvir - MAVIRET \(CAP\) - EMEA/H/C/004430/II/0012](#)

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Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication to extend the Maviret (glecaprevir/pibrentasvir) indication to adolescents (from 12 to 18 years of age) with chronic hepatitis C infection, based on new clinical data from study M16-123: an open-label, multicentre study to evaluate the pharmacokinetics, safety, and efficacy of glecaprevir/pibrentasvir in paediatric subjects with genotypes 1-6 chronic hepatitis C virus infection (DORA), using the adult co-formulated tablets in adolescents. 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 4.0) in line with revision 2 of the guidance on the format of RMP in the EU (template) are updated accordingly

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

#### 5.3.15. [Golimumab - SIMPONI \(CAP\) - EMEA/H/C/000992/X/0083/G](#)

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Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped applications consisting of: 1) extension application to add a new strength of 100 mg/ml solution for injection for paediatric use; 2) extension of indication to include

paediatric patients from the age of 2 years and older for the treatment of polyarticular juvenile idiopathic arthritis (pJIA) with Simponi (golimumab) 100 mg/mL solution for injection. As a consequence, sections 4.1, 4.2, 5.1 and section 4.1 of the 50mg strength are updated; 3) update of the RMP (version 18.0) to delete the following safety concerns: vasculitis, psoriasis (new onset or worsening of pre-existing), and sarcoidosis/sarcoid like reaction as requested in the outcome of variation II/068/G concluded in May 2016; 4) update of the RMP (version 18.0) to change the due date of study MK-8259-050 (listed as a category 3 study in the RMP) as requested by CHMP in the conclusion of MEA 033 dated April 2017. Finally, the MAH took the opportunity to update the product information in line with the latest QRD template (version 10) to implement the recommendations stated in the revised Annex to the European Commission (EC) guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' with regard to the excipient sorbitol (E420); to add a statement in section 4.4 of the SmPC to record the name and the batch number of the administered product in line with GVP Module P.II on 'Biological medicinal products' (EMA/168402/2014 Corr\*)

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

#### 5.3.16. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/II/0214

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of Annex II-D of the product information to remove the educational material for health care professionals. As a consequence, the RMP (version 17.0) is updated. In addition, the MAH took the opportunity to update the package leaflet with some missing warnings and adverse drug reactions (ADRs) already reflected in the SmPC, as requested by CHMP, and to introduce some minor QRD related changes

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

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

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Ulla Wändel Liminga

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

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

#### 5.3.18. Insulin glargine - TOUJEO (CAP) - EMEA/H/C/000309/II/0105/G

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations to introduce a new 3 mL pre-filled pen. As a consequence, Annex A, I, IIA and IIIB are amended. In addition, the RMP (version 5.0) in line with revision 2 of the guidance on the format of RMP in the EU (template) is updated accordingly

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

### 5.3.19. Insulin human - RYZODEG (CAP) - EMEA/H/C/002499/II/0028

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Applicant: Novo Nordisk A/S

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 5.1 of the SmPC based on new clinical data from cardiovascular outcome trial EX1250-4080 (DEVOTE): a randomised, double-blind and event-driven clinical trial with a median duration of 2 years comparing the cardiovascular safety of insulin degludec versus insulin glargine (100 units/mL) in patients with type 2 diabetes mellitus (T2DM) at high risk of cardiovascular events. Based on the long-term exposure and safety data from DEVOTE which are also relevant for insulin degludec/insulin aspart, the product information for Ryzodeg (insulin human) is updated with data from the trial in alignment with a recent update of the product information for insulin degludec-containing product(s). Section 6.5 of the SmPC is also amended to introduce editorial changes relating to the plunger stopper. The RMP (version 7) is updated accordingly

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

### 5.3.20. Irinotecan hydrochloride trihydrate - ONIVYDE (CAP) - EMEA/H/C/004125/II/0008, Orphan

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Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: David Olsen

Scope: Update of sections 1, 2, 4.2, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC in order to reflect the expression of strength based on irinotecan anhydrous free-base. The labelling, package leaflet and the RMP (version 2.1) are updated accordingly. In addition the MAH took the opportunity to introduce minor editorial changes

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

### 5.3.21. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/II/0069, Orphan

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Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to include treatment of cystic fibrosis in children age 12 to less than 24 months who have one of the currently approved gating mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene for Kalydeco (ivacaftor) 50 mg and 75 mg granules. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. Relevant consequential changes are made to Kalydeco (ivacaftor) 150 mg film-coated tablet product information. The package leaflet and the RMP (version 7.2) are updated accordingly

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

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

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Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Grouped variations consisting of: 1) extension application to introduce a new

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

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

#### 5.3.23. [Nintedanib - OFEV \(CAP\) - EMEA/H/C/003821/II/0021, Orphan](#)

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Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

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

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

#### 5.3.24. [Ocrelizumab - OCREVUS \(CAP\) - EMEA/H/C/004043/II/0002](#)

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Julie Williams

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

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

#### 5.3.25. [Octocog alfa - ADVATE \(CAP\) - EMEA/H/C/000520/II/0092](#)

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Applicant: Baxter AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 5.1 of the SmPC in order to add new data on immune tolerance induction (ITI) following the final results from study PASS-INT-004: a prospective, multicentre, uncontrolled, open-label, non-interventional post-authorisation safety surveillance study conducted to evaluate Advate (octocog alfa) in ITI therapy in subjects with moderate or severe haemophilia A (baseline factor VIII (FVIII)  $\leq$  2%) and a high titre (> 5 Bethesda units (BU)) inhibitor to FVIII. The RMP (version 16.0) is updated accordingly

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

#### 5.3.26. [Olaparib - LYNPARZA \(CAP\) - EMEA/H/C/003726/II/0020](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include the use of Lynparza (olaparib) tablets as monotherapy for the treatment of adult patients with BRCA-1/2-mutated human epidermal growth factor receptor 2 (HER2) negative metastatic breast cancer who have previously been treated with chemotherapy. These patients could have received chemotherapy in the neoadjuvant, adjuvant or metastatic setting. 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 16) are updated accordingly

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

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

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Kirsti Villikka

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

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

### 5.3.28. Pegaspargase - ONCASPAR (CAP) - EMEA/H/C/003789/II/0016/G

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Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Patrick Batty

Scope: Grouped variations consisting of an update of sections 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC with the final results from 2 studies, namely: 1) study DFCI 11-001 (listed as a category 3 study in the RMP): a phase 2, open-label, randomized, multicentre study to determine the safety and feasibility of administering an investigational asparaginase product (asparaginase formulation) compared with Oncaspar (pegaspargase) in subjects aged 1 to <22 years with newly diagnosed acute lymphoblastic leukaemia (ALL) or lymphoblastic lymphoma; 2) study AALL07P4 (listed as a category 3 study in the RMP): a multicentre, open label, randomized, active-controlled, parallel design clinical pilot study conducted to evaluate the pharmacokinetics (PK), pharmacodynamics (PD), safety, immunogenicity and efficacy of an investigational asparaginase product in comparison with Oncaspar (pegaspargase) in patients aged 1 to <31 years newly diagnosed with high risk B-precursor ALL. The package leaflet and the RMP (version 3.0) are updated accordingly

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

### 5.3.29. Peginterferon beta-1a - PLEGRIDY (CAP) - EMEA/H/C/002827/II/0046

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Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning and



safety information on 'anaphylaxis'. The RMP (version 3.2) is updated accordingly

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

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

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Applicant: Pfizer Limited

PRAC Rapporteur: Ulla Wändel Liminga

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

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

#### 5.3.31. [Prepandemic influenza vaccine \(H5N1\) \(surface antigen, inactivated, adjuvanted\) - AFLUNOV \(CAP\) - EMEA/H/C/002094/II/0044/G](#)

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Applicant: Seqirus S.r.l

PRAC Rapporteur: Amelia Cupelli

Scope: Grouped variations consisting of an update of sections 4.4, 4.6, 4.8 and 5.1 of the SmPC following the completion of clinical study reports for 1) study V87\_25: a phase 3, prospective, controlled, observer-blind, multicentre study to evaluate the safety, tolerability and immunogenicity of two doses of a monovalent A/H5N1 influenza vaccine adjuvanted with MF59 when administered to subjects with and without underlying medical conditions; 2) study V87\_26: a phase 3, prospective, controlled, observer-blind, multicentre study to evaluate the safety, tolerability and immunogenicity of two doses of a monovalent A/H5N1 influenza vaccine adjuvanted with MF59 when administered to adults and elderly subjects with immunosuppressive disorders. The package leaflet, labelling and RMP (version 3.0) are updated accordingly. In addition, the MAH took the opportunity to implement some amendments to the product information and introduce some additional minor editorial corrections

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

#### 5.3.32. [Ribociclib - KISQALI \(CAP\) - EMEA/H/C/004213/II/0003/G](#)

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Doris Stenver

Scope: Grouped variations consisting of: 1) update of section 5.2 of the SmPC in order to reflect on results from study CLEE011A2109: a phase 1, open label, multicentre, parallel cohort, single dose study to evaluate the pharmacokinetics (PK) of ribociclib (LEE011) in healthy subjects with normal hepatic function and subjects with impaired hepatic function; 2) update of section 4.2 and 5.2 of the SmPC in order to reflect on results from study CLEE011A2116-Part I: a phase 1, open label, multicentre, parallel-group, single dose two-staged study to evaluate the pharmacokinetics and safety of a single 400 mg oral dose of ribociclib (LEE011) in subjects with varying degrees of impaired renal function compared to matched healthy volunteers with normal renal function. The RMP (version 2.0) is updated



accordingly

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

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

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Doris Stenver

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

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

### 5.3.34. Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0152

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Update of sections 4.2 and 4.4 of the SmPC following the submission of the final study report for the non-interventional drug utilisation study (DUS) BA28478: MabThera drug utilisation study and patient alert card evaluation in non-oncology patients in Europe: an infusion centre-based approach. Annex II.E is updated to remove the patient alert card as an additional risk minimisation measure for the risks of progressive multifocal leukoencephalopathy (PML) and infections for the non-oncology indications. The package leaflet and the RMP (version 18) are updated accordingly. This submission fulfils FUM-68.1 and FUM-71

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

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

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Applicant: Tesaro UK Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Grouped variations consisting of: 1) update of SmPC section 4.5 regarding interaction with organic cation transporter 1 (OCT1) substrates to reflect results from non-

clinical study 17TESAP2R1: an in vitro evaluation of the substrate and inhibitor potential of rolapitant for efflux and update of transporters; 2) update of SmPC section 4.5 regarding interaction with UDP-glucuronosyltransferase (UGT) substrates following the submission of the results from non-clinical studies, namely: study 170594: evaluation of potential UGT inhibition by rolapitant in cryopreserved human hepatocytes and study TSRP/REP/07CRD75486/2017: evaluation of potential rolapitant metabolism by recombinantly expressed human UGT enzymes; 3) update of SmPC section 4.5 following the submission of the results for study 1000-01-001: an open-label, single-dose study to assess the effects of rolapitant (oral) on the pharmacokinetics of caffeine (CYP1A2) in healthy subjects. The RMP (version 1.2) is updated accordingly

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

### 5.3.36. [Rucaparib - RUBRACA \(CAP\) - EMEA/H/C/004272/II/0001, Orphan](#)

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Applicant: Clovis Oncology UK Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include a new indication for Rubraca 'as monotherapy for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy'. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated with the expanded clinical efficacy and safety data. The package leaflet and the RMP (version 2.0) are updated accordingly. In addition, the applicant took the opportunity to propose the move of one paragraph from section 4.4 to 5.1 in the SmPC for consistency with other SmPC agents in this class with this indication

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

### 5.3.37. [Secukinumab - COSENTYX \(CAP\) - EMEA/H/C/003729/II/0033/G](#)

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations consisting of: 1) update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to include information on dose up-titration for psoriatic arthritis (PsA) and update the radiographic sub-section for PsA based on results from the 24-week data from study CAIN457F2342: a phase 3, randomized, double-blind, placebo controlled multicentre study of subcutaneous secukinumab (150 mg and 300 mg) in prefilled syringe to demonstrate efficacy (including inhibition of structural damage), safety, and tolerability up to 2 years in subjects with active psoriatic arthritis (FUTURE 5), the pooled data from PsA phase 3 studies, the pooled data from patients who up-titrated their secukinumab dose in the following studies, namely: study CAIN457F2306E1: a three-year extension study to evaluate the long term efficacy, safety and tolerability of secukinumab in patients with active PsA; study CAIN457F2312: efficacy at 24 weeks with long term safety, tolerability and efficacy up to 5 years of secukinumab in patients of active psoriatic arthritis (FUTURE 2) as well as study CAIN457F2318: 24 week efficacy and 3-year safety and efficacy of secukinumab in active psoriatic arthritis, and long-term study observations which demonstrate higher rates of discontinuation for patients on secukinumab 150 mg compared to patients on secukinumab 300 mg. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the

package leaflet and to bring it in line with the latest approved SmPC as per procedure IB/0028 finalised in July 2017; 2) the RMP (version 3.0) is updated to include suicidal ideation and behaviour as an important potential risk in the RMP and including minor administrative/editorial changes (LEG 005.2)

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

#### 5.3.38. [Ticagrelor - BRILIQUE \(CAP\) - EMEA/H/C/001241/II/0042](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

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

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

#### 5.3.39. [Tocilizumab - ROACTEMRA \(CAP\) - EMEA/H/C/000955/II/0076](#)

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include as a paediatric indication 'treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 1 year of age and older, who have responded inadequately to previous therapy with non-steroidal anti-inflammatory drugs (NSAIDs) and systemic corticosteroids' to RoActemra (tocilizumab) 162 mg solution for injection in pre-filled syringe formulation, based on data from phase Ib pharmacokinetic/pharmacodynamic bridging study WA28118 (JIGSAW 118), designed to confirm the RoActemra subcutaneous dosing regimens in patients aged 1 to 17 years old with sJIA, as well as assess the safety of the RoActemra subcutaneous formulation. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 24.0) are updated accordingly. In addition, sections 4.2, 4.8 and 5.2 of the SmPC of RoActemra (tocilizumab) 20 mg/mL concentrate for solution for infusion formulation are updated to reflect data from the pivotal intravenous study WA18221 (TENDER): a randomised, placebo-controlled study to evaluate the effect of tocilizumab on disease response in patients with active sJIA

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

#### 5.3.40. [Trastuzumab - HERZUMA \(CAP\) - EMEA/H/C/002575/II/0006](#)

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Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Addition of a new presentation (420 mg/vial) drug product for single-dose, partial use. The strength (concentration after reconstitution) is identical to the previously authorised 150mg/vial presentation. The RMP (version 3.1) is updated accordingly

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

### 5.3.41. Vardenafil - LEVITRA (CAP) - EMEA/H/C/000475/WS1390/0062; VIVANZA (CAP) - EMEA/H/C/000488/WS1390/0058

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Applicant: Bayer AG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of sections 4.4 and 4.8 of the SmPC to reflect data from two post-marketing observational studies namely: 1) study NCT00759174: 'a study to assess whether phosphodiesterase type 5 inhibitor (PDE5) inhibitors increase the chance of triggering the onset of acute non-arteritic anterior ischaemic optic neuropathy (NAION)', 2) study NCT01131104: 'a study to determine if there is a possible association between NAION and PDE5 inhibitors'; indicating an increased risk of NAION when using PDE5 inhibitors. The MAH also proposed to terminate the NAION study 12912: a prospective case crossover study to assess whether PDE5 inhibitor exposure in men with erectile dysfunction increases the risk for the development of NAION. The RMP (version 5.0) is updated accordingly. In addition, the product information is brought in line with the QRD template (version 10.0) and the contact details of the Bulgarian local representative are updated in the package leaflet. The package leaflets for the 5 mg, 10 mg and 20 mg film-coated tablet strengths are combined into a single package leaflet and the product information for the 10 mg orodispersible tablet is updated for aspartame and sorbitol, according to the annex to the European Commission (EC) guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. Furthermore, the MAH took the opportunity to introduce some editorial amendments to the product information

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

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

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Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Patrick Batty

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

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

## 6. Periodic safety update reports (PSURs)

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

#### 6.1.1. Agomelatine - THYMANAX (CAP); VALDOXAN (CAP) - PSUSA/00000071/201802

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

PRAC Rapporteur: Karen Pernille Harg  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

#### 6.1.2. [Albutrepenonacog alfa - IDELVION \(CAP\) - PSUSA/00010497/201801](#)

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Applicant: CSL Behring GmbH  
PRAC Rapporteur: Menno van der Elst  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

#### 6.1.3. [Allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor \( \$\Delta\$ LNGFR\) and the herpes simplex I virus thymidine kinase \(HSV-TK Mut2\) - ZALMOXIS \(CAP\) - PSUSA/00010530/201802](#)

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Applicant: MolMed S.p.A, ATMP<sup>7</sup>  
PRAC Rapporteur: Brigitte Keller-Stanislawski  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CAT and CHMP

#### 6.1.4. [Atazanavir, cobicistat - EVOTAZ \(CAP\) - PSUSA/00010404/201801](#)

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

#### 6.1.5. [Axitinib - INLYTA \(CAP\) - PSUSA/00010022/201801](#)

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Applicant: Pfizer Limited  
PRAC Rapporteur: David Olsen  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

#### 6.1.6. [Baricitinib - OLUMIANT \(CAP\) - PSUSA/00010578/201802](#)

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Applicant: Eli Lilly Nederland B.V.  
PRAC Rapporteur: Patrick Batty  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

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<sup>7</sup> Advanced therapy medicinal product

#### 6.1.7. Bevacizumab - AVASTIN (CAP); MVASI (CAP) - PSUSA/00000403/201802

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Applicant(s): Amgen Europe B.V. (Mvasi), Roche Registration GmbH (Avastin)

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.8. Brentuximab vedotin - ADCETRIS (CAP) - PSUSA/00010039/201802

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Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.9. Brimonidine<sup>8</sup> - MIRVASO (CAP) - PSUSA/00010093/201802 (with RMP)

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Applicant: Galderma International

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.10. Brivaracetam - BRIVIACT (CAP) - PSUSA/00010447/201801

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Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.11. Carfilzomib - KYPROLIS (CAP) - PSUSA/00010448/201801

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Applicant: Amgen Europe B.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.12. Ceftazidime, avibactam - ZAVICEFTA (CAP) - PSUSA/00010513/201802

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Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

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

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<sup>8</sup> Centrally authorised product(s) only

#### 6.1.13. Chlormethine - LEDAGA (CAP) - PSUSA/00010587/201802

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Applicant: Actelion Registration Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.14. Cladribine<sup>9</sup> - MAVENCLAD (CAP) - PSUSA/00010634/201801

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Applicant: Merck Europe B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.15. Cobimetinib - COTELLIC (CAP) - PSUSA/00010450/201802

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.16. Colistimethate sodium<sup>10</sup> - COLOBREATHE (CAP) - PSUSA/00009112/201802

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Applicant: Teva B.V.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.17. Collagenase clostridium histolyticum<sup>11</sup> - XIAPEX (CAP) - PSUSA/00000871/201802

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Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.18. Dapagliflozin, metformin - EBYMECT (CAP); XIGDUO (CAP) - PSUSA/00010294/201801

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Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

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<sup>9</sup> Indicated in the treatment of multiple sclerosis (MS)

<sup>10</sup> Dry inhalation powder only

<sup>11</sup> Indicated in the treatment of Dupuytren's contracture and treatment of Peyronie's disease

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.19. [Dasabuvir - EXVIERA \(CAP\) - PSUSA/00010363/201801](#)

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Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.20. [Dexamethasone<sup>12</sup> - OZURDEX \(CAP\) - PSUSA/00000985/201801 \(with RMP\)](#)

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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

#### 6.1.21. [Diphtheria, tetanus, pertussis \(acellular, component\), hepatitis B \(rDNA\), poliomyelitis \(inactivated\), haemophilus type b conjugate vaccine \(adsorbed\) - VAXELIS \(CAP\) - PSUSA/00010469/201802](#)

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Applicant: MCM Vaccine B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.22. [Dolutegravir - TIVICAY \(CAP\); dolutegravir, abacavir, lamivudine - TRIUMEQ \(CAP\) - PSUSA/00010075/201801](#)

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Applicants: ViiV Healthcare B.V. (Tivicay), ViiV Healthcare UK Limited (Triumeq)

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.23. [Elosulfase alfa - VIMIZIM \(CAP\) - PSUSA/00010218/201802](#)

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Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

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

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<sup>12</sup> Centrally authorised product(s) only, indicated in the treatment of uveitis and macular oedema



6.1.24. [Emtricitabine, rilpivirine, tenofovir alafenamide - ODEFSEY \(CAP\) - PSUSA/00010514/201802](#)

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Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

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

6.1.25. [Etanercept<sup>13</sup> - BENEPALI \(CAP\); ERELZI \(CAP\) - PSUSA/00010452/201801](#)

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Applicant(s): Samsung Bioepis UK Limited (Benepali), Sandoz GmbH (Erelzi)

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

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

6.1.26. [Etanercept<sup>14</sup> - ENBREL \(CAP\) - PSUSA/00001295/201802](#)

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

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

6.1.27. [Evolocumab - REPATHA \(CAP\) - PSUSA/00010405/201801](#)

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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

6.1.28. [Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR \(CAP\) - PSUSA/00010352/201802](#)

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Applicant: Chiesi Farmaceutici S.p.A., ATMP<sup>15</sup>

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

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

6.1.29. [Fenofibrate, simvastatin - CHOLIB \(CAP\) - PSUSA/00010096/201802](#)

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Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Julie Williams

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<sup>13</sup> Biosimilar products only

<sup>14</sup> All products except biosimilar

<sup>15</sup> Advanced therapy medicinal product

Scope: Evaluation of a PSUSA procedure

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

#### **6.1.30. Ferric maltol - FERACCRU (CAP) - PSUSA/00010476/201802**

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Applicant: Shield TX (UK) Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

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

#### **6.1.31. Fingolimod - GILENYA (CAP) - PSUSA/00001393/201802**

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

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

#### **6.1.32. Florbetaben (<sup>18</sup>F) - NEURACEQ (CAP) - PSUSA/00010094/201802**

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Applicant: Life Radiopharma Berlin GmbH

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

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

#### **6.1.33. Fluticasone, salmeterol<sup>16</sup> - AERIVIO SPIROMAX (CAP); AIREXAR SPIROMAX (CAP) - PSUSA/00010531/201802**

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Applicant: Teva B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

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

#### **6.1.34. Gimeracil, oteracil monopotassium, tegafur - TEYSUNO (CAP) - PSUSA/00002875/201801**

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Applicant: Nordic Group B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

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<sup>16</sup> Centrally authorised product(s) only

#### 6.1.35. Glecaprevir, pibrentasvir - MAVIRET (CAP) - PSUSA/00010620/201801

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Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.36. Hepatitis B (rDNA) vaccine (adjuvanted, adsorbed) - FENDRIX (CAP) - PSUSA/00001598/201802

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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

#### 6.1.37. Infliximab<sup>17</sup> - FLIXABI (CAP); INFLECTRA (CAP); REMSIMA (CAP) - PSUSA/00010106/201801

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Applicant(s): Celltrion Healthcare Hungary Kft. (Remsima), Pfizer Europe MA EEIG (Inflectra), Samsung Bioepis UK Limited (Flixabi)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.38. Ingenol mebutate - PICATO (CAP) - PSUSA/00010035/201801

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Applicant: LEO Laboratories Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.39. Insulin glargine, lixisenatide - SULIQUA (CAP) - PSUSA/00010577/201801 (with RMP)

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Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.40. Lenvatinib - LENVIMA (CAP) - PSUSA/00010380/201802

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Applicant: Eisai Europe Ltd.

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<sup>17</sup> Biosimilar products only

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

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6.1.41. [Lonoctocog alfa - AFSTYLA \(CAP\) - PSUSA/00010559/201801](#)

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Applicant: CSL Behring GmbH  
PRAC Rapporteur: Daniela Philadelphly  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

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6.1.42. [Meningococcal group-B vaccine \(rDNA, component, adsorbed\) - BEXSERO \(CAP\) - PSUSA/00010043/201801 \(with RMP\)](#)

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Applicant: GSK Vaccines S.r.l  
PRAC Rapporteur: Ulla Wändel Liminga  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

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6.1.43. [Mercaptamine<sup>18</sup> - CYSTADROPS \(CAP\) - PSUSA/00010574/201801](#)

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Applicant: Orphan Europe SARL  
PRAC Rapporteur: Eva Segovia  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

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6.1.44. [Modified vaccinia Ankara virus - IMVANEX \(CAP\) - PSUSA/00010119/201801](#)

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

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6.1.45. [Nalmefene - SELINCRO \(CAP\) - PSUSA/00010120/201802](#)

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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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<sup>18</sup> Indicated in the treatment of corneal cystine

#### 6.1.46. Nilotinib - TASIGNA (CAP) - PSUSA/00002162/201801

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.47. Nitisinone - ORFADIN (CAP) - PSUSA/00002169/201802

Applicant: Swedish Orphan Biovitrum International AB

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.48. Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - PSUSA/00010367/201801

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.49. Ospemifene - SENSHIO (CAP) - PSUSA/00010340/201802

Applicant: Shionogi Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.50. Palbociclib - IBRANCE (CAP) - PSUSA/00010544/201802

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.51. Phenylephrine, ketorolac - OMIDRIA (CAP) - PSUSA/00010419/201801

Applicant: Omeros London Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.52. Pirfenidone - ESBRIET (CAP) - PSUSA/00002435/201802

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.53. Pomalidomide - IMNOVID (CAP) - PSUSA/00010127/201802

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Applicant: Celgene Europe Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.54. Prasugrel - EFIENT (CAP) - PSUSA/00002499/201802 (with RMP)

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Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.55. Ranolazine - RANEXA (CAP) - PSUSA/00002611/201801 (with RMP)

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Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.56. Reslizumab - CINQAERO (CAP) - PSUSA/00010523/201802

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Applicant: Teva Pharmaceuticals Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.57. Ribociclib - KISOALI (CAP) - PSUSA/00010633/201802

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.58. Rolapitant - VARUBY (CAP) - PSUSA/00010592/201802

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Applicant: Tesaro UK Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.59. Ruxolitinib - JAKAVI (CAP) - PSUSA/00010015/201802 (with RMP)

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.60. Sacubitril, valsartan - ENTRESTO (CAP); NEPARVIS (CAP) - PSUSA/00010438/201801

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.61. Safinamide - XADAGO (CAP) - PSUSA/00010356/201802

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Applicant: Zambon S.p.A.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.62. Sebelipase alfa - KANUMA (CAP) - PSUSA/00010422/201802

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Applicant: Alexion Europe SAS

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.63. Silodosin - SILODYX (CAP); UROREC (CAP) - PSUSA/00002701/201801

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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

#### 6.1.64. Simoctocog alfa - NUWIQ (CAP); VIHUMA (CAP) - PSUSA/00010276/201801

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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

#### 6.1.65. Telotristat - XERMELO (CAP) - PSUSA/00010639/201802

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Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.66. Tivozanib - FOTIVDA (CAP) - PSUSA/00010636/201802

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Applicant: EUSA Pharma (UK) Limited

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.67. Trastuzumab emtansine - KADCYLA (CAP) - PSUSA/00010136/201802

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.68. Ulipristal acetate<sup>19</sup> - ESMYA (CAP) - PSUSA/00009325/201802

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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

#### 6.1.69. Umeclidinium - INCRUSE ELLIPTA (CAP); ROLUFTA ELLIPTA (CAP) - PSUSA/00010263/201712

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Applicant(s): Glaxo Group Ltd (Incruse Ellipta), GlaxoSmithKline Trading Services Limited (Rolufta Ellipta)

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

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<sup>19</sup> Indicated in the treatment of moderate to severe symptoms of uterine fibroids



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

#### 6.1.70. Vismodegib - ERIVEDGE (CAP) - PSUSA/00010140/201801

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

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

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

#### 6.2.1. Alitretinoin - PANRETIN (CAP); NAP - PSUSA/00000090/201801

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Applicants: Eisai Ltd (Panretin), various

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

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

#### 6.2.2. Pregabalin - LYRICA (CAP); PREGABALIN PFIZER (CAP); NAP - PSUSA/00002511/201801

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Applicants: Pfizer Europe MA EEIG (Lyrica, Pregabalin Pfizer), various

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

#### 6.2.3. Repaglinide - NOVONORM (CAP); PRANDIN (CAP); NAP - PSUSA/00002618/201712

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Applicants: Novo Nordisk A/S (NovoNorm, Prandin), various

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

#### 6.2.4. <sup>13</sup>C-urea - HELICOBACTER TEST INFAI (CAP); PYLOBACTELL (CAP); NAP - PSUSA/00000006/201801

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Applicants: INFAI GmbH (Helicobacter Test INFAI), Torbet Laboratories Limited (Pylobactell), various

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

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

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

#### 6.3.1. 5-fluorouracil<sup>20</sup> (NAP) - PSUSA/00000007/201712

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Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.2. 5-fluorouracil<sup>21</sup> (NAP) - PSUSA/00010000/201712

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Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.3. Acebutolol (NAP) - PSUSA/00000018/201712

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Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.4. Aldesleukin (NAP) - PSUSA/00000076/201712

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Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.5. Allopurinol (NAP) - PSUSA/00000095/201712

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Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.6. Altizide, spironolactone (NAP) - PSUSA/00002781/201801

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Applicant(s): various

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<sup>20</sup> Intravenous (I.V) application only

<sup>21</sup> Topical application only

PRAC Lead: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

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

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#### 6.3.7. [Amantadine \(NAP\) - PSUSA/00000126/201801](#)

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Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

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#### 6.3.8. [Amiodarone \(NAP\) - PSUSA/00000166/201712](#)

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Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

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#### 6.3.9. [Amitriptyline, perphenazine \(NAP\) - PSUSA/00000170/201801](#)

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Applicant(s): various

PRAC Lead: Agni Kapou

Scope: Evaluation of a PSUSA procedure

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

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#### 6.3.10. [Amitriptyline \(NAP\); amitriptyline, amitriptylinoxide \(NAP\); amitriptylinoxide \(NAP\) - PSUSA/00010374/201801](#)

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Applicant(s): various

PRAC Lead: Agni Kapou

Scope: Evaluation of a PSUSA procedure

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

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#### 6.3.11. [Azelastine \(NAP\) - PSUSA/00000277/201712](#)

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Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

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

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#### 6.3.12. [Bendamustine hydrochloride \(NAP\) - PSUSA/00003162/201801](#)

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Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

6.3.13. [Bendroflumethiazide \(NAP\); bendroflumethiazide, potassium chloride \(NAP\) - PSUSA/00010583/201801](#)

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Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

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

6.3.14. [Betahistine \(NAP\) - PSUSA/00000389/201712](#)

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Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

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

6.3.15. [Calcitriol \(NAP\) - PSUSA/00000495/201801](#)

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Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

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

6.3.16. [Cefprozil \(NAP\) - PSUSA/00000605/201712](#)

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Applicant(s): various

PRAC Lead: Gabriela Jazbec

Scope: Evaluation of a PSUSA procedure

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

6.3.17. [Celecoxib \(NAP\) - PSUSA/00000616/201712](#)

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Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

6.3.18. [Cimicifuga racemosa \(L.\) Nutt., rhizoma \(NAP\) - PSUSA/00000755/201801](#)

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Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.19. Cisplatin (NAP) - PSUSA/00000778/201712

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Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.20. Cyproheptadine (NAP) - PSUSA/00000902/201712

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Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.21. Dapoxetine (NAP) - PSUSA/00000928/201712

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Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.22. Desmopressin (NAP) - PSUSA/00000964/201712

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Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.23. Enalapril, nitrendipine (NAP) - PSUSA/00001213/201801

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Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.24. Famciclovir (NAP) - PSUSA/00001349/201712

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Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.25. Felodipine (NAP) - PSUSA/00001356/201712

Applicant(s): various

PRAC Lead: Tatiana Magalova

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.26. Felodipine, metoprolol (NAP) - PSUSA/00001357/201712

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.27. Furosemide (NAP) - PSUSA/00001491/201801

Applicant(s): various

PRAC Lead: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.28. Gemcitabine (NAP) - PSUSA/00001519/201801

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.29. Haemophilus influenzae, klebsiella ozaenae, klebsiella pneumoniae, moraxella catarrhalis, staphylococcus aureus, streptococcus pneumoniae, streptococcus pyogenes, streptococcus viridans vaccine (NAP) - PSUSA/00001582/201712

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.30. Hydrochlorothiazide, ramipril (NAP) - PSUSA/00001660/201801

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

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

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#### 6.3.31. [Hydrochlorothiazide, spironolactone \(NAP\) - PSUSA/00001662/201801](#)

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Applicant(s): various

PRAC Lead: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

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

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#### 6.3.32. [Hypericum perforatum L., herba \(NAP\) - PSUSA/00001701/201801](#)

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Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

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

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#### 6.3.33. [Ibutilide \(NAP\) - PSUSA/00001713/201712](#)

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Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

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#### 6.3.34. [Landiolol \(NAP\) - PSUSA/00010570/201802](#)

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Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

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#### 6.3.35. [Levobupivacaine \(NAP\) - PSUSA/00001848/201712](#)

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Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

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#### 6.3.36. [Levonorgestrel \(NAP\) - PSUSA/00001856/201712](#)

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Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

6.3.37. [Levonorgestrel, ethinylestradiol; ethinylestradiol<sup>22</sup> \(NAP\) - PSUSA/00010442/201801](#)

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Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

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

6.3.38. [Lidocaine hydrochloride, phenylephrine hydrochloride, tropicamide \(NAP\) - PSUSA/00010390/201801](#)

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Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

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

6.3.39. [Lormetazepam \(NAP\) - PSUSA/00001910/201712](#)

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Applicant(s): various

PRAC Lead: Daniela Philadelphy

Scope: Evaluation of a PSUSA procedure

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

6.3.40. [Lubiprostone \(NAP\) - PSUSA/00010290/201801](#)

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Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

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

6.3.41. [Pseudoephedrine, triprolidine \(NAP\) - PSUSA/00003047/201712](#)

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Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

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<sup>22</sup> Combination pack only



#### 6.3.42. Sertindole (NAP) - PSUSA/00002695/201801

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Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.43. Tetanus vaccine (NAP) - PSUSA/00002910/201801

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Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.44. Tobramycin<sup>23 24</sup> (NAP) - PSUSA/00009316/201712

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Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.45. Valproic acid (NAP); sodium valproate (NAP); valproate pivoxil (NAP); valproate semisodium (NAP); valproamide (NAP); valproate bismuth (NAP); calcium valproate (NAP); valproate magnesium (NAP) - PSUSA/00003090/201801

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Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

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

#### 6.4.1. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/LEG 027.1

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Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to LEG 027 [cumulative review of cases of headache, dizziness, and abdominal pain/gastrointestinal (GI) pain from all available sources (post marketing cases, clinical trial data and literature) as requested in the conclusions of PSUSA/00000226/201705 adopted at the December 2017 PRAC] as per the request for supplementary information (RSI) adopted in April 2018

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

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<sup>23</sup> Nebuliser solution only

<sup>24</sup> All medicinal products except Centrally Authorised Products (CAP)

#### 6.4.2. Bosentan - STAYVEER (CAP) - EMEA/H/C/002644/LEG 010.1

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Applicant: Marklas Nederlands BV

PRAC Rapporteur: Adrien Inoubli

Scope: MAH's response to LEG 010 [overview of the educational materials with the controlled distribution systems implemented at national levels, together with a discussion on the effectiveness of each measure in place to minimise any risk (including educational material and controlled distribution system), as requested in the conclusions of PSUSA/00000425/201611 adopted in July 2017] as per the request for supplementary information (RSI) adopted in February 2018

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

#### 6.4.3. Bosentan - TRACLEER (CAP) - EMEA/H/C/000401/LEG 086.1

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Applicant: Actelion Registration Limited

PRAC Rapporteur: Adrien Inoubli

Scope: MAH's responses LEG 086 [overview of the educational materials with the controlled distribution systems implemented at national levels, together with a discussion on the effectiveness of each measure in place to minimise any risk (including educational material and controlled distribution system), as requested in the conclusions of PSUSA/00000425/201611 adopted in July 2017] as per the request for supplementary information (RSI) adopted in February 2018

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

#### 6.4.4. Decitabine - DACOGEN (CAP) - EMEA/H/C/002221/LEG 009.1

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ghania Chamouni

Scope: MAH's response to LEG 009 [cumulative review of cases of hepatic failure, fibrosis, cirrhosis and other liver damage-related conditions from all available sources as requested in the conclusions of PSUSA/00009118/201705 adopted at the December 2017 PRAC] as per the request for supplementary information (RSI) adopted in April 2018

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

#### 6.4.5. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/LEG 036.1

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: MAH's response to LEG 036 [review of cases of tumefactive lesions reported in the literature and in post marketing setting, as requested in the conclusions of PSUSA/00001393/201702 adopted by PRAC at its October 2017 meeting] as per the request for supplementary information (RSI) adopted in March 2018

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

#### 6.4.6. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/LEG 066

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Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Detailed study report of the retrospective analysis of extended interval dosing (EID) versus standard interval dosing (SID), a proposal for further investigation of efficacy and safety in terms of progressive multifocal leukoencephalopathy (PML) risk reduction with EID relative to SID, and updated pharmacokinetic/pharmacodynamic (PK/PD) modelling taking into account body weight and extended dosing intervals, as requested in the conclusions of PSUSA/00002127/201708 adopted by PRAC in March 2018

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

#### 6.4.7. Regorafenib - STIVARGA (CAP) - EMEA/H/C/002573/LEG 011

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Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

Scope: Cumulative review of cases of 'necrotising fasciitis' (NF) from all sources as requested in the conclusions of PSUSA/00010133/201709 adopted by PRAC in April 2018

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

#### 6.4.8. Thalidomide - THALIDOMIDE CELGENE (CAP) - EMEA/H/C/000823/LEG 036

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Applicant: Celgene Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: Cumulative review and analysis of cases of progressive multifocal leukoencephalopathy (PML) reported in patients treated with thalidomide as requested in the conclusions of PSUSA/00002919/201710 adopted by PRAC in May 2018

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

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

### 7.1. Protocols of PASS imposed in the marketing authorisation(s)<sup>25</sup>

None

### 7.2. Protocols of PASS non-imposed in the marketing authorisation(s)<sup>26</sup>

#### 7.2.1. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/MEA 016

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Applicant: Bayer AG

PRAC Rapporteur: Ghania Chamouni

Scope: Protocol for a follow-up survey measuring the effectiveness of the updated

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<sup>25</sup> In accordance with Article 107n of Directive 2001/83/EC

<sup>26</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

educational material for healthcare professionals (HCPs): a survey to investigate whether physicians have received the revised educational materials, measuring physician knowledge and understanding of the key information in the revised educational materials, and whether physicians have provided the patient booklet to their patients [result due date expected within 6 months after completion of the survey] (from variation II/39 finalised in April 2018)

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

#### 7.2.2. Alectinib - ALECENSA (CAP) - EMEA/H/C/004164/MEA 002

Applicant: Roche Registration GmbH

PRAC Rapporteur: Patrick Batty

Scope: Protocol for study BO40643: a survey measuring the effectiveness of the risk minimisation activities to prescribers: correct implementation of Alecensa (alectinib) label guidance by prescribers of the following important identified risks: interstitial lung disease (ILD)/pneumonitis, hepatotoxicity, photosensitivity, bradycardia, severe myalgia and creatine phosphokinase (CPK) elevations (from variation II/01 finalised in October 2017)

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

#### 7.2.3. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/MEA 004

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Protocol for study D3250R00042: a descriptive study of the incidence of malignancy in patients with severe asthma overall and among those receiving benralizumab and other therapies in real-world settings (from initial MAA/opinion)

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

#### 7.2.4. Dimethyl fumarate - SKILARENCE (CAP) - EMEA/H/C/002157/MEA 001.2

Applicant: Almirall S.A

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 001 [protocol for study M-41008-40 (listed as a category 3 study in the RMP): an observational PASS in European psoriasis registers to evaluate the long-term safety of Skilarence (dimethyl fumarate) used for the treatment of patients with moderate to severe psoriasis [future due date(s): end of data collection: Q1 2027; final study report expected within a year of availability of the final data set] (from initial MAA/opinion)] as per the request for supplementary information (RSI) adopted in March 2018

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

#### 7.2.5. Dimethyl fumarate - SKILARENCE (CAP) - EMEA/H/C/002157/MEA 002.1

Applicant: Almirall S.A

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 002 [protocol for study M-41008-44: a PASS retrospective chart review to assess the effectiveness of Skilarence (dimethyl fumarate) risk minimisation activities in daily practice] as per the request for supplementary information (RSI) adopted in March 2018

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

#### 7.2.6. Eliglustat - CERDELGA (CAP) - EMEA/H/C/003724/MEA 006.4

Applicant: Genzyme Europe BV

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 006.3 [protocol for drug utilisation study (DUS) ELIGL C06912 conducted in the US population using the MarketScan database to assess adherence to the labelling with regard to drug-drug interactions (DDI) and to genotyping assessment prior to the initiation of eliglustat therapy] as per the request for supplementary information (RSI) adopted in March 2018

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

#### 7.2.7. Guanfacine - INTUNIV (CAP) - EMEA/H/C/003759/MEA 005.2

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA005.1 [protocol for a non-imposed, non-interventional PASS safety study: a drug utilisation study (DUS) of Intuniv (guanfacine extended release) in European countries (DUS-database) and protocol for a prescriber survey (DUS-survey) conducted in European countries] as per the request for supplementary information (RSI) adopted in April 2018

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

#### 7.2.8. Insulin glargine, lixisenatide - SULIQUA (CAP) - EMEA/H/C/004243/MEA 002.2

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 002.1 [protocol for a study/survey (listed as a category 3 study in the RMP): a cross-sectional multinational, multichannel survey conducted among healthcare professionals and patients to measure the effectiveness of Suliqua (insulin glargine/lixisenatide) educational materials set up to evaluate the knowledge and understanding of the key safety messages in the healthcare professional guide and the patient guide] as per the request for supplementary information (RSI) adopted in March 2018

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

#### 7.2.9. Lutetium (<sup>177</sup>Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/MEA 001.2

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA 001.1 [protocol for study A-LUT-T-E02-402 (SALUS study, listed as a category 3 study in the RMP): an international post-authorisation safety registry to assess the long-term safety of Lutathera (lutetium (<sup>177</sup>Lu)) for unresectable or metastatic, somatostatin receptor positive gastroenteropancreatic neuroendocrine tumours (GEP-NETs)] as per the request for supplementary information (RSI) adopted in April 2018

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

#### 7.2.10. Mercaptamine - CYSTADROPS (CAP) - EMEA/H/C/003769/MEA 001.2

Applicant: Orphan Europe SARL

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 001.1 [PASS protocol for study CYT-DS-001 (listed as a category 3 study in the RMP): an open-label longitudinal PASS to assess the safety of Cystadrops (mercaptopamine) in paediatric and adult cystinosis patients in long term use [final clinical study report (CSR) due date: by 2021] (from initial opinion/MA)] as per the request for supplementary information (RSI) adopted in June 2018

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

#### 7.2.11. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/MEA 003.5

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 003.4 [protocol for study NB-451: a protocol synopsis for an observational retrospective database study based on secondary data analysis using existing databases, as suitable] as per the request for supplementary information (RSI) adopted in April 2018

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

#### 7.2.12. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/MEA 067

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Protocol for study IMA-06-02: the TOP study (Tysabri Observational Programme): an open label, multinational, multicentre, prospective, observational study to address the long-term safety profile and long-term impact on disease activity and progression of natalizumab with marketed use, and the impact of treatment on disability in particular by comparing the results with prospectively determined controls from established databases

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

#### 7.2.13. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/MEA 004

Applicant: Roche Registration GmbH

PRAC Rapporteur: Julie Williams

Scope: Protocol for study BA39730 (listed as a category 3 study in the RMP): a long term

surveillance study to assess and characterize the long-term safety data from the use of ocrelizumab in treated patients with multiple sclerosis (MS) [final report due date expected in 12/2028] (from initial MA/opinion)

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

#### 7.2.14. Sarilumab - KEVZARA (CAP) - EMEA/H/C/004254/MEA 002.1

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 002 [PASS protocol for a safety surveillance programme using existing EU rheumatoid arthritis (RA) registries conducted in four countries: Germany (German Register for Rheumatoid Arthritis Observation of Biologic Therapy (RABBIT) (OBS15180)), Spain (Spanish Registry for Adverse Events for Biological Therapy in Rheumatic Diseases (BIOBASASER) (6R88-RA-1720)), Sweden (Register for Antirheumatic Therapies in Sweden (ARTIS) (OBS15220)) and UK (British Society for Rheumatology Biologicals Register (BSRBR) (6R88-RA-1634)) (from initial MAA/opinion)] as per the request for supplementary information (RSI) adopted in March 2018

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

#### 7.2.15. Semaglutide - OZEMPIC (CAP) - EMEA/H/C/004174/MEA 002

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Protocol for study NN9535-4447: an epidemiological database study to estimate the risk of pancreatic cancer in users of Ozempic (semaglutide) [final study report expected 5 years after start of study] (from initial MA/opinion)

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

#### 7.2.16. Susoctocog alfa - OBIZUR (CAP) - EMEA/H/C/002792/MEA 008

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Protocol for a study to evaluate the effectiveness of risk minimisation measures (RMM): a survey among healthcare professionals to assess their knowledge on dosing and administration of Obizur (susoctocog alfa) in six European countries

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

#### 7.2.17. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 007.1

Applicant: Pfizer Limited

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 007 [protocol for a non-interventional PASS study A3921298 (listed as a category 3 study in the RMP) evaluating the effectiveness of additional risk minimisation measures (aRMM) for Xeljanz (tofacitinib) in the European Union via a survey of healthcare professionals (HCPs) considered as an additional pharmacovigilance activity in

the RMP] as per the request for supplementary information (RSI) adopted in April 2018

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

#### 7.2.18. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 008

Applicant: Pfizer Limited

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study A3921312 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the British Society for Rheumatology Biologics Register-Rheumatoid Arthritis (BSRBR-RA)

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

#### 7.2.19. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 009

Applicant: Pfizer Limited

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study A3921314 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the Swedish (ARTIS) register

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

#### 7.2.20. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 010

Applicant: Pfizer Limited

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study A3921316 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the Spanish registry of adverse events of biological therapies and biosimilars in rheumatoid diseases (BIOBADASER)

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

#### 7.2.21. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 011

Applicant: Pfizer Limited

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study A3921317 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other adverse event rates among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within within the



German registry Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT)

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

#### 7.2.22. [Velaglucerase alfa - VPRIV \(CAP\) - EMEA/H/C/001249/MEA 025.3](#)

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Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Amendment to protocol version 4 previously agreed in September 2017 as part of MEA 025.2, to evaluate the effectiveness of risk minimisation measures: a survey among healthcare professionals (HCPs) and patient/caregivers to assess their knowledge and attitudes on prescribing and home administration conditions of Vpriv (velaglucerase alfa) relating to the risk of serious hypersensitivity/allergic reactions

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

### 7.3. **Results of PASS imposed in the marketing authorisation(s)**<sup>27</sup>

#### 7.3.1. [Domperidone \(NAP\) - EMEA/H/N/PSR/J/0015](#)

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Applicant: Janssen Pharmaceutical Companies of Johnson & Johnson

PRAC Rapporteur: Adrien Inoubli

Scope: MAH's response to PSR/S/0016 [results of a drug utilisation study (DUS) of domperidone in Europe using databases to investigate the effectiveness of risk minimisation measures and to describe the prescribing patterns before and after the changes to the domperidone label in routine clinical practice in selected European countries, as required in the conclusions of the referral procedure under Article 31 of Directive 2001/83/EC concluded in 2013] as per the request for supplementary information (RSI) adopted in March 2018

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

#### 7.3.2. [Magnesium sulphate heptahydrate, sodium sulphate anhydrous, potassium sulphate \(NAP\) - EMEA/H/N/PSR/S/0016](#)

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Applicant: Ipsen Pharma (Eziclen, Izinova)

PRAC Rapporteur: Adrien Inoubli

Scope: MAH's response to PSR/S/0016 [results for a multicentre, European, observational, drug utilisation study (DUS) of Eziclen/Izinova (BLI800) (magnesium sulfate heptahydrate/sodium sulfate anhydrous/potassium sulfate) as a bowel cleansing preparation to document the misuse of BLI800, defined as non-compliance in terms of sufficient liquid intake, during the post approval period in the real life setting; and to describe the safety profile of BLI800 in routine clinical practice, overall and in cases of misuse defined as non-compliance in terms of sufficient liquid intake, and identify any immediate/acute adverse events associated with the use of BLI800 in special populations (i.e. the elderly and patients at risk for electrolyte shifts)] as per the request for supplementary information (RSI) adopted in May 2018

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<sup>27</sup> In accordance with Article 107p-q of Directive 2001/83/EC

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

### 7.3.3. [Piperaquine tetraphosphate, arteminol – EURARTESIM \(CAP\) - EMEA/H/C/PSR/S/0018](#)

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Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Julie Williams

Scope: Results of a safety registry study in the EU assessing the association between the QTc prolongation induced by Eurartesim (piperaquine tetraphosphate/arteminol) and various factors, co-morbidities and concomitant medications, as well as at monitoring patterns of drug utilisation

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

## 7.4. [Results of PASS non-imposed in the marketing authorisation\(s\)<sup>28</sup>](#)

### 7.4.1. [Agomelatine - THYMANAX \(CAP\) - EMEA/H/C/000916/II/0038](#)

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Applicant: Servier (Ireland) Industries Ltd.

PRAC Rapporteur: Karen Pernille Harg

Scope: Submission of the final report for study CLE-20098-096 (listed as a category 3 study in the RMP): a non-interventional PASS, drug utilisation study (DUS) to assess the effectiveness of risk-minimisation measures of Thymanax/Valdoxan (agomelatine)

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

### 7.4.2. [Agomelatine - VALDOXAN \(CAP\) - EMEA/H/C/000915/II/0039](#)

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Applicant: Les Laboratoires Servier

PRAC Rapporteur: Karen Pernille Harg

Scope: Submission of the final report for study CLE-20098-096 (listed as a category 3 study in the RMP): a non-interventional PASS, drug utilisation study (DUS) to assess effectiveness of risk-minimisation measures of Thymanax/Valdoxan (agomelatine)

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

### 7.4.3. [Crizotinib - XALKORI \(CAP\) - EMEA/H/C/002489/II/0058](#)

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Applicant: Pfizer Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Submission of the final study report for study A8081038 (listed as a category 3 study in the RMP): a multinational active safety surveillance study of crizotinib in Europe and the United States to evaluate safety outcomes among lung cancer patients

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

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<sup>28</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

#### 7.4.4. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/WS1270/0216; LIFMIOR (CAP) - EMEA/H/C/004167/WS1270/0013

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Patrick Batty

Scope: Submission of the final report from study B1801396 (listed as a category 3 study in the RMP): a non-interventional, population-based, multi-country, observational cohort register study to evaluate the risk of adverse pregnancy outcomes in patients with rheumatoid arthritis and related inflammatory diseases, who were treated with etanercept compared to patients with the same diseases of interest who were treated with non-biologic systemic drugs, but without etanercept or other biologics during pregnancy, using merged data from Sweden, Denmark and Finland

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

#### 7.4.5. Everolimus - VOTUBIA (CAP) - EMEA/H/C/002311/II/0055, Orphan

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from non-interventional study CRAD001MIC03 (listed as a category 3 study in the RMP): an international disease registry collecting data on manifestations, interventions and outcomes in patients with tuberous sclerosis complex

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

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

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Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Patrick Batty

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

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

#### 7.4.7. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/II/0186

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Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of the final report from study GS-EU-174-1846 (listed as a category 3 study in the RMP, in fulfilment of MEA 273): a multicentre, non-interventional, retrospective, matched cohort study of patients mono-infected with chronic hepatitis B and with moderate or severe renal impairment treated with Viread (tenofovir disoproxil) or entecavir

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

#### 7.4.8. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/II/0188

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Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of the final report from study GS-EU-174-0224 (listed as a category 3 study in the RMP): a cross-sectional drug utilisation study (DUS) in children and adolescents with chronic hepatitis B (CHB) to assess whether physicians prescribing Viread (tenofovir disoproxil) to paediatric patients with CHB in the EU follow the relevant recommendations in the SmPC and educational brochures

**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. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.6

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Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to MEA 007.5 [third annual report for study OBS13434: a prospective, multicentre, observational PASS to evaluate the long term safety profile of Lemtrada (alemtuzumab) treatment in patients with relapsing forms of multiple sclerosis (MS) and to determine the incidence of adverse events of special interest (AESIs)] as per the request for supplementary information (RSI) adopted in May 2018

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

#### 7.5.2. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 024.9

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Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: MAH's response to MEA 024.8 [annual report for the Pompe registry: a global, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease. The registry aims at detecting adverse events and/or lack of efficacy in patients, and at collecting immunological data, and follow-up growth disturbances in children] as per the request for supplementary information (RSI) adopted in April 2018

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

#### 7.5.3. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 053.6

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Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: MAH's response to MEA 053.5 [second interim study report for PASS study ALGMYC07390 evaluating the prevalence of immunology testing in patients treated with alglucosidase alfa with significant hypersensitivity/anaphylactic reactions, including MAH's response to MEA 053.4 on first interim report as per the request for supplementary

information adopted in July 2017 [final clinical study report (CSR): due 31 August 2019] as per the request for supplementary information (RSI) adopted in March 2018

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

#### 7.5.4. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/MEA 006.3

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Applicant: Celgene Europe BV

PRAC Rapporteur: Eva Segovia

Scope: Interim results for the UK clinical practice research datalink (CPRD) database data analysis for psoriatic arthritis (PsA) and psoriasis [due date: CPRD data analysis at years 1, 3 and 5 starting from the date of first commercial availability in the UK. Final study report due for submission within 6 months after the 5 year-data analysis cut-off date]

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

#### 7.5.5. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/MEA 002.3

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Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Menno van der Elst

Scope: Three year interim report for study PTC124-GD-025o-DMD (listed as a category 3 study in the RMP): a post-approval registry observational study exploring the long-term of ataluren safety and effectiveness in usual care setting [final clinical study report (CSR) expected in: April 2023]

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

#### 7.5.6. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/MEA 007

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Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: Interim study result for study 109MS401 (ESTEEM study): a multicentre, global, observational study to collect information on safety and to document the drug utilisation of Tecfidera (dimethyl fumarate) when used in routine medical practice in the treatment of relapsing multiple sclerosis [final clinical study report (CSR) expected due date: Q4/2024]

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

#### 7.5.7. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/MEA 008

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Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: Annual progress report (version 2.0) for study 109MS402: Biogen multiple sclerosis pregnancy exposure registry [final clinical study report (CSR) expected due date: Q4 2021]

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

#### 7.5.8. Florbetaben (<sup>18</sup>F) - NEURACEQ (CAP) - EMEA/H/C/002553/MEA 005.2

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Applicant: Life Radiopharma Berlin GmbH

PRAC Rapporteur: Patrick Batty

Scope: Second interim results for study FBB-01\_02\_13: a prospective observational study to assess the effectiveness of the training and risk minimisation measures recommended for the usage of the diagnostic agent Neuraceq (florbetaben (<sup>18</sup>F)) in post-authorisation clinical settings [final clinical study report (CSR) expected due date: Q1/2019]

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

#### 7.5.9. [Infliximab - INFLECTRA \(CAP\) - EMEA/H/C/002778/MEA 007.3](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Patrick Batty

Scope: Annual interim safety and efficacy report for registry CT-P13 4.2: an observational, prospective cohort study to evaluate safety and efficacy of Inflectra (infliximab) in patients with rheumatoid arthritis (EU and Korea) [final report expected by May 2026] and MAH's response to MEA 007.2 as per the request for supplementary information (RSI) adopted in September 2017

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

#### 7.5.10. [Infliximab - INFLECTRA \(CAP\) - EMEA/H/C/002778/MEA 010.3](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Patrick Batty

Scope: Annual interim safety and efficacy report for registry CT-P13 4.3: an observational, prospective cohort study to evaluate the safety and efficacy of Inflectra (infliximab) in patients with Crohn's disease (CD), and ulcerative colitis (UC) (EU and Korea) [final report expected by May 2026] and MAH's response to MEA 010.2 as per the request for supplementary information (RSI) adopted in September 2017

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

#### 7.5.11. [Infliximab - REMSIMA \(CAP\) - EMEA/H/C/002576/MEA 007.3](#)

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Patrick Batty

Scope: Annual interim safety and efficacy report for registry CT-P13 4.2: an observational, prospective cohort study to evaluate safety and efficacy of Remsima (infliximab) in patients with rheumatoid arthritis (EU and Korea) [final report expected by May 2026] and MAH's response to MEA 007.2 as per the request for supplementary information (RSI) adopted in September 2017

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

#### 7.5.12. [Infliximab - REMSIMA \(CAP\) - EMEA/H/C/002576/MEA 010.3](#)

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Patrick Batty

Scope: Annual interim safety and efficacy report for registry CT-P13 4.3: an observational, prospective cohort study to evaluate the safety and efficacy of Inflectra (infliximab) in patients with Crohn's disease (CD), and ulcerative colitis (UC) (EU and Korea) [final report expected by May 2026] and MAH's response to MEA 010.2 as per the request for supplementary information (RSI) adopted in September 2017

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

#### 7.5.13. [Influenza vaccine \(live attenuated, nasal\) - FLUENZ TETRA \(CAP\) - EMEA/H/C/002617/MEA 004.9](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Annual interim report for the passive enhanced safety surveillance study (ESS) D2560C00008: a postmarketing non-interventional cohort study of the safety of live attenuated influenza vaccine (LAIV) in subjects 2 through 17 years of age for the 2017-2018 influenza season in England

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

#### 7.5.14. [Liraglutide - SAXENDA \(CAP\) - EMEA/H/C/003780/MEA 015.2](#)

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Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Interim results for study NN8022-4246: a drug utilisation study (DUS) in the UK using UK clinical practice research datalink (CPRD) database evaluating if liraglutide (Saxenda) is used according to approved indication and posology and if liraglutide (Victoza) is used for weight management

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

#### 7.5.15. [Meningococcal group B vaccine \(recombinant, component, adsorbed\) - BEXSERO \(CAP\) - EMEA/H/C/002333/MEA 017.6](#)

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Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 017.5 [first interim report for study V72\_36OB: a post-licensure observational safety study after Bexsero (meningococcal B vaccine 4CMenB) vaccination in routine UK care [final report due date: 31/12/2019]] as per the request for supplementary information (RSI) adopted in April 2018

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

#### 7.5.16. [Meningococcal group B vaccine \(recombinant, component, adsorbed\) - BEXSERO \(CAP\) - EMEA/H/C/002333/MEA 017.7](#)

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Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fifth progress report for study V72\_36OB: a post-licensure observational safety

study after Bexsero (meningococcal B vaccine 4CMenB) vaccination in routine UK care [final report due date expected in December 2019]

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

#### **7.5.17. Octocog alfa - KOVALTRY (CAP) - EMEA/H/C/003825/MEA 005**

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Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Interim results for epidemiological study 15689: an evaluation of adverse events of special interest (AESI) in the PEDIatric NETwork (PedNet) haemophilia registry (from MA/opinion)

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

#### **7.5.18. Ospemifene - SENSHIO (CAP) - EMEA/H/C/002780/ANX 001.5**

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Applicant: Shionogi Limited

PRAC Rapporteur: Julie Williams

Scope: Third annual interim report for a PASS (ENCEPP/SDPP/8585) (listed as a category 1 in the RMP): an observational retrospective cohort study of ospemifene utilising existing databases in Germany, Italy, Spain, and the United States to evaluate the incidence of venous thromboembolism and other adverse events in vulvar and vaginal atrophy (VVA) patients treated with ospemifene as compared to: 1) patients newly prescribed selective oestrogen receptor modulators (SERM) for oestrogen-deficiency conditions or breast cancer prevention and; 2) the incidence in untreated VVA patients [final report expected in February 2021]

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

#### **7.5.19. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/MEA 023.4**

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Applicant: Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim results for study 16167 (Wave 2): a risk minimisation study/survey evaluating the adherence to the prescriber's guide on deep vein thrombosis treatment (DVT-T) and stroke prevention in atrial fibrillation (SPAF) indication

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

#### **7.5.20. Roflumilast - DAXAS (CAP) - EMEA/H/C/001179/ANX 002.6**

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Applicant: AstraZeneca AB

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Second interim results for PASS D7120R00003 (previously RO-2455-403-RD): a long-term post-marketing observational study exploring the safety of roflumilast in the treatment of chronic obstructive pulmonary disease (COPD), combined data results from Sweden, Germany and the US (Annex II-D condition) [final clinical study report (CSR) expected in March 2021]



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

#### 7.5.21. Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/MEA 004.3

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 004.2 [annual progress report for study GENA-99: a prospective, multinational, non-interventional post-authorisation study to document the long-term immunogenicity, safety, and efficacy of simoctocog alfa in patients with haemophilia A treated in routine clinical practice [final report due date expected in 2020]] as per the request for supplementary information (RSI) adopted in April 2018

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

#### 7.5.22. Simoctocog alfa - VIHUMA (CAP) - EMEA/H/C/004459/MEA 004.2

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 004.1 [annual progress report for study GENA-99: a prospective, multinational, non-interventional post-authorisation study to document the long-term immunogenicity, safety, and efficacy of simoctocog alfa in patients with haemophilia A treated in routine clinical practice [final report due date expected in 2020]] as per the request for supplementary information (RSI) adopted in April 2018

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

#### 7.5.23. Trastuzumab emtansine - KADCYLA (CAP) - EMEA/H/C/002389/MEA 011.4

Applicant: Roche Registration GmbH

PRAC Rapporteur: Doris Stenver

Scope: Fifth 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 (trastuzumab), pertuzumab in combination with Herceptin, or pertuzumab during pregnancy or within 7 months prior to conception [final report expected in May 2024]

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

#### 7.5.24. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 022.14

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Patrick Batty

Scope: MAH's response to MEA 022.13 [annual report for study C0168Z03 (PSOLAR: PSOriasis Longitudinal Assessment and Registry): an international prospective cohort study/registry programme designed to collect data on psoriasis (PSO) patients that are eligible to receive systemic therapies, including generalised phototherapy and biologics] as per the request for supplementary information (RSI) adopted in April 2018

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

#### 7.5.25. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 023.10

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Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Patrick Batty

Scope: Eighth annual interim report for study CNTO1275PSO4005 (Nordic database initiative): a prospective cohort registry, five-year observational study of adverse events (AEs) observed in patients exposed to ustekinumab

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

### 7.6. Others

#### 7.6.1. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 009.1

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Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Martin Huber

Scope: Updated feasibility assessment within 2 years (e.g. by Q2/2018) to evaluate the drug utilisation patterns of canagliflozin-containing medicines including off-label usage in type 1 diabetes mellitus (T1DM) and the risk of diabetic ketoacidosis (DKA) using 3 EU databases (United Kingdom, Spain and Italy) on market uptake and exposure within the UK, Spain and Italy

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

#### 7.6.2. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 008.1

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Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Updated feasibility assessment within 2 years (e.g. by Q2/2018) to evaluate the drug utilisation patterns of canagliflozin-containing medicines including off-label usage in type 1 diabetes mellitus (T1DM) and the risk of diabetic ketoacidosis (DKA) using 3 EU databases (United Kingdom, Spain and Italy) on market uptake and exposure within the UK, Spain and Italy

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

#### 7.6.3. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/MEA 024.1

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Applicant: AstraZeneca AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 024 [signal of incorrect use of device associated with (serious) adverse reactions including hyperglycaemia and hypoglycaemia (EPITT 18688) to review the instructions for use (IFU) for Bydureon (exenatide) and propose improvements of the IFU as applicable] as per the request for supplementary information (RSI) adopted in March 2018

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

## 7.7. New Scientific Advice

None

## 7.8. Ongoing Scientific Advice

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

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

None

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

## 8.1. Annual reassessments of the marketing authorisation

None

## 8.2. Conditional renewals of the marketing authorisation

None

## 8.3. Renewals of the marketing authorisation

### 8.3.1. Agomelatine - THYMANAX (CAP) - EMEA/H/C/000916/R/0040 (with RMP)

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Applicant: Servier (Ireland) Industries Ltd.

PRAC Rapporteur: Karen Pernille Harg

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.2. Agomelatine - VALDOXAN (CAP) - EMEA/H/C/000915/R/0042 (with RMP)

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Applicant: Les Laboratoires Servier

PRAC Rapporteur: Karen Pernille Harg

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.3. Brimonidine - MIRVASO (CAP) - EMEA/H/C/002642/R/0021 (without RMP)

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Applicant: Galderma International

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

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

#### 8.3.4. Elosulfase alfa - VIMIZIM (CAP) - EMEA/H/C/002779/R/0024 (without RMP)

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Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Patrick Batty

Scope: 5-year renewal of the marketing authorisation

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

#### 8.3.5. Florbetaben (<sup>18</sup>F) - NEURACEQ (CAP) - EMEA/H/C/002553/R/0025 (with RMP)

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Applicant: Life Radiopharma Berlin GmbH

PRAC Rapporteur: Patrick Batty

Scope: 5-year renewal of the marketing authorisation

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

#### 8.3.6. Follitropin alfa - BEMFOLA (CAP) - EMEA/H/C/002615/R/0019 (without RMP)

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Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

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

#### 8.3.7. Influenza vaccine (live attenuated, nasal) - FLUENZ TETRA (CAP) - EMEA/H/C/002617/R/0079 (with RMP)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: 5-year renewal of the marketing authorisation

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

#### 8.3.8. Japanese encephalitis vaccine (inactivated, adsorbed) - IXIARO (CAP) - EMEA/H/C/000963/R/0091 (without RMP)

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Applicant: Valneva Austria GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

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

#### 8.3.9. Levetiracetam - LEVETIRACETAM HOSPIRA (CAP) - EMEA/H/C/002783/R/0018 (with RMP)

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Applicant: Hospira UK Limited

PRAC Rapporteur: Laurence de Fays

Scope: 5-year renewal of the marketing authorisation

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

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8.3.10. [Lurasidone - LATUDA \(CAP\) - EMEA/H/C/002713/R/0020 \(with RMP\)](#)

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Applicant: Aziende Chimiche Riunite Angelini Francesco S.p.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

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

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8.3.11. [Obeticholic acid - OCALIVA \(CAP\) - EMEA/H/C/004093/R/0009 \(without RMP\)](#)

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Applicant: Intercept Pharma Ltd

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

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

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8.3.12. [Pneumococcal polysaccharide conjugate vaccine \(adsorbed\) - SYNFLORIX \(CAP\) - EMEA/H/C/000973/R/0128 \(without RMP\)](#)

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Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

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

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8.3.13. [Riociguat - ADEMPAS \(CAP\) - EMEA/H/C/002737/R/0026 \(without RMP\)](#)

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Applicant: Bayer AG

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

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

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8.3.14. [Travoprost - IZBA \(CAP\) - EMEA/H/C/002738/R/0011 \(without RMP\)](#)

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: 5-year renewal of the marketing authorisation

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

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8.3.15. [Vedolizumab - ENTYVIO \(CAP\) - EMEA/H/C/002782/R/0032 \(without RMP\)](#)

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Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

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

#### 8.3.16. Vortioxetine - BRINTELLIX (CAP) - EMEA/H/C/002717/R/0019 (with RMP)

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Applicant: H. Lundbeck A/S

PRAC Rapporteur: Laurence de Fays

Scope: 5-year renewal of the marketing authorisation

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

#### 8.3.17. Zoledronic acid - ZOLEDRONIC ACID ACCORD (CAP) - EMEA/H/C/002667/R/0006 (without RMP)

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Applicant: Accord Healthcare Limited

PRAC Rapporteur: Doris Stenver

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. Ustekinumab – STELARA (CAP) - EMEA/H/C/000958/II/0066

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Applicant: Janssen-Cilag International

PRAC Rapporteur: Patrick Batty

Scope: Consultation on a type II variation to update section 4.8 of the SmPC to add 'allergic alveolitis' and 'eosinophilic pneumonia' as adverse drug reactions with a frequency 'rare'. The package leaflet is updated accordingly

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

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

None

## 10.3. Other requests

None

## 10.4. Scientific Advice

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

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

## 11.1. Safety related variations of the marketing authorisation

### 11.1.1. Celecoxib (NAP) - SE/H/xxxx/WS/186, SE/H/xxxx/WS/204, SE/H/xxxx/WS/210

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Applicant(s): Pfizer AB (Celebra, Celecoxib Pfizer, Solexa)

PRAC Lead: Ulla Wändel Liminga

Scope: PRAC consultation on variation procedures assessing the final results of a post-approval study: 'a prospective randomized evaluation of celecoxib integrated safety vs. ibuprofen or naproxen (PRECISION)' and proposed changes in the product information, on request of Sweden

**Action:** For adoption of advice to Member States

### 11.1.2. Dienogest, estradiol valerate (NAP) - NL/H/1230/001/II/034

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Applicant(s): Bayer BV (Qlaira)

PRAC Lead: Menno van der Elst

Scope: PRAC follow-up consultation on a national variation procedure to assess the final results of an imposed cohort study INAS-SCORE: 'an international active surveillance study, safety of contraceptives: role of estrogens' conducted in the US and Europe and the proposed amendments to the product information on the risk of venous thromboembolism (VTE), on request of the Netherlands

**Action:** For adoption of advice to Member States

### 11.1.3. General anaesthetics and sedatives: Desflurane (NAP); enflurane (NAP); etomidate (NAP); esketamine (NAP); halothane (NAP); isoflurane (NAP); ketamine (NAP); midazolam (NAP); propofol (NAP); sevoflurane (NAP); thiopental (NAP)

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Applicants: various

PRAC Lead: Ghania Chamouni

Scope: PRAC follow-up consultation on the scientific relevance to update the product information for general anaesthetics and sedative medicines regarding the risk of developmental disorders when used in children and pregnant women, in light of available safety data from preclinical and clinical studies, FDA action taken in April 2017, national variations submitted for isoflurane-, sevoflurane- and propofol-containing medicines, and PRAC advice adopted in January 2018 including the Safety Working Party (SWP) responses, on request of France

**Action:** For adoption of advice to Member States

## 11.2. Other requests

### 11.2.1. Thiocolchicoside (NAP) - EMEA/H/N/PSA/J/0010

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Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: PRAC follow-up consultation on the evaluation of a progress report for a non-interventional imposed PASS: a drug utilisation study assessing the effectiveness of risk minimisation measures (routine and additional) and further characterising the prescribing patterns for thiocolchicoside-containing medicinal products for systemic use, following the conclusions of a referral procedure under Article 31 of Directive 2001/83/EC finalised in 2014, on request of Italy

**Action:** For adoption of advice to Member States

## 12. Organisational, regulatory and methodological matters

### 12.1. Mandate and organisation of the PRAC

#### 12.1.1. PRAC Vice-Chairperson - election

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**Action:** For adoption

### 12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

#### 12.3.1. Scientific Advice Working Party (SAWP) – call for expression of interest for a joint SAWP-PRAC alternate

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**Action:** For adoption

### 12.4. Cooperation within the EU regulatory network

None



## 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, Maia Uusküla

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

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PRAC lead: To be announced

**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 plan (RMP) – Results of the monitoring exercise of the quality of submissions under RMP revision 2

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**Action:** For discussion

### 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. Communication on safety referrals at the time of CMDh position and European Commission (EC) decision – Proposal for review process amendment

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**Action:** For discussion

### 12.18.2. PRAC communication – call for expression of interest to review communication strategy and materials

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**Action:** For adoption

### 12.18.3. Public participation in pharmacovigilance

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None

### 12.18.4. Safety communication

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None

## 12.19. Continuous pharmacovigilance

### 12.19.1. Incident management

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None

## 12.20. Others

### 12.20.1. Brexit preparedness - EMA measures and business continuity plan

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**Action:** For discussion

### 12.20.2. EMA funded post-authorisation efficacy and safety research - Generating evidence to support regulatory decision-making

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**Action:** For adoption

### 12.20.3. Good Pharmacovigilance Practices (GVP) – revisions during 2018 - 2019 revision cycle

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**Action:** For discussion

#### 12.20.4. Telematics - Concept paper on strategy 2020-2025

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**Action:** For discussion

### 13. Any other business

Next meeting on: 01-04 October 2018

## 14. Explanatory notes

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

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

(Items 2 and 3 of the PRAC agenda)

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

[http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general\\_content\\_000150.jsp&mid=WCOB01ac05800240d0](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000150.jsp&mid=WCOB01ac05800240d0)

### **Signals assessment and prioritisation**

(Item 4 of the PRAC agenda)

A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine and that warrants further investigation. Signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. The evaluation of safety signals is a routine part of pharmacovigilance and is essential to ensuring that regulatory authorities have a comprehensive knowledge of a medicine's benefits and risks.

The presence of a safety signal does not mean that a medicine has caused the reported adverse event. The adverse event could be a symptom of another illness or caused by another medicine taken by the patient. The evaluation of safety signals is required to establish whether or not there is a causal relationship between the medicine and the reported adverse event.

The evaluation of safety signals may not necessarily conclude that the medicine caused the adverse event in question. In cases where a causal relationship is confirmed or considered likely, regulatory action may be necessary and this usually takes the form of an update of the summary of product characteristics and the package leaflet.

### **Risk Management Plans (RMPs)**

(Item 5 of the PRAC agenda)

The RMP describes what is known and not known about the side effects of a medicine and states how these risks will be prevented or minimised in patients. It also includes plans for studies and other activities to gain more knowledge about the safety of the medicine and risk factors for developing side effects.

RMPs are continually modified and updated throughout the lifetime of the medicine as new information becomes available.

### **Assessment of Periodic Safety Update Reports (PSURs)**

(Item 6 of the PRAC agenda)

A PSUR is a report providing an evaluation of the benefit-risk balance of a medicine, which is submitted by marketing authorisation holders at defined time points following a medicine's authorisation.

PSURs summarises data on the benefits and risks of a medicine and includes the results of all studies carried out with this medicine (in the authorised and unauthorised indications).

### **Post-authorisation Safety Studies (PASS)**

(Item 7 of the PRAC agenda)

A PASS is a study of an authorised medicinal product carried out to obtain further information on its safety, or to measure the effectiveness of risk management measures. The results of a PASS help regulatory agencies to evaluate the safety and benefit-risk profile of a medicine.

### **Product related pharmacovigilance inspections**

(Item 9 of the PRAC agenda)

Inspections carried out by regulatory agencies to ensure that marketing authorisation holders comply with their pharmacovigilance obligations.

More detailed information on the above terms can be found on the EMA website: [www.ema.europa.eu/](http://www.ema.europa.eu/)