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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 10-13 February 2020

Chair: Sabine Straus – Vice-Chair: Martin Huber

10 February 2020, 13:00 – 19:30, room 1/C

11 February 2020, 08:30 – 19:30, room 1/C

12 February 2020, 08:30 – 19:30, room 1/C

13 February 2020, 08:30 – 16:00, room 1/C

Organisational, regulatory and methodological matters (ORGAM)

27 February 2020, 09:00 – 12:00, room 1/F, 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](#)).



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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 on 10 – 13 February 2020. See February 2020 PRAC minutes (to be published post March 2020 PRAC meeting).

### **1.2. Agenda of the meeting on 10-13 February 2020**

**Action:** For adoption

### **1.3. Minutes of the previous meeting on 13-16 January 2020**

**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

#### 3.3.1. Cyproterone acetate (NAP) - EMEA/H/A-31/1488

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Applicant(s): various

PRAC Rapporteur: Menno van der Elst; PRAC Co-rapporteur: Adam Przybylkowski

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

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

### 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. Adalimumab - AMGEVITA (CAP); HALIMATOZ (CAP); HEFIYA (CAP); HULIO (CAP); HUMIRA (CAP); HYRIMOZ (CAP); IDACIO (CAP); IMRALDI (CAP)

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Applicant(s): AbbVie Deutschland GmbH & Co. KG (Humira), Amgen Europe B.V. (Amgevita), Fresenius Kabi Deutschland GmbH (Idacio), Mylan S.A.S (Hulio), Samsung Bioepis NL B.V. (Imraldi), Sandoz GmbH (Halimatoz, Hefiya, Hyrimoz)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of abnormal weight gain

**Action:** For adoption of PRAC recommendation

EPITT 19520 – New signal

Lead Member State(s): SE

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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

#### 4.1.2. Macrogol 3350<sup>3 4</sup> (NAP); macrogol 4000<sup>5 6</sup> (NAP)

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Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of colitis ischaemic

**Action:** For adoption of PRAC recommendation

EPITT 19517 – New signal

Lead Member State(s): MS: IT, FR, NL

#### 4.1.3. Lisdexamfetamine (NAP)

---

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of QT prolongation and cardiac arrhythmia

**Action:** For adoption of PRAC recommendation

EPITT 19533 – New signal

Lead Member State(s): SE

#### 4.1.4. Teriparatide - FORSTEO (CAP), MOVYMIA (CAP); TERROSA (CAP); NAP

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

PRAC Rapporteur: To be appointed

Scope: Signal of myeloma

**Action:** For adoption of PRAC recommendation

EPITT 19511 – New signal

Lead Member State(s): FR

#### 4.1.5. Tramadol (NAP); tramadol, dexketoprofen (NAP); tramadol, paracetamol (NAP)

---

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of hiccups

**Action:** For adoption of PRAC recommendation

EPITT 19529 – New signal

Lead Member State(s): ES, FR

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<sup>3</sup> With or without electrolytes

<sup>4</sup> and combination(s)

<sup>5</sup> With or without electrolytes

<sup>6</sup> and combination(s)

#### 4.1.6. Sevoflurane (NAP)

---

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of diabetes insipidus

**Action:** For adoption of PRAC recommendation

EPITT 19531 – New signal

Lead Member State(s): IE

### 4.2. New signals detected from other sources

#### 4.2.1. Azithromycin (NAP)

---

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of increased cancer risk among patients with bronchiolitis obliterans after hematopoietic cell transplantation

**Action:** For adoption of PRAC recommendation

EPITT 19528 – New signal

Lead Member State(s): FI

#### 4.2.2. Lorlatinib – LORVIQUA (CAP)

---

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Signal of nephrotic syndrome

**Action:** For adoption of PRAC recommendation

EPITT 19518 – New signal

Lead Member State(s): HR

### 4.3. Signals follow-up and prioritisation

#### 4.3.1. Bevacizumab – AVASTIN (CAP) - EMEA/H/C/000582/SDA/088; MVASI (CAP) - EMEA/H/C/004728/SDA/003; ZIRABEV (CAP) - EMEA/H/C/004697/SDA/003

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

PRAC Rapporteur: Hans Christian Siersted

Scope: Signal of Guillain–Barré syndrome (GBS)

**Action:** For adoption of PRAC recommendation

EPITT 19472 – Follow up to October 2019

#### 4.3.2. Ifosfamide (NAP)

---

Applicant(s): various

PRAC Rapporteur: Annika Folin

Scope: Signal of increased risk of encephalopathy

**Action:** For adoption of PRAC recommendation

EPITT 19433 – Follow up to December 2019

#### 4.3.3. Nivolumab – OPDIVO (CAP) - EMEA/H/C/003985/SDA/040

---

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of haemophagocytic lymphohistiocytosis

**Action:** For adoption of PRAC recommendation

EPITT 19467 – Follow up to October 2019

#### 4.3.4. Vismodegib – ERIVEDGE (CAP) - EMEA/H/C/002602/SDA/019

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Signal of pancreatitis

**Action:** For adoption of PRAC recommendation

EPITT 19470 – Follow up to October 2019

## 5. Risk management plans (RMPs)

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

#### 5.1.1. Bupivacaine, meloxicam - EMEA/H/C/005205

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Scope: Reduction of postoperative pain

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

#### 5.1.2. Cabazitaxel - EMEA/H/C/005178

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Scope: Treatment of adult patients with metastatic castration resistant prostate cancer previously treated with a docetaxel-containing regimen

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



### 5.1.3. Ebola vaccine (rDNA<sup>7</sup>, replication-incompetent) - EMEA/H/C/005343

---

Scope (accelerated assessment): Active immunisation for the prevention of disease caused by Ebola virus

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

### 5.1.4. Ebola vaccine (rDNA<sup>8</sup>, replication-incompetent) - EMEA/H/C/005337

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Scope (accelerated assessment): Active immunisation for the prevention of disease caused by Ebola virus (Zaire ebolavirus species)

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

### 5.1.5. Fingolimod - EMEA/H/C/005191

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Scope: Treatment of multiple sclerosis

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

### 5.1.6. Fingolimod - EMEA/H/C/005282

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Scope: Treatment of multiple sclerosis

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

### 5.1.7. Glasdegib - EMEA/H/C/004878, Orphan

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Applicant: Pfizer Europe MA EEIG

Scope: Treatment of newly diagnosed de novo or secondary acute myeloid leukaemia

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

### 5.1.8. Imlifidase - EMEA/H/C/004849, Orphan

---

Applicant: Hansa Biopharma AB

Scope: Desensitisation treatment of highly sensitised adult kidney transplant patients with positive crossmatch against an available deceased donor

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

### 5.1.9. Insulin aspart - EMEA/H/C/005033

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Scope: Treatment of diabetes mellitus

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

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<sup>7</sup> Ribosomal deoxyribonucleic acid

<sup>8</sup> Ribosomal deoxyribonucleic acid

#### 5.1.10. Ivosidenib - EMEA/H/C/005056, Orphan

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Applicant: Agios Netherlands B.V.

Scope: Treatment of adult patients ( $\geq 18$  years old) with relapsed or refractory acute myeloid leukaemia (AML) with an isocitrate dehydrogenase-1 (IDH1) R132 mutation

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

#### 5.1.11. Luspatercept - EMEA/H/C/004444, Orphan

---

Applicant: Celgene Europe BV

Scope: Treatment of adult patients with very low- to intermediate-risk myelodysplastic syndromes (MDS)-associated anaemia and treatment of adult patients with beta-thalassaemia ( $\beta$ -thalassaemia)-associated anaemia who require red blood cell (RBC) transfusions

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

#### 5.1.12. Sodium oxybate – HOPVEUS (CAP MAA) - EMEA/H/C/004962

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Applicant: D&A Pharma

Scope (re-examination): Medium to long-term maintenance of alcohol abstinence and treatment of mild to moderate alcohol withdrawal syndrome

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

#### 5.1.13. Teriparatide - EMEA/H/C/005087

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Scope: Treatment of osteoporosis

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

#### 5.1.14. Teriparatide - EMEA/H/C/005388

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Scope: Treatment of osteoporosis

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

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

#### 5.2.1. 5-aminolevulinic acid - AMELUZ (CAP) - EMEA/H/C/002204/II/0040

---

Applicant: Biofrontera Bioscience GmbH

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 11.1) brought in line with revision 2 of GVP module V on 'Risk management systems', including also the implementation of changes as requested by PRAC in the conclusions of the periodic safety update report single assessment (PSUSA) procedure PSUSA/00010006/201806 adopted in February 2019

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

#### 5.2.2. [Alogliptin, pioglitazone - INCRESYNC \(CAP\) - EMEA/H/C/002178/II/0029](#)

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Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 10.0) in order to remove additional risk minimisation measures (aRMMs) as requested in the outcome of periodic safety update report single assessment (PSUSA) procedure PSUSA/00002417/201807 for pioglitazone, glimepiride/pioglitazone and metformin/pioglitazone adopted in March 2019 and consequently the removal of the drug utilisation study (DUS) on the utilisation of pioglitazone-alogliptin containing medicinal product(s) in clinical practice with regard to diabetic treatment regimen and comorbidities as well as the removal of relevant commitments as per the conclusions of LEG 008 adopted in September 2015. In addition, the RMP is brought in line with revision 2 of the guidance on the format of RMP in the EU (template) reflecting changes in the categorisation of safety concerns. Furthermore, the targeted adverse event (AE) follow-up questionnaires related to AEs of severe hypersensitivity skin reactions, hepatic events, pancreatitis, bladder cancer, malignancies (including pancreatic cancer), bone fractures, and macular oedema are removed. Finally, the RMP is updated to reflect the removal of the additional monitoring inverted black triangle as per the conclusion of the renewal procedure R/0023 finalised in March 2018. Annex II is updated accordingly. The MAH took the opportunity to update the product information to amend the details of the local representative for Poland

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

#### 5.2.3. [Bedaquiline - SIRTURO \(CAP\) - EMEA/H/C/002614/II/0038, Orphan](#)

---

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 4.3) to revise the summary of safety concerns as requested by PRAC/CHMP in the conclusions of the renewal procedure of the conditional marketing authorisation R/0035 adopted in November 2019. As requested by the PRAC/CHMP, data on co-administration of bedaquiline and human immunodeficiency virus (HIV)-protease inhibitors are also summarised

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

#### 5.2.4. [Bortezomib - VELCADE \(CAP\) - EMEA/H/C/000539/II/0093](#)

---

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of an updated RMP (version 30.1) in order to revise the list of safety concerns as requested in the conclusions of periodic single assessment procedure (PSUSA) PSUSA/00000424/201804 adopted in December 2018. As a consequence, Annex II is updated to reflect the removal of the additional risk minimisation activities. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet.

Furthermore, the product information is being brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

#### 5.2.5. [Daptomycin - CUBICIN \(CAP\) - EMEA/H/C/000637/II/0074](#)

---

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Pernille Harg

Scope: Submission of an updated RMP (version 11.1) in order to delete all risks and additional risk minimisation measures in line with revision 2 of GVP module V on 'Risk management systems'. Annex II is updated accordingly. In addition, the MAH took the opportunity to align the product information with the quality review of documents (QRD) template (version 10.1) and update the list of local representatives

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

#### 5.2.6. [Epoetin zeta - RETACRIT \(CAP\) - EMEA/H/C/000872/II/0094](#)

---

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 11.1) in order to align the safety concerns of Retacrit (epoetin zeta – biosimilar) to the medicinal product of reference containing epoetin alfa (Eprex). The RMP (version 15.0) is updated accordingly

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

#### 5.2.7. [Etanercept - ENBREL \(CAP\) - EMEA/H/C/000262/WS1747/0231; LIFMIOR \(CAP\) - EMEA/H/C/004167/WS1747/0025](#)

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Eva Segovia

Scope: Submission of an updated RMP (version 7.0) to revise the list of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' and revision 2.0.1 of the guidance on the format of RMP in the EU (template). In addition, the MAH took the opportunity to implement the outcomes of variation WS/1270 adopted in January 2019 and periodic single assessment procedure (PSUSA) PSUSA/001295/201902 adopted in September 2019 as requested by PRAC/CHMP in order to remove or consolidate several risks. Finally, the MAH removed the addendum to RMP (version 6.3), introduced some clinical and post-marketing data updates and reflected the completion of post-authorisation studies

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

#### 5.2.8. [Interferon beta-1a - REBIF \(CAP\) - EMEA/H/C/000136/II/0144](#)

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Applicant: Merck Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 11) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' and to ensure the appropriate time needed for the effective review and analysis of all RMP sections

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

#### 5.2.9. Tegafur, gimeracil, oteracil - TEYSUNO (CAP) - EMEA/H/C/001242/II/0042

Applicant: Nordic Group B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 9.0) in order to revise the list of safety concerns in line with revision 2 of GVP module V on 'Risk management systems' as requested in the conclusions of the periodic safety update report single assessment (PSUSA) procedure PSUSA/00002875/201801 adopted in September 2018

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

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

#### 5.3.1. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/II/0029

Applicant: Celgene Europe BV

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include treatment of adult patients with oral ulcers associated with Behçet's disease (BD) who are candidates for systemic therapy. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 12.0) are updated accordingly

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

#### 5.3.2. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/II/0013

Applicant: Merck Europe B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Update of section 5.1 of the SmPC in order to update efficacy information following results from study EMR100070-003 Part B (listed as a specific obligation in Annex II): a phase 2, open-label, multicentre trial to investigate the clinical activity and safety of avelumab (MSB0010718C) in subjects with Merkel cell carcinoma. The MAH took the opportunity to update Annex II proposing the deletion of the specific obligation and proposing the switch from conditional to full marketing authorisation. The package leaflet and the RMP (version 2.1) are updated accordingly

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

#### 5.3.3. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/II/0076

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information based on the final results from study BEL115467 (listed as an imposed PASS in Annex II): a Randomized, double-blind, placebo-controlled 52-week study to assess adverse events of special interest in adults with active, autoantibody-positive systemic lupus erythematosus receiving belimumab. The package leaflet is updated accordingly. The RMP (version 36) is updated in accordance and includes minor updates. In addition, the MAH took the opportunity to introduce minor editorial changes to Annex II and the labelling

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

#### 5.3.4. [Bictegravir, emtricitabine, tenofovir alafenamide - BIKTARVY \(CAP\) - EMEA/H/C/004449/II/0027](#)

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Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.8 and 5.1 of the SmPC to reflect pooled efficacy and safety data from the final clinical study reports of two antiretroviral therapy-naïve adult studies (listed as category 3 studies in the RMP) through 144 weeks of treatment, namely study GS-US-380-1489: a phase 3, randomized, double-blind study to evaluate the safety and efficacy of GS-9883 (bictegravir)/emtricitabine/tenofovir alafenamide versus abacavir [ABC]/dolutegravir [DTG]/lamivudine [3TC] in human immunodeficiency virus-1 (HIV-1) infected, antiretroviral treatment-naïve adults) and study GS-US-380-1490: a phase 3, randomized, double-blinded study to evaluate the safety and efficacy of GS-9883/emtricitabine/tenofovir alafenamide versus dolutegravir + emtricitabine/tenofovir alafenamide in HIV-1 infected, antiretroviral treatment-naïve adults (in fulfilment of MEA 001 and MEA 002). The RMP (version 2.1) is updated accordingly. In addition, the MAH took the opportunity to make some minor editorial changes to the product information and update Annex II with regards to PSUR requirements

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

#### 5.3.5. [Brigatinib, brigatinib - ALUNBRIG \(CAP\) - EMEA/H/C/004248/II/0003](#)

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Applicant: Takeda Pharma A/S

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously untreated with an ALK inhibitor for Alunbrig (brigatinib). The addition of a new indication is supported by data from study AP26113-13-301 (ALTA 1L): a phase 3, randomized, open label, comparative, multicentre, international phase 3 study of brigatinib versus crizotinib in patients With ALK-positive advanced lung cancer. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The package leaflet, labelling and the RMP (version (version 5.1) are updated accordingly. The MAH took the opportunity to introduce minor editorial corrections in the product information

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

### 5.3.6. [Buprenorphine, naloxone - SUBOXONE \(CAP\) - EMEA/H/C/000697/X/0042](#)

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Applicant: Indivior Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Extension application to introduce a new pharmaceutical form (sublingual film) associated with four new strengths (2/0.5 mg, 4/1 mg, 8/2 mg and 16/4 mg) and a new route of administration (either sublingual or buccal administration). The RMP (version 14.0) is updated accordingly

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

### 5.3.7. [Canagliflozin - INVOKANA \(CAP\) - EMEA/H/C/002649/II/0046](#)

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Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to add the treatment of stage 2 or 3 chronic kidney disease (CKD) and albuminuria, as an adjunct to standard of care, in adults with type 2 diabetes mellitus (T2DM), based on new clinical efficacy and safety data from study DNE3001 (CREDENCE): a randomised, double-blind, event-driven, placebo-controlled, multicentre phase 3 study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with T2DM and diabetic nephropathy. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 8.1) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

### 5.3.8. [Canagliflozin, metformin - VOKANAMET \(CAP\) - EMEA/H/C/002656/II/0051](#)

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Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to add the treatment of stage 2 or 3 chronic kidney disease (CKD) and albuminuria, as an adjunct to standard of care, in adults with type 2 diabetes mellitus (T2DM), based on new clinical efficacy and safety data from study DNE3001 (CREDENCE): a randomised, double-blind, event-driven, placebo-controlled, multicentre phase 3 study of the effects of canagliflozin on renal and cardiovascular outcomes in subjects with T2DM and diabetic nephropathy. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 8.1) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

### 5.3.9. [Carmustine - CARMUSTINE OBVIUS \(CAP\) - EMEA/H/C/004326/II/0002](#)

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Applicant: Obvius Investment B.V

PRAC Rapporteur: Jan Neuhauser



Scope: Extension of indication to add carmustine with or without total body irradiation (TBI), as conditioning treatment prior to allogeneic or autologous haematopoietic progenitor cell transplantation (HPCT) in haematological diseases. As a consequence, sections 4.1, 4.2 and 6.3 of the SmPC are updated. 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

#### 5.3.10. [Dabigatran etexilate - PRADAXA \(CAP\) - EMEA/H/C/000829/X/0122/G](#)

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Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Grouped applications consisting of: 1) extension application to add two new pharmaceutical forms coated granules (20 mg, 30 mg, 40 mg, 50 mg, 110 mg, 150 mg) and powder and solvent for oral solution (6.25 mg/mL); 2) extension of indication to include treatment of venous thromboembolic events (VTE) and prevention of recurrent VTE in paediatric patients from birth to less than 18 years of age for Pradaxa (dabigatran etexilate) 75 mg, 110 mg, 150 mg capsules based on paediatric trials, namely study 1160.106: an open-label, randomized, parallel-group, active-controlled, multi-centre non-inferiority study of dabigatran etexilate versus standard of care for venous thromboembolism treatment in children from birth to less than 18 years of age, and study 1160.108: an open label, single arm safety prospective cohort study of dabigatran etexilate for secondary prevention of venous thromboembolism in children from 0 to less than 18 years. As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and labelling are updated in accordance. The RMP (version 37.0) is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

#### 5.3.11. [Dapagliflozin - EDISTRIDE \(CAP\) - EMEA/H/C/004161/WS1737/0034; FORXIGA \(CAP\) - EMEA/H/C/002322/WS1737/0053](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to add a new indication for the treatment of symptomatic heart failure with reduced ejection fraction in adults. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and labelling are updated in accordance. The RMP (version 18) is updated accordingly. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1). Finally, the MAH took the opportunity to introduce an editorial change in the product information

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

#### 5.3.12. [Delamanid - DELTYBA \(CAP\) - EMEA/H/C/002552/II/0040, Orphan](#)

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Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: Extension of indication to include adolescents and children above 6 years with a body weight of at least 30 kg. As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 3.2) are updated accordingly. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

### 5.3.13. Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/II/0014/G

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Grouped variations consisting of: 1) extension of indication to include the use of Imfinzi (durvalumab) in combination with etoposide and either carboplatin or cisplatin for the first-line treatment of adults with extensive-stage small cell lung cancer (ES-SCLC). The proposed indication is supported by study D419QC00001 (CASPIAN): an ongoing phase 3 randomised, multicentre, open-label, comparative study designed to determine the efficacy and safety of durvalumab, or durvalumab and tremelimumab, in combination with etoposide and platinum-based chemotherapy (EP) for the first-line treatment of patients with ES-SCLC; 2) update of sections 4.4 and 4.8 of the SmPC to update the safety information based on the durvalumab pan-tumour pool: a safety dataset comprising of 9 clinical studies building on the existing safety database and summarising the safety information for durvalumab monotherapy characterised across tumour types in the durvalumab clinical programme to date, The package leaflet and the RMP (version 2) are updated in accordance

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

### 5.3.14. Emtricitabine, tenofovir alafenamide - DESCOVY (CAP) - EMEA/H/C/004094/II/0044

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report from study GS-US-311-1717 (listed as a category 3 in the RMP): a phase 3b, randomized, double-blind, switch study to evaluate emtricitabine/tenofovir alafenamide (F/TAF) in human immunodeficiency virus type 1 (HIV-1) infected subjects who are virologically suppressed on regimens containing abacavir/lamivudine (ABC/3TC). The RMP (version 4.1) is updated accordingly

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

### 5.3.15. Entecavir - BARACLUDGE (CAP) - EMEA/H/C/000623/II/0064

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to reflect the completion of the two paediatric studies, namely: study AI463028: evaluation of the pharmacokinetics, safety, tolerability and efficacy of entecavir (ETV) in paediatric subjects with chronic

hepatitis B virus (HBV) infection who are hepatitis B e-antigen (HBeAg)-positive; and study AI463189: a comparative study of the antiviral efficacy and safety of ETV versus placebo in paediatric subjects with chronic HBV infection who are HBeAg-positive. In addition, section 5.3 of the SmPC is updated to reflect the outcome of study AI463080 (REALM Study): a randomized, observational study of entecavir to assess long-term outcomes associated with nucleoside/nucleotide monotherapy for patients with chronic HBV infection. Section 5.2 of the SmPC is also updated to remove information on the pharmacokinetics of entecavir in lamivudine-experienced paediatric patients, at the request of the CHMP. The RMP (version 15) is updated accordingly and in line with revision 2.0 of the guidance on the format of RMP in the EU (template). In addition, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1) and to introduce minor editorial changes to the product information

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

#### 5.3.16. Insulin degludec, liraglutide - XULTOPHY (CAP) - EMEA/H/C/002647/II/0034

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 4.2 of the SmPC in order to change the wording 'transfer from basal insulin' to 'transfer from any insulin regimen', based on data from study NN9068-4184 (DUAL II Japan): a double-blinded trial comparing the efficacy and safety of insulin degludec/liraglutide and insulin degludec both in combination with metformin in Japanese subjects with type 2 diabetes mellitus (T2DM) inadequately controlled with basal or pre-mix/combination insulin therapy and oral anti-diabetic drugs, together with data from the post-marketing setting. In addition, the MAH took the opportunity to make a minor correction in section 5.1 of the SmPC and to implement changes in Annexes in line with the latest quality review of documents (QRD) template (version 10.1). The RMP (version 9.0) is updated accordingly

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

#### 5.3.17. Ledipasvir, sofosbuvir - HARVONI (CAP) - EMEA/H/C/003850/X/0081/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Grouped applications consisting of: 1) extension application to introduce a new strength (45/200 mg film-coated tablets) and a new pharmaceutical form (oral granules) associated with new strengths (33.75/150 mg and 45/200 mg). The new presentations are indicated in combination with other medicinal products for the treatment of chronic hepatitis C (CHC) in patients aged 3 to <12 years; 2) inclusion of paediatric use in patients aged 3 to < 12 years who weigh greater than or equal to 35 kg to the existing presentations of 90/400 mg film-coated tablets. The RMP (version 8.3) is updated accordingly. In addition, the MAH took the opportunity to implement minor linguistic corrections throughout the product information

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

### 5.3.18. Nintedanib - OFEV (CAP) - EMEA/H/C/003821/II/0026, Orphan

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Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to include a new indication for the treatment of systemic sclerosis associated interstitial lung disease (SSc-ILD). As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 7.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to introduce minor linguistic corrections to the Annexes in French and Swedish

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

### 5.3.19. Obinutuzumab - GAZYVARO (CAP) - EMEA/H/C/002799/II/0036, Orphan

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.8 and 5.1 of the SmPC based on data from the final clinical study report (CSR) of pivotal study GA04753g/GO01297 (GADOLIN) (listed as category 3 study in the RMP): an open-label, multicentre, randomized, phase 3 Study to investigate the efficacy and safety of bendamustine compared with bendamustine+ obinutuzumab (RO5072759 (GA101)) in patients with rituximab-refractory, indolent non-Hodgkin's lymphoma. The package leaflet and the RMP (version 6.0) are updated accordingly

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

### 5.3.20. Obinutuzumab - GAZYVARO (CAP) - EMEA/H/C/002799/II/0038, Orphan

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Submission of final clinical study report (CSR) for study MO28543/GREEN: a multicentre, open-label, single-arm, phase 3b, international study evaluating the safety of obinutuzumab alone or in combination with chemotherapy in patients with previously untreated or relapsed/refractory chronic lymphocytic leukaemia (in fulfilment of the post authorisation commitment MEA 005). The RMP (version 6.1) is updated accordingly

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

### 5.3.21. Omalizumab - XOLAIR (CAP) - EMEA/H/C/000606/II/0101

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to include treatment of nasal polyps in adult patients with inadequate response to intranasal corticosteroids. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 16.0) are updated in accordance. In addition, the MAH took the opportunity to introduce minor editorial changes in section 4.2 of the SmPC and in the package leaflet and to update

the details of the Dutch local representative. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

#### 5.3.22. [Oseltamivir - TAMIFLU \(CAP\) - EMEA/H/C/000402/II/0142](#)

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC following completion of paediatric studies NV25719 and NV20234 and downstream population pharmacokinetic (PK) and PK/pharmacodynamic (PD) analysis in order to include a dose recommendation for the treatment of paediatric immunocompromised (IC) patients. Study NV25719 was a prospective, open-label, randomized study which investigated PK and PD of two weight adjusted oseltamivir doses for the treatment of influenza-infected immunocompromised (IC) children less than 13 years of age. Study NV20234 was a prospective, double-blind, randomized trial which investigated safety and viral resistance to oseltamivir treatment in influenza-infected IC adults, adolescents and children. The package leaflet, labelling and the RMP (version 19.0) are updated accordingly

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

#### 5.3.23. [Pembrolizumab - KEYTRUDA \(CAP\) - EMEA/H/C/003820/II/0057](#)

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Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include first line treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) tumours expressing programmed death-ligand 1 (PD-L1) with a  $\geq 1\%$  tumour proportion score (TPS), based on data from study KEYNOTE-042: an international, randomized, open-label phase 3 study investigating Keytruda (pembrolizumab) monotherapy compared to standard of care platinum-based chemotherapy in patients with locally advanced or metastatic PD-L1 positive (TPS  $\geq 1\%$ ) NSCLC, and on supportive data from the final planned analysis of KEYNOTE-024: a phase 3 randomized open-label study of Keytruda (pembrolizumab) monotherapy compared to platinum-based chemotherapy in metastatic NSCLC with PD-L1 TPS  $\geq 50\%$ . As a result, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated. The RMP (version 18.1) is updated accordingly

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

#### 5.3.24. [Ribociclib - KISQALI \(CAP\) - EMEA/H/C/004213/II/0021](#)

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Hans Christian Siersted

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to add a warning on interstitial lung disease (ILD)/pneumonitis and related dose modification recommendations. 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

#### 5.3.25. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/II/0057

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years who are candidates for systemic therapy for Cosentyx (secukinumab). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 of the SmPC are updated. Section 6.6 of the SmPC for the solution for injection is also updated. The package leaflet and the RMP (version 6.0) are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. Furthermore, Annex II is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

#### 5.3.26. Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/X/0059/G

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Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Grouped applications consisting of: 1) extension application to introduce a new strength (200 mg film-coated tablets) and a new pharmaceutical form (oral granules) associated with new strengths (150 and 200 mg). The new presentations are indicated in combination with other medicinal products for the treatment of chronic hepatitis C (CHC) in patients aged 3 to <12 years; 2) inclusion of paediatric use in patients aged 3 to <12 years who weigh greater than or equal to 35 kg to the existing presentations of 400 mg film-coated tablets. The RMP (version 8.3) is updated in accordance. In addition, the MAH took the opportunity to implement minor linguistic corrections throughout the product information

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

#### 5.3.27. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/X/0043/G

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Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Grouped applications consisting of: 1) extension application to introduce a new strength (200/50 mg film-coated tablets). The new formulation is indicated for the treatment of chronic hepatitis C (CHC) in patients aged 6 years and older; 2) inclusion of paediatric use in patients aged 6 to <18 years who weigh greater than or equal to 35 kg to the existing presentation (400/100 mg film-coated tablets). 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 5.1) are updated in accordance

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

### 5.3.28. Tedizolid phosphate - SIVEXTRO (CAP) - EMEA/H/C/002846/II/0035

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Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to include adolescent population from 12 years old and older to the existing indication of treatment of acute bacterial skin and skin-structure infections (ABSSSI) in adult. As a consequence, sections 4.1, 4.2, 4.8 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 5.1) are updated in accordance. In addition, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

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

### 5.3.29. Tezacaftor, ivacaftor - SYMKEVI (CAP) - EMEA/H/C/004682/II/0016, Orphan

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Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the information based on final results from study VX14-661-110 (listed as a category 3 study in the RMP): a phase 3, multicentre, open label, rollover study for studies 103, 106, 107, 108, 109, 111, 112 and 114 designed to evaluate the long-term safety and tolerability of tezacaftor/ivacaftor (TEZ/IVA) treatment for 96 weeks in cystic fibrosis (CF) subjects 12 years and older, homozygous or heterozygous for the phenylalanine in position 508 of the cystic fibrosis transmembrane conductance regulator (F508del CFTR) mutation. In addition, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1). The RMP (version 2.2) is updated accordingly

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

### 5.3.30. Tisagenlecleucel - KYMRIAHA (CAP) - EMEA/H/C/004090/II/0013/G, Orphan

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Applicant: Novartis Europharm Limited, ATMP<sup>9</sup>

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of: 1) update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC to implement 24 month follow-up results from study CCTL019C2201: a phase 2, single arm, multicentre trial to determine the efficacy and safety of CTL019 (tisagenlecleucel) in adult patients with relapsed or refractory diffuse large b-cell lymphoma (DLBCL); 2) update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC based on interim results from study CCTL019B2202: a phase 2, single arm, multicentre trial to determine the efficacy and safety of CTL019 in paediatric patients with relapsed and refractory b-cell acute lymphoblastic leukaemia; 3) update of section 5.2 of the SmPC based on interim results from study CCTL019B2205J: a phase 2, single arm, multicentre trial to determine the efficacy and safety of CTL019 in paediatric patients with relapsed and refractory b-cell acute lymphoblastic leukaemia. Annex II, the package leaflet and the RMP (version 2.0) are updated accordingly. In addition, the MAH took the opportunity to clarify the wording of the

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<sup>9</sup> Advanced therapy medicinal product



indication in order to reflect that patients of 25 years of age are being included and to introduce some minor editorial corrections throughout the SmPC and the package leaflet

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

### 5.3.31. [Trastuzumab - HERCEPTIN \(CAP\) - EMEA/H/C/000278/II/0158](#)

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report from study BO29159 (MetaPHER) (listed as a category 3 study in the RMP): a phase 3b study to evaluate the safety and tolerability of Herceptin (trastuzumab) subcutaneous (SC) with Perjeta (pertuzumab) and docetaxel in patients with HER2-positive Advanced Breast Cancer in order to generate and evaluate additional safety and tolerability data for the approved triplet regimen in the advanced breast cancer setting. In addition, bioanalytical supportive studies are presented. The RMP (version 21) is 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. [Aclidinium bromide - BRETARIS GENUAIR \(CAP\); EKLIRA GENUAIR \(CAP\) - PSUSA/00009005/201907](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.2. [Aflibercept<sup>10</sup> - ZALTRAP \(CAP\) - PSUSA/00010019/201908](#)

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Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.3. [Alirocumab - PRALUENT \(CAP\) - PSUSA/00010423/201907](#)

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Applicant: Sanofi-aventis groupe

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<sup>10</sup> In oncological indication(s) only

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.4. [Apalutamide - ERLEADA \(CAP\) - PSUSA/00010745/201907](#)

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.5. [Ataluren - TRANSLARNA \(CAP\) - PSUSA/00010274/201907](#)

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Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.6. [Beclometasone, formoterol, glycopyrronium bromide - RIARIFY \(CAP\); TRIMBOW \(CAP\); TRYDONIS \(CAP\) - PSUSA/00010617/201907](#)

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Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.7. [Bictegravir, emtricitabine, tenofovir alafenamide - BIKTARVY \(CAP\) - PSUSA/00010695/201908](#)

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Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.8. [Birch bark extract<sup>11</sup> - EPISALVAN \(CAP\) - PSUSA/00010446/201907](#)

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Applicant: Amryt AG

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

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

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<sup>11</sup> Centrally authorised product(s) only

#### 6.1.9. Brodalumab - KYNTHEUM (CAP) - PSUSA/00010616/201907

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Applicant: LEO Pharma A/S

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.10. Catridecacog - NOVOTHIRTEEN (CAP) - PSUSA/00010034/201907

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Applicant: Novo Nordisk A/S

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.11. Daunorubicin, cytarabine - VYXEOS LIPOSOMAL (CAP) - PSUSA/00010701/201908

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Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.12. Dolutegravir – TIVICAY (CAP); dolutegravir, lamivudine - DOVATO (CAP); dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - PSUSA/00010075/201907

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Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.13. Evolocumab - REPATHA (CAP) - PSUSA/00010405/201907

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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

#### 6.1.14. Glecaprevir, pibrentasvir - MAVIRET (CAP) - PSUSA/00010620/201907

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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

#### 6.1.15. Guselkumab - TREMFYA (CAP) - PSUSA/00010652/201907

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.16. Idursulfase - ELAPRASE (CAP) - PSUSA/00001722/201907

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.17. Ingenol mebutate - PICATO (CAP) - PSUSA/00010035/201907

Applicant: LEO Laboratories Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.18. Lomitapide - LOJUXTA (CAP) - PSUSA/00010112/201907

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.19. Metreleptin - MYALEPTA (CAP) - PSUSA/00010700/201907

Applicant: Aegerion Pharmaceuticals B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.20. Natalizumab - TYSABRI (CAP) - PSUSA/00002127/201908 (with RMP)

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.21. Neratinib - NERLYNX (CAP) - PSUSA/00010712/201907

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.22. Palbociclib - IBRANCE (CAP) - PSUSA/00010544/201908

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.23. Pegaspargase<sup>12</sup> - ONCASPAR (CAP) - PSUSA/00010457/201907

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.24. Peginterferon beta-1A - PLEGRIDY (CAP) - PSUSA/00010275/201907

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.25. Perampanel - FYCOMPA (CAP) - PSUSA/00009255/201907

Applicant: Eisai GmbH

PRAC Rapporteur: Ghania Chamouni

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

6.1.26. [Rotavirus vaccine monovalent \(live, oral\) - ROTARIX \(CAP\) - PSUSA/00002665/201907](#)

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Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

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

6.1.27. [Sacubitril, valsartan - ENTRESTO \(CAP\); NEPARVIS \(CAP\) - PSUSA/00010438/201907](#)

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

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

6.1.28. [Sarilumab - KEVZARA \(CAP\) - PSUSA/00010609/201907](#)

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Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

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

6.1.29. [Saxagliptin, dapagliflozin - QTERN \(CAP\) - PSUSA/00010520/201907](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

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

6.1.30. [Smallpox vaccine \(live modified vaccinia Ankara virus\) - IMVANEX \(CAP\) - PSUSA/00010119/201907 \(with RMP\)](#)

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Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

6.1.31. [Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI \(CAP\) - PSUSA/00010619/201907](#)

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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

#### 6.1.32. Tocofersolan - VEDROP (CAP) - PSUSA/00002981/201907

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Applicant: Recordati Rare Diseases

PRAC Rapporteur: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.33. Voretigene neparvovec - LUXTURNA (CAP) - PSUSA/00010742/201907

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Applicant: Novartis Europharm Limited, ATMP<sup>13</sup>

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.34. Zanamivir<sup>14</sup> - DECTOVA (CAP) - PSUSA/00010763/201907

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Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Ulla Wändel Liminga

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. Aripiprazole - ABILIFY (CAP); ABILIFY MAINTENA (CAP); ARIPIPRAZOLE SANDOZ (CAP); NAP - PSUSA/00000234/201907

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Applicant(s): Otsuka Pharmaceutical Netherlands B.V. (Abilify, Abilify Maintena), Sandoz GmbH (Aripiprazole Sandoz), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

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

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<sup>13</sup> Advanced therapy medicinal product

<sup>14</sup> Centrally authorised product(s) only

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

#### 6.3.1. Clebopride - PSUSA/00000789/201906

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Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.2. Dienogest, estradiol<sup>15</sup> (NAP) - PSUSA/00010443/201906

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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

#### 6.3.3. Ganciclovir (NAP) - PSUSA/00001516/201906

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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

#### 6.3.4. Human plasma proteins<sup>16</sup> (NAP) - PSUSA/00010605/201907

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Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislowski

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.5. Ibuprofen, pseudoephedrine (NAP) - PSUSA/00001711/201907

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Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

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

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<sup>15</sup> Hormone replacement therapy (HRT) indication(s) only

<sup>16</sup> With not less than 95% albumin



### 6.3.6. Itopride (NAP) - PSUSA/00010606/201906

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Applicant(s): various

PRAC Lead: Rugilė Pilvinienė

Scope: Evaluation of a PSUSA procedure

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

### 6.3.7. Lidocaine hydrochloride, phenylephrine hydrochloride, tropicamide (NAP) – PSUSA/00010390/201907

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Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

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

### 6.3.8. Misoprostol<sup>17</sup> (NAP) - PSUSA/00010291/201906

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Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

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

### 6.3.9. Mitoxantrone (NAP) - PSUSA/00002076/201906

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Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

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

### 6.3.10. Octenidine (NAP) - PSUSA/00010748/201907

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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

### 6.3.11. Pitavastatin (NAP) - PSUSA/00010502/201907

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Applicant(s): various

PRAC Lead: Menno van der Elst

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<sup>17</sup> Gastrointestinal indication(s) only

Scope: Evaluation of a PSUSA procedure

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

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

### 6.4.1. Lacosamide - VIMPAT (CAP) - EMEA/H/C/000863/LEG 035.1

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Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to LEG 035 [cumulative review of cases of metabolic/toxic encephalopathy as requested in the conclusions of periodic safety update single assessment procedure PSUSA/00001816/201808 adopted in April 2019] as per the request for supplementary information (RSI) adopted in September 2019

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

### 6.4.2. Levetiracetam - KEPPRA (CAP) - EMEA/H/C/000277/LEG 087

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Applicant: UCB Pharma S.A.

PRAC Rapporteur: Laurence de Fays

Scope: Cumulative review of cases of seizure worsening as requested in the conclusions of periodic safety update single assessment procedure PSUSA/00001846/201811 adopted in July 2019

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

### 6.4.3. Levetiracetam - KEPPRA (CAP) - EMEA/H/C/000277/LEG 088

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Applicant: UCB Pharma S.A.

PRAC Rapporteur: Laurence de Fays

Scope: Cumulative review of cases of cardiac arrhythmia and cases of torsades de pointes/QT prolongation as requested in the conclusions of periodic safety update single assessment procedure PSUSA/00001846/201811 adopted in July 2019

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

### 6.4.4. Pirfenidone - ESBRIET (CAP) - EMEA/H/C/002154/LEG 015

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Detailed reviews of cases of hyponatraemia and cases of serious hepatic reactions, including the adequacy of the current risk minimisation measures (RMM) of the product information as requested in the conclusions of periodic safety update single assessment procedure PSUSA/00002435/201902 adopted in September 2019

**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>18</sup>

#### 7.1.1. Aprotinin (NAP) - EMEA/H/N/PSA/J/0046

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Applicant: Nordic Group BV

PRAC Rapporteur: Laurence de Fays

Scope: Substantial amendment to a previously agreed protocol (N/PSP/0004.1) in March 2015 for a joint non-interventional study: Nordic aprotinin patient registry to record utilisation information on patients at cardiac surgery centres

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

#### 7.1.2. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/PSP/S/0071.2

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Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: MAH's response to PSP/S/0071.1 [protocol for study 20180130: an observational PASS to describe the long-term safety profile of first-relapse B-precursor acute lymphoblastic leukaemia (ALL) paediatric patients who have been treated with blinatumomab or chemotherapy prior to undergoing haematopoietic stem cell transplant] as per the request for supplementary information (RSI) adopted in October 2019

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

#### 7.1.3. Buprenorphine - SIXMO (CAP) - EMEA/H/C/PSP/S/0086

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Applicant: L. Molteni & C. dei Fratelli Alitti Societa di Esercizio S.p.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Protocol for study MOLTeNI-2019-01: a prospective, observational (non-interventional), post-authorisation safety cohort study to evaluate the incidence of the breakages and insertion/removal complications of buprenorphine implants (Sixmo) in the routine clinical care

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

#### 7.1.4. Dinutuximab beta - QARZIBA (CAP) - EMEA/H/C/PSA/S/0047

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Applicant: EUSA Pharma (UK) Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Substantial amendment to a previously agreed protocol (PSP/S/0065) in July 2018: a registry of patients with high-risk neuroblastoma being treated with Qarziba (dinutuximab

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<sup>18</sup> In accordance with Article 107n of Directive 2001/83/EC

beta) to assess: 1) pain severity and use of analgesics during treatment; 2) incidence of neurotoxicity, visual impairment, capillary leak syndrome, cardiovascular events and hypersensitivity reactions; 3) long term safety

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

#### 7.1.5. Nonacog beta pegol - REFIXIA (CAP) - EMEA/H/C/PSA/S/0041.2

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to PSA/S/0041.1 [substantial amendment to a protocol previously endorsed in June 2018 (PSP/S/0059) for a non-interventional PASS in male patients with haemophilia B receiving nonacog beta pegol (N9-GP) prophylaxis treatment to investigate safety of N9-GP during long-term routine use] as per the request for supplementary information (RSI) adopted in November 2019

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

#### 7.1.6. Sotagliflozin - ZYNQUISTA (CAP) - EMEA/H/C/PSP/S/0084.1

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSP/S/0084 [protocol for an observational retrospective cohort study using existing data sources on the incidence of diabetic ketoacidosis (DKA) in adult patients with type 1 diabetes mellitus (T1DM) treated with sotagliflozin as an adjunct to insulin versus insulin alone, as required in the outcome of the initial opinion/marketing authorisation (EMEA/H/C/004889) finalised in February 2019] as per the request for supplementary information (RSI) adopted in September 2019

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

#### 7.1.7. Valproate (NAP) - EMEA/H/N/PSP/J/0072.3

Applicant: Sanofi-Aventis Recherche & Développement

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to PSP/J/0072.2 [protocol for a joint retrospective observational study to investigate the association between paternal exposure to valproate and the risk of congenital anomalies and neurodevelopmental disorders including autism in offspring, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in February 2018 (EMEA/H/A-31/1454)] as per the request for supplementary information (RSI) adopted in December 2019

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

#### 7.1.8. Valproate (NAP) - EMEA/H/N/PSP/J/0073.3

Applicant: Sanofi-Aventis Recherche & Développement

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to PSP/J/0073.2 [protocol for a joint survey among healthcare professionals (HCP) to assess the knowledge of HCP and behaviour with regard to the pregnancy prevention programme (PPP), the receipt/use of direct healthcare professional communication (DHPC) and educational materials as well as for a survey among patients to assess the knowledge of patients with regards to PPP and receipt/use of educational materials, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in February 2018 (EMA/H/A-31/1454)] as per the request for supplementary information (RSI) adopted in December 2019

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

### 7.1.9. Valproate (NAP) - EMA/H/N/PSP/J/0075.3

Applicant: Sanofi-Aventis Recherche & Développement

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to PSP/J/0075.2 [protocol for a joint drug utilisation study (DUS) to assess the effectiveness of the new risk minimisation measures (RMMs) and to further characterise the prescribing patterns for valproate as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in February 2018 (EMA/H/A-31/1454)] as per the request for supplementary information (RSI) adopted in December 2019

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

## **7.2. Protocols of PASS non-imposed in the marketing authorisation(s)<sup>19</sup>**

### 7.2.1. Apalutamide - ERLEADA (CAP) - EMA/H/C/004452/MEA 004.1

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ghania Chamouni

Scope: MAH's response to MEA 004 [protocol for a prospective, observational safety study to characterise the risks of the use of apalutamide in non-metastatic castration-resistant prostate cancer (NM-CRPC) patients on androgen deprivation therapy (ADT) with clinically significant cardiovascular conditions [final report expected in 2023] as per the request for supplementary information (RSI) adopted in June 2019

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

### 7.2.2. Axicabtagene ciloleucel - YESCARTA (CAP) - EMA/H/C/004480/MEA 003.2

Applicant: Kite Pharma EU B.V., ATMP<sup>20</sup>

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to MEA 003.1 [protocol for study KT-EU-471-0116: a prescriber

<sup>19</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

<sup>20</sup> Advanced therapy medicinal product

survey to assess the prescribers' understanding of serious neurologic adverse reactions and cytokine release syndrome (CRS)] as per the request for supplementary information (RSI) adopted in October 2019

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

#### 7.2.3. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/MEA 053.2

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Amendment to a previously agreed protocol for study M07-001: a prospective registry for an observational, multicentre, multinational study of patients with paroxysmal nocturnal haemoglobinuria (PNH)

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

#### 7.2.4. Eluxadoline - TRUBERZI (CAP) - EMEA/H/C/004098/MEA 005.3

Applicant: Allergan Pharmaceuticals International Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Amendment to a previously agreed protocol (version 2.0) for study EVM-19596-00-001 (listed as a category 3 study in the RMP): a drug utilisation study (DUS) using relevant healthcare databases at two different time periods in order to define the compliance to contraindications over time and the number of subjects diagnosed with pancreatitis after eluxadoline treatment

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

#### 7.2.5. Galcanezumab - EMGALITY (CAP) - EMEA/H/C/004648/MEA 003.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: MAH's response to MEA 003 [protocol for study I5Q-MC-B002 (listed as a category 3 study in the RMP): galcanezumab European drug utilisation and safety outcomes study to describe, in real-world clinical practice the utilisation of galcanezumab in Europe, and the incidence of important safety outcomes such as serious hypersensitivity and long-term safety including serious cardio-vascular events, and malignancies [final clinical study report (CSR) expected in Q4 2026] as per the request for supplementary information (RSI) adopted in September 2019

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

#### 7.2.6. L-lysine hydrochloride, L-arginine hydrochloride - LYSAKARE (CAP) - EMEA/H/C/004541/MEA 001

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Protocol for study CAAA001A12401 (listed as a category 3 study in the RMP): an international PASS to assess the effect of LysaKare (L-lysine hydrochloride/L-arginine hydrochloride) administration on potassium blood levels concentration up to 24hr compared to baseline (from MAA initial/opinion)

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

#### 7.2.7. Lurasidone - LATUDA (CAP) - EMEA/H/C/002713/MEA 010.1

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

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 010 [protocol for study 151(A)PO19107 (lurasidone PASS programme): an evaluation of the safety profile of lurasidone: a PASS using United States administrative claims databases] as adopted in October 2019

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

#### 7.2.8. Mexiletine - NAMUSCLA (CAP) - EMEA/H/C/004584/MEA 001.2

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Applicant: Lupin Europe GmbH

PRAC Rapporteur: Eva Jirsová

Scope: MAH's response to MEA 001.1 [protocol for a registry study to determine the long-term safety and tolerability of Namuscla (mexiletine) for the symptomatic treatment of myotonia in adult patients with non-dystrophic myotonic disorder] as per the request for supplementary information (RSI) adopted in October 2019

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

#### 7.2.9. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/MEA 003.2

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Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA 003.1 [MAH's response to MEA 003 [protocol for study M-14745-40: European psoriasis registry to collect long-term safety data for tildrakizumab and to further characterise the long-term safety profile of tildrakizumab in the treatment of psoriasis under conditions of routine clinical practice (from initial MAA/opinion)] as per the request for supplementary information (RSI) adopted in September 2019

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

### 7.3. Results of PASS imposed in the marketing authorisation(s)<sup>21</sup>

#### 7.3.1. Mannitol – BRONCHITOL (CAP) - EMEA/H/C/PSR/S/0020

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Applicant: Pharmaxis Pharmaceuticals Limited

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<sup>21</sup> In accordance with Article 107p-q of Directive 2001/83/EC

PRAC Rapporteur: Adrien Inoubli

Scope: MAH's response to PSR/S/0020 [results of an observational 5 year safety study to assess the identified and potential risks of Bronchitol (mannitol) in cystic fibrosis (CF) through a comparison between Bronchitol-exposed patients and unexposed patients matched for key characteristics] as per the request for supplementary information (RSI) adopted in June 2019

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

### 7.3.2. Thiocolchicoside (NAP) - EMEA/H/N/PSR/J/0023

Applicant: Sanofi (on behalf of a consortium)

PRAC Rapporteur: Amelia Cupelli

Scope: Results for a joint drug utilisation study of thiocolchicoside (TCC) containing medicinal products for systemic use in France and Italy: an electronic medical records databases study

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

## **7.4. Results of PASS non-imposed in the marketing authorisation(s)<sup>22</sup>**

### 7.4.1. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0086

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study UP0038 (listed as a category 3 study in the RMP): a non-interventional PASS with the aim to evaluate the effectiveness of Cimzia (certolizumab pegol) risk minimisation educational materials for healthcare professionals and patients

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

### 7.4.2. Colistimethate sodium - COLOBREATHE (CAP) - EMEA/H/C/001225/II/0044/G

Applicant: Teva B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Grouped variations consisting of the submission of the final report for study CLB-MD-05 (listed as a category 3 study in the RMP): an observational safety study of Colobreathe (colistimethate sodium dry powder for inhalation) compared with other inhaled anti-pseudomonal antibiotics in cystic fibrosis patients using cystic fibrosis registries. The RMP (version 9.0) is updated accordingly, together with the results from study CLB-MD-08: (listed as a category 3 study in the RMP): a non-interventional PASS cross-sectional survey study to evaluate the effectiveness of Colobreathe (colistimethate sodium) risk minimisation educational programme among healthcare professionals and patients, as per the outcome of variation II/39 adopted in February 2019

<sup>22</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



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

#### **7.4.3. Degarelix - FIRMAGON (CAP) - EMEA/H/C/000986/II/0035**

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Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Ghania Chamouni

Scope: Revised PASS report for study FE 200486 CS39: a prospective observational safety study in patients with advanced prostate cancer treated with Firmagon (degarelix) or a gonadotropin-releasing hormone (GnRH) agonist

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

#### **7.4.4. Fampridine - FAMPYRA (CAP) - EMEA/H/C/002097/II/0046**

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Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.2, 4.3, 4.4, 4.8 and 5.1 of the SmPC in order to update the existing contraindication for renal impaired patients, update the frequency of seizure to 'uncommon' and reflect safety information based on the final results from study 218MS401 (LIBERATE) (listed as category 3 study in the RMP): a phase 4 prospective, non-interventional, multicentre, observational study in multiple sclerosis (MS) patients who began Fampyra (fampridine) treatment in the post-marketing setting. The package leaflet is updated accordingly. The RMP (version 13.1) is also updated accordingly and in line with revision 2.0 of the guidance on the format of RMP in the EU (template)

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

#### **7.4.5. Linaclotide - CONSTELLA (CAP) - EMEA/H/C/002490/II/0043**

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Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study 'linaclotide utilisation study in selected European populations' (listed as a category 3 study in the RMP): a drug utilisation study (DUS) addressing the potential for off-label use and abuse/excessive use, the extent of use in pregnancy and lactation, and male patients as well as assessing the extent of off-label use and the extent of use in males and in pregnant females

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

#### **7.4.6. Liraglutide - SAXENDA (CAP) - EMEA/H/C/003780/II/0025**

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Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study NN8022-4241 (listed as a category 3 study in the RMP): a retrospective drug utilisation study (DUS) to investigate patterns of use of Saxenda and Victoza (liraglutide) in routine clinical practice in order to assess the use of Saxenda (liraglutide) according to the approved indication (adjunct to a reduced-calorie diet

and increased physical activity for weight management in adult patients with an initial body mass index (BMI) of  $\geq 30$  kg/m<sup>2</sup> (obese), or  $\geq 27$  kg/m<sup>2</sup> to  $< 30$  kg/m<sup>2</sup> (overweight) in the presence of at least one weight-related comorbidity) and the use of Victoza (liraglutide) for the treatment of weight management while the approved indication is for the treatment of adults with type 2 diabetes mellitus (T2DM). The RMP (version 31) is updated accordingly

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

#### 7.4.7. [Mirabegron - BETMIGA \(CAP\) - EMEA/H/C/002388/II/0033](#)

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Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final study report for study 178-CL-114: an evaluation of cardiovascular events in users of mirabegron and other treatments for overactive bladder

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

#### 7.4.8. [Rasagiline - AZILECT \(CAP\) - EMEA/H/C/000574/WS1749/0084; RASAGILINE RATIOPHARM \(CAP\) - EMEA/H/C/003957/WS1749/0016](#)

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Applicant: Teva B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report from study TV1030-CNS-50024 (listed as a category 3 study in the RMP): a non-interventional retrospective cohort study which was conducted using the United States Medicare research database to assess the potential risk of melanoma associated with the use of rasagiline mesylate in patients with Parkinson's disease

**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. [Etanercept - ENBREL \(CAP\) - EMEA/H/C/000262/MEA 166.2](#)

---

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Eva Segovia

Scope: Third biennial interim analysis report for study B1801023: an open-label extension study to assess the long-term safety and clinical benefit of etanercept in children and adolescents with extended oligoarticular juvenile idiopathic arthritis, enthesitis-related arthritis, or psoriatic arthritis who were previously enrolled in protocol 0881A1-3338-WW (B1801014)

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

### 7.5.2. Etanercept - LIFMIOR (CAP) - EMEA/H/C/004167/MEA 002.1

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Eva Segovia

Scope: Third biennial interim analysis report for study B1801023: an open-label extension study to assess the long-term safety and clinical benefit of etanercept in children and adolescents with extended oligoarticular juvenile idiopathic arthritis, enthesitis-related arthritis, or psoriatic arthritis who were previously enrolled in protocol 0881A1-3338-WW (B1801014)

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

### 7.5.3. Filgrastim - NIVESTIM (CAP) - EMEA/H/C/001142/MEA 015.4

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Third annual report for study ZOB-NIV-1513 (C1121008): a multinational, multicentre, prospective, non-interventional PASS in healthy donors (HDs) exposed to Nivestim (biosimilar filgrastim) for haematopoietic stem cell (HSC) mobilisation (NEST) [final clinical study report (CSR) due date: March 2023]

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

### 7.5.4. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 027.7

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Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fourth annual progress report of the ENEIDA registry (study MK-8259-042): a long-term, non-interventional observational study of patients with inflammatory bowel disease (IBD) in Spain to evaluate whether the use of golimumab is associated with a risk of colectomy for intractable disease, advanced neoplasia (colorectal cancer or high grade dysplasia), and hepatosplenic T-cell lymphoma (HSTCL) in patients with ulcerative colitis (UC) as compared with alternative therapies for similar severity of disease [final clinical study report (CSR) expected: March 2023]

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

### 7.5.5. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/ANX 003.4

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Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Annual report for study VX14 809 108: an observational study to evaluate the utilisation patterns and long-term effects of lumacaftor/ivacaftor therapy in patients with cystic fibrosis (CF) [final report expected: December 2021]

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

#### 7.5.6. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 002.5

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Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Ronan Grimes

Scope: Annual progress report for PASS D3820R00006: a post-marketing observational drug utilisation study (DUS) of Moventig (naloxegol) conducted in selected European populations in order to describe demographic, clinical, and treatment characteristics in the baseline of patients treated with naloxegol as well as to describe treatment pattern characteristics of naloxegol utilisation at initiation and follow-up

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

#### 7.5.7. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 006.8

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Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Ronan Grimes

Scope: Annual progress report for study D3820R00009: an observational PASS of Moventig (naloxegol) among patients aged 18 years and older treated with opioids chronically

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

#### 7.5.8. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58<sup>23</sup>) - EMEA/H/W/002300/MEA 002.2

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Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Interim result for study EPI-MAL-002: a prospective study to estimate the incidence of diseases specified as adverse events of special interest (AESI) leading to hospitalisation or death, and of meningitis in infants and young children in sub-Saharan Africa prior to implementation of Mosquirix (RTS, S/AS01E) [final clinical study report due in December 2022]

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

#### 7.5.9. Radium-223 - XOFIGO (CAP) - EMEA/H/C/002653/MEA 004.2

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Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Second interim result for study 16913 (REASSURE): an observational PASS to assess the long term safety profile and risks of developing second primary malignancies and their potential relationship to radium-223 in the routine clinical practice setting

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

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<sup>23</sup> Article 58 of Regulation (EC) No 726/2004 allows the Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO) on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)

#### 7.5.10. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/MEA 005.2

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Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Annual progress reports for: 1) pregnancy registry OBS12751 (international): an international pregnancy exposure registry of women with multiple sclerosis (MS) exposed to Aubagio (teriflunomide) and; 2) pregnancy registry OBS13499 (US/CA): teriflunomide pregnancy outcome exposure registry: a 'teratology information specialists (OTIS)' autoimmune diseases in pregnancy project

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

#### 7.5.11. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/MEA 006.1

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Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Annual progress report 2019 for study OBS12753: a prospective cohort study of long-term safety of Aubagio (teriflunomide) in multiple sclerosis (MS) patients in Europe

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

### 7.6. Others

#### 7.6.1. Filgrastim - FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/MEA 007.6

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Applicant: Hexal AG

PRAC Rapporteur: Menno van der Elst

Scope: MAH's request to close study EP06-501 (SMART): a non-interventional, prospective, long-term safety data collection of Zarzio/Filgrastim Hexal (filgrastim) in healthy unrelated stem cell donors undergoing peripheral blood progenitor cell mobilisation, in light of available data

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

#### 7.6.2. Filgrastim - ZARZIO (CAP) - EMEA/H/C/000917/MEA 007.6

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Applicant: Sandoz GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's request to close study EP06-501 (SMART): a non-interventional, prospective, long-term safety data collection of Zarzio/Filgrastim Hexal (filgrastim) in healthy unrelated stem cell donors undergoing peripheral blood progenitor cell mobilisation, in light of available data

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

### 7.6.3. Somatropin - OMNITROPE (CAP) - EMEA/H/C/000607/MEA 012.4

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Applicant: Sandoz GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's request to close post-marketing surveillance study EP00-501 [PATRO Children]: a multicentre, non-interventional study to monitor the long-term safety and efficacy of Omnitrope (somatropin) in paediatric patients for the approved indications within routine clinical practice

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

### 7.6.4. Vernakalant - BRINAVESS (CAP) - EMEA/H/C/001215/LEG 033

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Applicant: Correvio

PRAC Rapporteur: Menno van der Elst

Scope: Submission of a detailed analysis of a case of hypotension (KW-C14001-19-00239) including the CIOMS<sup>24</sup> form, causality assessment report

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

## 7.7. New Scientific Advice

None

## 7.8. Ongoing Scientific Advice

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

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

None

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

## 8.1. Annual reassessments of the marketing authorisation

### 8.1.1. Cholic acid - ORPHACOL (CAP) - EMEA/H/C/001250/S/0033 (without RMP)

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Applicant: Laboratoires CTRS

PRAC Rapporteur: Sofia Trantza

Scope: Annual reassessment of the marketing authorisation

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<sup>24</sup> Council for International Organisations of Medical Sciences

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

#### 8.1.2. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/S/0045 (without RMP)

Applicant: Gentium S.r.l.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual reassessment of the marketing authorisation

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

#### 8.1.3. Galsulfase - NAGLAZYME (CAP) - EMEA/H/C/000640/S/0078 (without RMP)

Applicant: BioMarin International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Annual reassessment of the marketing authorisation

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

#### 8.1.4. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/S/0019 (without RMP)

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Annual reassessment of the marketing authorisation

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

#### 8.1.5. Susoctocog alfa - OBIZUR (CAP) - EMEA/H/C/002792/S/0028 (without RMP)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual reassessment of the marketing authorisation

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

#### 8.1.6. Tocofersolan - VEDROP (CAP) - EMEA/H/C/000920/S/0035 (without RMP)

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Melinda Palfi

Scope: Annual reassessment of the marketing authorisation

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

## 8.2. Conditional renewals of the marketing authorisation

### 8.2.1. Autologous CD34<sup>+</sup> cell enriched population that contains hematopoietic stem cells transduced with lentiglobin BB305 lentiviral vector encoding the beta-A-T87Q-globin gene - ZYNTEGLO (CAP) - EMEA/H/C/003691/R/0005 (without RMP)

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Applicant: bluebird bio (Netherlands) B.V, ATMP<sup>25</sup>

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

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

### 8.2.2. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/R/0041 (without RMP)

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Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: 5-year renewal of the marketing authorisation

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

### 8.2.3. Parathyroid hormone - NATPAR (CAP) - EMEA/H/C/003861/R/0022 (without RMP)

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Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Conditional renewal of the marketing authorisation

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

### 8.2.4. Obeticholic acid - OCALIVA (CAP) - EMEA/H/C/004093/R/0018 (without RMP)

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Applicant: Intercept Pharma International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Conditional renewal of the marketing authorisation

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

### 8.2.5. Rucaparib - RUBRACA (CAP) - EMEA/H/C/004272/R/0016 (without RMP)

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Applicant: Clovis Oncology Ireland Limited

PRAC Rapporteur: Annika Folin

Scope: 5-year renewal of the marketing authorisation

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

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<sup>25</sup> Advanced therapy medicinal product



## 8.3. Renewals of the marketing authorisation

### 8.3.1. Asfotase alfa - STRENSIQ (CAP) - EMEA/H/C/003794/R/0044 (without RMP)

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Applicant: Alexion Europe SAS

PRAC Rapporteur: Rhea Fitzgerald

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.2. Bortezomib - BORTEZOMIB ACCORD (CAP) - EMEA/H/C/003984/R/0022 (without RMP)

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Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.3. Ceftolozane, tazobactam - ZERBAXA (CAP) - EMEA/H/C/003772/R/0026 (without RMP)

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Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.4. Human alpha1-proteinase inhibitor - RESPREEZA (CAP) - EMEA/H/C/002739/R/0036 (without RMP)

---

Applicant: CSL Behring GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.5. Lenvatinib - LENVIMA (CAP) - EMEA/H/C/003727/R/0031 (with RMP)

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Applicant: Eisai GmbH

PRAC Rapporteur: Annika Folin

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.6. Lutetium (<sup>177</sup>Lu) chloride - LUMARK (CAP) - EMEA/H/C/002749/R/0014 (with RMP)

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Applicant: I.D.B. Holland B.V.

PRAC Rapporteur: Ronan Grimes

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.7. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/R/0074 (with RMP)

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Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.8. Panobinostat - FARYDAK (CAP) - EMEA/H/C/003725/R/0020 (with RMP)

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Applicant: Secura Bio Limited

PRAC Rapporteur: Sofia Trantza

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.9. Sebelipase alfa - KANUMA (CAP) - EMEA/H/C/004004/R/0025 (without RMP)

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Applicant: Alexion Europe SAS

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

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

## 9. Product related pharmacovigilance inspections

### 9.1. List of planned pharmacovigilance inspections

None

### 9.2. Ongoing or concluded pharmacovigilance inspections

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

### 9.3. Others

None

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

### 10.1. Safety related variations of the marketing authorisation

None

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

None

### 10.3. Other requests

#### 10.3.1. Nitrosamine impurities in medicinal products for human use containing chemically synthesised active pharmaceutical ingredients (API) - EMEA/H/A-5(3)/1490

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Applicant(s): various

PRAC Lead: Martin Huber, Ulla Wändel Liminga

Scope: PRAC consultation on a CHMP review under Article 5(3) of Regulation (EC) No 726/2004 on nitrosamine impurities in human medicinal products containing chemically synthesised API

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

### 10.4. Scientific Advice

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

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

### 11.1. Safety related variations of the marketing authorisation

None

## 11.2. Other requests

# 12. Organisational, regulatory and methodological matters

## 12.1. Mandate and organisation of the PRAC

None

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

None

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

### 12.3.1. Scientific advice working party (SAWP) – re-nomination of PRAC representative(s)

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**Action:** For adoption

## 12.4. Cooperation within the EU regulatory network

### 12.4.1. EMA Regulatory science strategy to 2025

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**Action:** For discussion

## 12.5. Cooperation with International Regulators

### 12.5.1. Health Canada (HC) - overview of structure and processes

---

**Action:** For discussion

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

None

## 12.7. PRAC work plan

None

## 12.8. Planning and reporting

### 12.8.1. EU Pharmacovigilance system – quarterly workload measures and performance indicators – Q4 2019 and predictions

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**Action:** For discussion

## 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: Menno van der Elst

**Action:** For discussion

## 12.12. Adverse drug reactions reporting and additional monitoring

### 12.12.1. Management and reporting of adverse reactions to medicinal products

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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

### 12.13.2. EudraVigilance operational plan – milestones 2020 to 2022

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**Action:** For discussion

## 12.14. Risk management plans and effectiveness of risk minimisations

### 12.14.1. Risk management systems

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None

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

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None

## **12.15. Post-authorisation safety studies (PASS)**

### 12.15.1. Post-authorisation Safety Studies – imposed PASS

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None

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

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None

## **12.16. Community procedures**

### 12.16.1. Referral procedures for safety reasons

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None

## **12.17. Renewals, conditional renewals, annual reassessments**

None

## **12.18. Risk communication and transparency**

### 12.18.1. Public participation in pharmacovigilance

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None

### 12.18.2. Safety communication

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None

## **12.19. Continuous pharmacovigilance**

### 12.19.1. Incident management

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None

## **12.20. Others**

### 12.20.1. Medical Dictionary for Regulatory Activities (MedDRA) points to consider group – call for EU expert nomination

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**Action:** For discussion

12.20.2. Strategy on measuring the impact of pharmacovigilance - PRAC interest group (IG)  
Impact – impact guidance

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PRAC Lead: Antoine Pariente

**Action:** For discussion

12.20.3. UK withdrawal from the EU – update

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**Action:** For discussion

## 13. Any other business



## 14. Explanatory notes

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

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

(Items 2 and 3 of the PRAC agenda)

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

[http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general\\_content\\_000150.jsp&mid=WC0b01ac05800240d0](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000150.jsp&mid=WC0b01ac05800240d0)

### **Signals assessment and prioritisation**

(Item 4 of the PRAC agenda)

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

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

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

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

(Item 5 of the PRAC agenda)

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

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

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

(Item 6 of the PRAC agenda)

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

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

### **Post-authorisation Safety Studies (PASS)**

(Item 7 of the PRAC agenda)

A PASS is a study of an authorised medicinal product carried out to obtain further information on its safety, or to measure the effectiveness of risk management measures. The results of a PASS help regulatory agencies to evaluate the safety and benefit-risk profile of a medicine.

### **Product related pharmacovigilance inspections**

(Item 9 of the PRAC agenda)

Inspections carried out by regulatory agencies to ensure that marketing authorisation holders comply with their pharmacovigilance obligations.

More detailed information on the above terms can be found on the EMA website: [www.ema.europa.eu/](http://www.ema.europa.eu/)