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SCIENCE MEDICINES HEALTH

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Human Medicines Division

## Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 02-05 May 2022

Chair: Sabine Straus – Vice-Chair: Martin Huber

02 May 2022, 13:00 – 19:30, room 1C / via teleconference

03 May 2022, 08:30 – 19:30, room 1C / via teleconference

04 May 2022, 08:30 – 19:30, room 1C / via teleconference

05 May 2022, 08:30 – 16:00, room 1C / via teleconference

Organisational, regulatory and methodological matters (ORGAM)

19 May 2022, 09:00 – 12:00, 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.

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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 02-05 May 2022. See May 2022 PRAC minutes (to be published post June 2022 PRAC meeting).

### **1.2. Agenda of the meeting on 02-05 May 2022**

**Action:** For adoption

### **1.3. Minutes of the previous meeting on 04-07 April 2022**

**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

### 3.2.1. Chlormadinone (NAP); chlormadinone, ethinylestradiol (NAP); nomegestrol (NAP); nomegestrol, estradiol – ZOELY (CAP), NAP - EMEA/H/A-31/1510

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Applicant(s): Theramex Ireland Limited (Zoely), various

PRAC Rapporteur: Martin Huber; PRAC Co-rapporteur: Željana Margan Koletić

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 list of outstanding issues (LoOI)

## 3.3. Procedures for finalisation

None

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

None

## 3.5. Others

None

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

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

### 4.1.1. Apixaban – APIXABAN ACCORD (CAP), ELIQUIS (CAP); NAP

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Applicant(s): Accord Healthcare S.L.U. (Apixaban Accord), Bristol-Myers Squibb, Pfizer EEIG (Eliquis)

PRAC Rapporteur: To be appointed

Scope: Signal of masking of acquired haemophilia

**Action:** For adoption of PRAC recommendation

EPITT 19802 – New signal

Lead Member State(s): NL

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

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

#### 4.1.2. Cabozantinib – COMETRIQ (CAP), CABOMETYX (CAP)

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Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Signal of tumour lysis syndrome

**Action:** For adoption of PRAC recommendation

EPITT 19794 – New signal

Lead Member State(s): NL

#### 4.2. New signals detected from other sources

None

#### 4.3. Signals follow-up and prioritisation

##### 4.3.1. Calcitonin gene-related peptide (CGRP) antagonists: eptinezumab – VYEPTI (CAP) - EMEA/H/C/005287/SDA/001, erenumab – AIMOVIG (CAP) - EMEA/H/C/004447/SDA/004, fremanezumab – AJOVY (CAP) - EMEA/H/C/004833/SDA/006, galcanezumab – EMGALITY (CAP) - EMEA/H/C/004648/SDA/005

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Applicant(s): Eli Lilly Nederland B.V. (Emgality), H. Lundbeck A/S (Vyepsti), Novartis Europharm Limited (Aimovig), Teva GmbH (Ajovy)

PRAC Rapporteur: Kirsti Villikka

Scope: Signal of Raynaud's phenomenon

**Action:** For adoption of PRAC recommendation

EPITT 19766 – Follow-up to January 2022

#### 4.4. Variation procedure(s) resulting from signal evaluation

None

## 5. Risk management plans (RMPs)

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

#### 5.1.1. Bevacizumab - EMEA/H/C/005534

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Scope: Treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer; first-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer; first line treatment of patients with advanced and/or metastatic

renal cell cancer

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

#### 5.1.2. [Coronavirus \(COVID-19\) vaccine \(recombinant protein receptor binding domain fusion heterodimer\) – EMEA/H/C/006058](#)

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Scope: Active immunisation to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older

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

#### 5.1.3. [Faricimab - EMEA/H/C/005642](#)

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Scope: Treatment of neovascular (wet) age-related macular degeneration (nAMD) and visual impairment due to diabetic macular oedema (DME)

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

#### 5.1.4. [Lutetium \(<sup>177</sup>Lu\) chloride - EMEA/H/C/005859](#)

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Scope: Radiopharmaceutical precursor intended to be used only for the radiolabelling of carrier molecules specifically developed and authorised for radiolabelling with lutetium (<sup>177</sup>Lu) chloride

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

#### 5.1.5. [Mobocertinib - EMEA/H/C/005621](#)

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Scope: Treatment of adult patients with epidermal growth factor receptor (EGFR) exon 20 insertion mutation-positive locally advanced or metastatic non-small cell lung cancer (NSCLC)

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

#### 5.1.6. [Nirsevimab - EMEA/H/C/005304, PRIME](#)

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Scope (accelerated assessment): Prevention of respiratory syncytial virus (RSV) lower respiratory tract infection disease to immunise infants from birth entering their first RSV season

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

#### 5.1.7. [Octreotide - EMEA/H/C/005826, Orphan](#)

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Applicant: Amryt Pharmaceuticals DAC

Scope: Treatment of acromegaly

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

### 5.1.8. Pemetrexed - EMEA/H/C/005848

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Scope: Treatment of malignant pleural mesothelioma and non-small cell lung cancer (NSCLC)

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

### 5.1.9. Relatlimab, nivolumab - EMEA/H/C/005481

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Scope: First-line treatment of advanced (unresectable or metastatic) melanoma in adults and adolescents of 12 years and older and weighing at least 40 kg

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

### 5.1.10. Teclistamab - EMEA/H/C/005865, PRIME, Orphan

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Applicant: Janssen-Cilag International N.V.

Scope (accelerated assessment): Treatment of relapsed or refractory multiple myeloma

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

### 5.1.11. Thalidomide - EMEA/H/C/005715

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Scope: Treatment of multiple myeloma

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

### 5.1.12. Voclosporin - EMEA/H/C/005256

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Scope: Treatment of adult patients with class III, IV or V (including mixed class III/V and IV/V) lupus nephritis (LN) in combination with background immunosuppressive therapies

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

### 5.1.13. Vutrisiran - EMEA/H/C/005852, Orphan

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Applicant: Alnylam Netherlands B.V.

Scope: Treatment of hereditary transthyretin-mediated amyloidosis

**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. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/II/0041

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Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated RMP (version 10.0) in order to include the new important identified risk of 'autoimmune encephalitis' and to introduce changes in accordance to the

Rapporteurs' requests made in the conclusions of variation II/0038 finalised in January 2022

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

#### 5.2.2. [Infliximab - ZESSLY \(CAP\) - EMEA/H/C/004647/II/0020](#)

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Applicant: Sandoz GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 3.0) to remove the German registry Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT) as an additional pharmacovigilance activity in alignment with the RMP of the reference product and to remove the British Association of Dermatologists Biologic and Immunomodulators Register (BADBIR) registry as an additional pharmacovigilance activity

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

#### 5.2.3. [Nintedanib - VARGATEF \(CAP\) - EMEA/H/C/002569/II/0044](#)

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Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Georgia Gkegka

Scope: Submission of an updated RMP (version 10.0) in order to remove safety concerns that were classified as important identified risks, important potential risks and missing information, based on cumulative post-marketing experience. The MAH also proposed an update of the anatomical therapeutic chemical (ATC) code, an update of post-marketing exposure, the removal of adverse event follow-up forms and an update of search strategies

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

#### 5.2.4. [Pandemic influenza vaccine \(H5N1\) \(surface antigen, inactivated, adjuvanted\) - FOCLIVIA \(CAP\) - EMEA/H/C/001208/WS2151/0068; prepandemic influenza vaccine \(H5N1\) \(surface antigen, inactivated, adjuvanted\) - AFLUNOV \(CAP\) - EMEA/H/C/002094/WS2151/0071](#)

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Applicant: Seqirus S.r.l

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of an updated RMP (version 3.9) in order to align safety concerns of Aflunov (prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted)) and Foclivia (pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted)) and to reclassify some potential risks in line with revision 2 of GVP module V on 'Risk management systems'. In addition, reference to adverse drug reaction follow-up forms for routine pharmacovigilance activity are removed

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

#### 5.2.5. [Selexipag - UPTRAVI \(CAP\) - EMEA/H/C/003774/II/0035](#)

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nathalie Gault



Scope: Submission of an updated RMP (version 9.3) in order to reflect amendments to the protocol of ongoing EXPOSURE PASS study: an international, observational, cohort study of pulmonary arterial hypertension (PAH) patients newly treated with either Uptravi (selexipag) or any other PAH-specific therapy, in clinical practice; to add the EXTRACT study (67896049PAH0002): a retrospective medical chart review of patients with PAH newly treated with either Uptravi (selexipag) or any other PAH-specific therapy as an additional pharmacovigilance activity; and to reflect amendments to the protocol of study EDUCATE (listed as category 3 study in the RMP): a PASS to evaluate risk minimisation measures for medication errors with Uptravi (selexipag) during the titration phase in patients with PAH in clinical practice (assessed and approved in MEA 003.4)

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

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

#### 5.3.1. Acalabrutinib - CALQUENCE (CAP) - EMEA/H/C/005299/X/0009/G

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Applicant: AstraZeneca AB

PRAC Rapporteur: Željana Margan Koletić

Scope: Grouped application consisting of: 1) extension application to introduce a new pharmaceutical form, film-coated tablet; 2) change of the anatomical therapeutic chemical (ATC) code for acalabrutinib from L01XE51 to L01EL02. The RMP (version 4.1) is updated accordingly

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

#### 5.3.2. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/II/0046, Orphan

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Applicant: Kite Pharma EU B.V., ATMP<sup>3</sup>

PRAC Rapporteur: Anette Kirstine Stark

Scope: Extension of indication to include treatment of adult patients with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL). 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 5.3) are updated in accordance. In addition, the MAH took the opportunity to update the product information with minor editorial changes

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

#### 5.3.3. Budesonide - JORVEZA (CAP) - EMEA/H/C/004655/II/0015, Orphan

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Applicant: Dr. Falk Pharma GmbH

PRAC Rapporteur: Zane Neikena

Scope: Update of section 4.8 of the SmPC in order to update the list of adverse drug reactions based on final results from long-term maintenance study BUL-2/EER: a double-blind, randomised, placebo-controlled, phase 3 study on the efficacy and tolerability of a 48-

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<sup>3</sup> Advanced therapy medicinal product

week treatment with two different doses of budesonide effervescent tablets vs. placebo for maintenance of clinico-pathological remission in adult patients with eosinophilic esophagitis. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. The package leaflet and RMP (version 3.0) are updated accordingly. The MAH also submitted the final report of study BUL-6/BIO: an open-label, randomised, 3-period, 3-sequence, single dose change-over trial in 18 male and female healthy volunteers, previously assessed within procedure X/0007/G concluded in March 2020

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

#### 5.3.4. Bupivacaine - EXPAREL LIPOSOMAL (CAP) - EMEA/H/C/004586/II/0005

Applicant: Pacira Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension of indication to extend the existing indication of treatment of somatic post-operative pain from small- to medium-sized surgical wounds to children over 6 years old or older. 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 1.1) are updated accordingly

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

#### 5.3.5. Canakinumab - ILARIS (CAP) - EMEA/H/C/001109/II/0075

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of adult patients with Schnitzler syndrome. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 13.0) are updated in accordance

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

#### 5.3.6. Casirivimab, imdevimab - RONAPREVE (CAP) - EMEA/H/C/005814/II/0002

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include treatment of coronavirus (COVID-19) in hospitalised patients in adults and adolescents aged 12 years and older weighing at least 40 kg. As a consequence, sections 4.2, 4.4, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The package leaflet, the labelling and the RMP (version 1.1) are updated in accordance

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

#### 5.3.7. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) (NVX-CoV2373) - NUVAXOVID (CAP) - EMEA/H/C/005808/II/0009

Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include use in adolescents 12 to 17 years of age based on data from study 2019nCoV-301: a phase 3, randomised, observer-blinded, placebo-controlled study to evaluate the efficacy, safety, and immunogenicity of a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) recombinant spike protein nanoparticle vaccine (SARS-CoV-2 rS) with matrix-M adjuvant in adult participants  $\geq$  18 years with a paediatric expansion in adolescents (12 to < 18 years). 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 1.1) are updated in accordance

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

#### 5.3.8. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/II/0056, Orphan

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Applicant: Gentium S.r.l.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study 15-007 (listed as a specific obligation in Annex II): a phase 3, randomised, adaptive study of defibrotide vs. best supportive care in the prevention of hepatic veno-occlusive disease in adult and paediatric patients undergoing hematopoietic stem cell transplant (HSCT). The RMP (version 9.0) is updated accordingly. The MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) (template 10.2). In addition, the MAH introduced some minor correction throughout the product information

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

#### 5.3.9. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/II/0053, Orphan

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Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of section 4.8 of the SmPC in order to update the list of adverse drug reactions (ADRs) following the development of an improved methodology to identify relevant ADRs likely attributable to delamanid. The package leaflet and the RMP (version 3.6) are updated accordingly

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

#### 5.3.10. Dexamethasone - NEOFORDEX (CAP) - EMEA/H/C/004071/II/0017/G

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Applicant: Laboratoires CTRS

PRAC Rapporteur: Tiphaine Vaillant

Scope: 1. Grouped variations consisting of: 1) update of the RMP (version 4.3) with a completion of 'removal of the score line for sub-division of the 40 mg tablet and consequent deletion of the 20 mg posology' (as a category 3 activity) and to include the direct healthcare professional communication (DHPC). In addition, the MAH used the opportunity to update sections from Module 3 of the dossier with editorial changes

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

### 5.3.11. [Dexmedetomidine - DEXDOR \(CAP\) - EMEA/H/C/002268/II/0035](#)

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Applicant: Orion Corporation

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.4 of the SmPC in order to add a new warning on mortality in intensive care unit patients  $\leq 65$  years old, based on results from study SPICE III: an open-label, randomized trial on early sedation with dexmedetomidine in ventilated critically ill patients and heterogeneity of treatment effect and based on the completion of post-authorisation measure (LEG 16.4) finalised in November 2021. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. A proposal for a direct healthcare professional communication (DHPC) and a communication plan is submitted. The RMP (version 9) is updated accordingly

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

### 5.3.12. [Dolutegravir, abacavir, lamivudine - TRIUMEQ \(CAP\) - EMEA/H/C/002754/X/0101/G](#)

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Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Grouped application consisting of: 1) extension application to introduce a new pharmaceutical form associated with a new strength (5 mg/60 mg/30 mg dispersible tablet). The new presentation is indicated for the treatment of human immunodeficiency virus (HIV) infected children weighing at least 14 kg to less than 25 kg; 2) extension of indication to include treatment of human immunodeficiency virus (HIV) infected children weighing at least 25kg for the already approved film-coated tablets. As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC are updated. The package leaflet and labelling are updated in accordance. The RMP (version 19) is updated in accordance

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

### 5.3.13. [Elbasvir, grazoprevir - ZEPATIER \(CAP\) - EMEA/H/C/004126/II/0034](#)

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Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report from study MK-5172-017 (listed as a category 3 study in the RMP): a long-term follow-up study to evaluate the durability of virologic response and/or viral resistance patterns of subjects with chronic hepatitis C who have been previously treated with Zepatier (elbasvir/grazoprevir) in a prior clinical trial (in fulfilment of MEA 002.1). The RMP (version 5.1) is updated accordingly

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

### 5.3.14. [Emicizumab - HEMLIBRA \(CAP\) - EMEA/H/C/004406/II/0027](#)

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include treatment of adult and paediatric patients with

haemophilia A without factor VIII (FVIII) inhibitors who have mild or moderate disease for whom prophylaxis is clinically indicated. Consequently, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC are updated. In addition, section 4.2 of the SmPC is updated to make clearer that the maintenance dose for Hemlibra (emicizumab) applies from week 5 of dosing. 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

#### 5.3.15. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/II/0246

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Eva Segovia

Scope: Update of section 5.1 of the SmPC in order to update clinical information based on final results obtained from the clinical paediatric study B1801023 (CLIPPER 2): an open label extension study to assess the long-term safety 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). The RMP (version 7.5) is updated accordingly

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

#### 5.3.16. Gemtuzumab ozogamicin - MYLOTARG (CAP) - EMEA/H/C/004204/II/0024, Orphan

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Update of sections 4.8, 5.1 and 5.2 of the SmPC based on the final results from study B176103: a single-arm, open-label, phase 4 study evaluating the QT interval, pharmacokinetics, and safety of gemtuzumab ozogamicin as a single-agent regimen in patients with relapsed or refractory CD<sup>433</sup>-positive acute myeloid leukaemia. The RMP (version 2.0) is updated in accordance. In addition, the MAH took the opportunity to introduce some editorial changes in the product information

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

#### 5.3.17. Gilteritinib - XOSPATA (CAP) - EMEA/H/C/004752/II/0007, Orphan

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the report of an integrated analysis to demonstrate the safety of long-term treatment with gilteritinib when all patients enrolled in studies 2215-CL-0101, 2215-CL-0102 and 2215-CL-0301 have completed at least 3 years of treatment with gilteritinib or have withdrawn prior to completing at least 3 years of treatment. The studies refer to: 1) study 2215-CL-0101: a phase 1/2 open-label, dose escalation study investigating the safety, tolerability, pharmacokinetics, and pharmacodynamics of ASP2215 (gilteritinib) in patients with relapsed or refractory acute myeloid leukaemia (AML); 2) study 2215-CL-0102: a phase 1 open-label, dose escalation study investigating the safety, tolerability,

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<sup>4</sup> Cluster of differentiation

pharmacokinetics, and pharmacodynamics of ASP2215 in Japanese patients with relapsed or refractory AML; 3) study 2215-CL-0301: a phase 3 open-label, multicentre, randomized study of ASP2215 versus salvage chemotherapy in patients with relapsed or refractory AML with FMS-like tyrosine kinase 3 (FLT3) mutation. The RMP (version 2.0) is updated in order to address missing information regarding the safety of Xospata (gilteritinib)

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

#### 5.3.18. [Givosiran - GIVLAARI \(CAP\) - EMEA/H/C/004775/II/0006, Orphan](#)

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Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC to add 'blood homocysteine increase' as a new adverse drug reaction (ADR) and update of section 4.4 of the SmPC to add a related warning. The package leaflet and the RMP (version 1.1) are updated accordingly. In addition, the MAH took the opportunity to make editorial changes to the product information and to update the local representative details for Malta and Cyprus

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

#### 5.3.19. [Ibrutinib - IMBRUVICA \(CAP\) - EMEA/H/C/003791/II/0069](#)

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of section 4.4 of the SmPC to include information on fatal and serious cardiac arrhythmias and cardiac failure, relevant warnings and periodical monitoring of patients following a safety assessment for increased risk of sudden death/cardiac death with the use of ibrutinib. The MAH took the opportunity to correct typographical errors throughout the product information. The package leaflet and the RMP (version 11.0) are updated accordingly

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

#### 5.3.20. [Pegcetacoplan - ASPAVELI \(CAP\) - EMEA/H/C/005553/II/0002, Orphan](#)

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Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC based on final results from study APL2-302 (Pegasus) (listed as a category 3 study in the RMP): a global, phase 3, prospective, randomised, multicentre, open-label, active-comparator-controlled study in 80 subjects. The objective was to confirm treatment efficacy and safety of pegcetacoplan monotherapy for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) (in fulfilment of MEA 001). The package leaflet and the RMP (version 0.5) are updated accordingly

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

### 5.3.21. Pemigatinib - PEMAZYRE (CAP) - EMEA/H/C/005266/II/0005, Orphan

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Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC based on the final results from study INCB054828 (FIGHT-202) (listed as a specific obligation in the Annex II (SOB/002)): a phase 2 study investigating the efficacy and safety of pemigatinib in adults with advanced/metastatic or surgically unresectable cholangiocarcinoma including fibroblast growth factor receptor 2 (FGFR2) translocations who failed previous therapy. The RMP (version 2.0) and Annex II are updated accordingly

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

### 5.3.22. Pirfenidone - ESBRIET (CAP) - EMEA/H/C/002154/II/0074

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension of indication to include treatment of 'advanced' idiopathic pulmonary fibrosis (IPF) by the deletion of the current qualifier 'mild to moderate', based on the results from study MA29957: a 52-week phase 2b, multicentre, randomised, double-blind, placebo-controlled clinical trial in IPF-patients with advanced lung function impairment (carbon monoxide diffusion capacity (DLco) < 40% of predicted) and at high risk of grade 3 pulmonary hypertension, and additional analyses performed on the original pivotal trials for pirfenidone in IPF. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. In addition, the MAH took the opportunity to include information in section 4.4 of the SmPC related to the content of sodium. 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

### 5.3.23. Pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - APEXXNAR (CAP) - EMEA/H/C/005451/II/0002

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.5, 4.8 and 5.1 of the SmPC to add information regarding the co-administration of Apexxnar (pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed)) with seasonal quadrivalent influenza vaccine (QIV) based on final study results from study B7471004 (listed as a category 3 study in the RMP): a phase 3, randomised, double-blind trial to evaluate the safety and immunogenicity of a 20-valent pneumococcal conjugate vaccine (20vPnC) when co-administered with seasonal inactivated influenza vaccine (SIIV) in adults ≥65 years of age. The package leaflet and the RMP (version 1.1) are updated accordingly

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

### 5.3.24. Relugolix, estradiol, norethisterone acetate - RYEQO (CAP) - EMEA/H/C/005267/II/0006

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Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study MVT-601-035 (listed as a category 3 study in the RMP): an international phase 3 double-blind, placebo-controlled, randomised withdrawal study of relugolix co-administered with estradiol and norethisterone in women with heavy menstrual bleeding associated with uterine fibroids to evaluate the efficacy and safety of long-term use of Ryeqo (relugolix/estradiol/norethisterone acetate). The RMP (version 1.0) is updated accordingly

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

### 5.3.25. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/II/0035/G

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Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Grouped variations consisting of: 1) extension of indication for treatment of paediatric patients (at least 4 weeks of age and weighing at least 3 kg) with pneumonia requiring supplemental oxygen (low- or high-flow oxygen) or other non-invasive ventilation at start of treatment based on interim results from study GS-US-540-5823: a phase 2/3 single-arm, open-label study to evaluate the safety, tolerability, pharmacokinetics and efficacy of remdesivir in participants from birth to <18 years of age with coronavirus (COVID-19); 2) extension of indication for treatment of paediatric patients (weighing at least 40 kg) who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19 based on data from 8 adolescent patients who were included in study GS-US-540-9012: a phase 3 randomized, double-blind placebo-controlled trial to evaluate the efficacy and safety of remdesivir treatment of COVID-19 in an outpatient setting. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 3.2) are updated accordingly

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

### 5.3.26. Remimazolam - BYFAVO (CAP) - EMEA/H/C/005246/X/0002

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Applicant: PAION Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength (50 mg powder for concentrate for solution for injection/infusion). The new presentation comes with a new indication to include the intravenous induction and maintenance of general anaesthesia (GA) in adults for Byfavo (remimazolam) 50 mg, based on final results from two pivotal trials: 1) study ONO-2745-05: a phase 2b/3, single-blind, randomised, parallel-group study assessing safety and efficacy in induction and maintenance of anaesthesia in American Society of Anesthesiologists (ASA) I/II patients (general surgery); 2) study CNS-7056-022: a phase 3, randomised, propofol controlled, parallel group, confirmatory single-blind efficacy and safety trial during induction and maintenance of anaesthesia in ASA III/IV patients. A new combined version of the SmPC,



labelling and package leaflet solely for the 50 mg strength and the GA indication is provided accordingly. The RMP (version 1.1) is updated accordingly. Finally, the MAH also requested an extension of the market protection by one additional year

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

### 5.3.27. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/II/0079

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include treatment of juvenile idiopathic arthritis (enthesitis-related arthritis and juvenile psoriatic arthritis) in patients 2 years and older whose disease has responded inadequately to, or who cannot tolerate, conventional therapy. 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 10.0) are updated in accordance

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

### 5.3.28. Tadalafil - ADCIRCA (CAP) - EMEA/H/C/001021/X/0035/G

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Grouped application consisting of: 1) extension application to introduce a new pharmaceutical form associated with a new strength (2 mg/ml oral suspension); 2) extension of indication to paediatric use from 6 months to 17 years based on study 4 (H6D-MC-LVHV [LVHV]): a 24-week placebo-controlled efficacy and safety study with an open-label long-term extension phase. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and labelling are updated accordingly. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template and editorial changes have been implemented. The RMP (version 9.1) is updated in accordance

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

### 5.3.29. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0039

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Extension of indication to include treatment of active ankylosing spondylitis for Xeljanz (tofacitinib) prolonged release. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. The RMP (version 18.1) is updated accordingly

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

### 5.3.30. Zanubrutinib - BRUKINSA (CAP) - EMEA/H/C/004978/II/0003

Applicant: BeiGene Ireland Ltd

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include treatment of adult patients with chronic lymphocytic leukaemia (CLL) or small lymphocytic leukaemia (SLL) based on results from: 1) study BGB-3111-304: an ongoing, international, phase 3, open-label, multiple-cohort, randomised study designed to evaluate the efficacy of zanubrutinib versus bendamustine plus rituximab (B+R) in patients with previously untreated CLL/SLL; 2) study BGB-3111-305: an ongoing, international phase 3, open-label, randomised study of zanubrutinib versus ibrutinib with relapsed/refractory (R/R) CLL/SLL. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are being updated. The package leaflet and the RMP (version 1.1) are updated in accordance. In addition, as part of the application the MAH requested a 1-year extension of the market protection

**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. Abemaciclib - VERZENIOS (CAP) - PSUSA/00010724/202109

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Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.2. Adefovir - HEPSERA (CAP) - PSUSA/00000060/202109

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Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.3. Amikacin<sup>5</sup> - ARIKAYCE LIPOSOMAL (CAP) - PSUSA/00010882/202109

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Applicant: Insméd Netherlands B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

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

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<sup>5</sup> Centrally authorised product(s) only

#### 6.1.4. Brolucizumab - BEOVU (CAP) - PSUSA/00010829/202110

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.5. Bupivacaine - EXPAREL LIPOSOMAL (CAP) - PSUSA/00010889/202110

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Applicant: Pacira Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.6. Cemiplimab - LIBTAYO (CAP) - PSUSA/00010780/202109

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Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.7. Cenobamate - ONTOZRY (CAP) - PSUSA/00010921/202109

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Applicant: Angelini S.p.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.8. Chenodeoxycholic acid<sup>6 7</sup> - CHENODEOXYCHOLIC ACID LEADIANT (CAP) - PSUSA/00010590/202110

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Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.9. Dacomitinib - VIZIMPRO (CAP) - PSUSA/00010757/202109

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Applicant: Pfizer Europe MA EEIG

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<sup>6</sup> Indicated for the treatment of inborn errors of primary bile acid synthesis due to sterol 27 hydroxylase deficiency (presenting as cerebrotendinous xanthomatosis (CTX)) in infants, children and adolescents aged 1 month to 18 years and adults

<sup>7</sup> Centrally authorised product(s) only

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

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#### 6.1.10. Dapagliflozin - EDISTRIDE (CAP); FORXIGA (CAP) - PSUSA/00010029/202110

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

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#### 6.1.11. Daptomycin - CUBICIN (CAP) - PSUSA/00000931/202109

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Applicant: Merck Sharp & Dohme B.V.  
PRAC Rapporteur: Pernille Harg  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

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#### 6.1.12. Dexamethasone<sup>8 9</sup> - NEOFORDEX (CAP) - PSUSA/00010480/202109

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Applicant: Laboratoires CTRS  
PRAC Rapporteur: Tiphaine Vaillant  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

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#### 6.1.13. Ebola vaccine (rDNA<sup>10</sup>, replication-incompetent) - MVABEA (CAP); ZABDENO (CAP) - PSUSA/00010857/202109

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Applicant(s): Janssen-Cilag International N.V.  
PRAC Rapporteur: Jean-Michel Dogné  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

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#### 6.1.14. Eltrombopag - REVOLADE (CAP) - PSUSA/00001205/202109

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Applicant: Novartis Europharm Limited  
PRAC Rapporteur: Eva Segovia  
Scope: Evaluation of a PSUSA procedure

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<sup>8</sup> Indicated in symptomatic multiple myeloma only

<sup>9</sup> Centrally authorised product(s) only

<sup>10</sup> Recombinant deoxyribonucleic acid

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

#### 6.1.15. Galcanezumab - EMGALITY (CAP) - PSUSA/00010733/202109

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Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.16. Hepatitis A (inactivated), hepatitis B (rDNA) vaccines (adsorbed) - AMBIRIX (CAP); TWINRIX ADULT (CAP); TWINRIX PAEDIATRIC (CAP) - PSUSA/00001593/202109

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Applicant(s): GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.17. Herpes zoster vaccine (recombinant, adjuvanted) – SHINGRIX (CAP) – PSUSA/00010678/202110

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Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope : Evaluation of a PSUSA procedure

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

#### 6.1.18. Idecabtagene vicleucel – ABECMA (CAP) – PSUSA/00010954/202109

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Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP<sup>11</sup>

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.19. Insulin aspart - FIASP (CAP); INSULIN ASPART SANOFI (CAP); KIRSTY (CAP); NOVOMIX (CAP); NOVORAPID (CAP) - PSUSA/00001749/202109

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Applicant(s): Mylan IRE Healthcare Limited (Kirsty), Novo Nordisk A/S (Fiasp, NovoMix, NovoRapid), Sanofi-aventis groupe (Insulin Aspart Sanofi)

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

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

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<sup>11</sup> Advanced therapy medicinal product

#### 6.1.20. Lusutrombopag - MULPLEO (CAP) - PSUSA/00010755/202109

Applicant: Shionogi B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.21. Mogamulizumab - POTELIGEO (CAP) - PSUSA/00010741/202109

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.22. Netupitant, palonosetron - AKYNZEO (CAP) - PSUSA/00010393/202110

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.23. Ofatumumab - KESIMPTA (CAP) - PSUSA/00010927/202109

Applicant: Novartis Ireland Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.24. Panitumumab - VECTIBIX (CAP) - PSUSA/00002283/202109

Applicant: Amgen Europe B.V.

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.25. Pitolisant - OZAWADE (CAP); WAKIX (CAP) - PSUSA/00010490/202109

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.26. Raltegravir - ISENTRESS (CAP) - PSUSA/00010373/202109

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.27. Riociguat - ADEMPAS (CAP) - PSUSA/00010174/202109

Applicant: Bayer AG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.28. Selinexor - NEXPOVIO (CAP) - PSUSA/00010926/202109

Applicant: Karyopharm Europe GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.29. Selumetinib - KOSELUGO (CAP) - PSUSA/00010936/202110

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.30. Siponimod - MAYZENT (CAP) - PSUSA/00010818/202109

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.31. Sofosbuvir, ledipasvir - HARVONI (CAP) - PSUSA/00010306/202110

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. Vinflunine - JAVLOR (CAP) - PSUSA/00003123/202109

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Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Eva Segovia

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. Filgrastim - ACCOFIL (CAP), FILGRASTIM HEXAL (CAP), GRASTOFIL (CAP), NIVESTIM (CAP), RATIOGRASTIM (CAP), TEVAGRASTIM (CAP), ZARZIO (CAP); NAP - PSUSA/00001391/202109

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Applicants: Accord Healthcare S.L.U. (Accofil, Grastofil), Hexal AG (Filgrastim Hexal), Pfizer Europe MA EEIG (Nivestim), Ratiopharm GmbH (Ratiograstim), Sandoz GmbH (Zarzio), Teva GmbH (Tevagrastim), various

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

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

#### 6.2.2. Measles, mumps, rubella, varicella vaccines (live) - PROQUAD (CAP); NAP - PSUSA/00001936/202109

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Applicants: Merck Sharp & Dohme B.V. (ProQuad), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

#### 6.2.3. Oseltamivir - TAMIFLU (CAP); NAP - PSUSA/00002225/202109

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Applicants: Roche Registration GmbH (Tamiflu), various

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

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



#### 6.2.4. Sodium oxybate<sup>12</sup> - XYREM (CAP); NAP - PSUSA/00010612/202110

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Applicants: UCB Pharma S.A. (Xyrem), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

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

#### 6.2.5. Teriparatide - FORSTEO (CAP), LIVOGIVA (CAP), MOVYMIA (CAP); TERROSA (CAP); NAP - PSUSA/00002903/202109

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Applicants: Eli Lilly Nederland B.V. (Forsteo), Gedeon Richter Plc. (Terrosa), STADA Arzneimittel AG (Movymia), Theramex Ireland Limited (Livogiva), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

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

#### 6.2.6. Thalidomide - THALIDOMIDE BMS (CAP); NAP - PSUSA/00002919/202110

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Applicants: Bristol-Myers Squibb Pharma EEIG (Thalidomide BMS), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

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

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

#### 6.3.1. Alfentanil (NAP) - PSUSA/00000082/202109

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Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.2. Ambrosia artemisiifolia<sup>13 14 15 16</sup> (NAP) - PSUSA/00010693/202110

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Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

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<sup>12</sup> Oral use only

<sup>13</sup> Allergen for therapy

<sup>14</sup> (302)

<sup>15</sup> Sublingual use only

<sup>16</sup> Medicinal product(s) authorised via decentralised procedure

Scope: Evaluation of a PSUSA procedure

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

### 6.3.3. Carmustine<sup>17</sup> (NAP) - PSUSA/00010348/202109

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Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

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

### 6.3.4. Opium (NAP) - PSUSA/00010670/202109

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Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

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

### 6.3.5. Sodium oxybate<sup>18</sup> (NAP) - PSUSA/00010613/202110

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Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

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

### 6.3.6. Tolterodine (NAP) – PSUSA/00002993/202109

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Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

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

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

None

## 6.5. Variation procedure(s) resulting from PSUSA evaluation

None

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<sup>17</sup> Implant(s) only

<sup>18</sup> Intravenous use only

## 6.6. Expedited summary safety reviews<sup>19</sup>

### 6.6.1. Coronavirus (COVID-19) vaccine (Ad26.COVS-S, recombinant) - JCOVDEN (previously COVID-19 VACCINE JANSSEN) (CAP) – EMEA/H/C/005737/MEA 014.9

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Tenth expedited summary safety report (SSR) for COVID-19 Vaccine Janssen (COVID-19 vaccine (Ad26.COVS-S, recombinant)) during the coronavirus disease (COVID-19) pandemic

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

### 6.6.2. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 014.1

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Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: First expedited summary safety report (SSR) for Nuvaxovid (COVID-19 vaccine (recombinant, adjuvanted)) during the coronavirus disease (COVID-19) pandemic

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

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

### 7.1. Protocols of PASS imposed in the marketing authorisation(s)<sup>20</sup>

#### 7.1.1. Tisagenlecleucel - KYMRIAHA (CAP) - EMEA/H/C/PSA/S/0080.1

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Applicant: Novartis Europharm Limited, ATMP<sup>21</sup>

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's responses to PSA/S/0080.1 [substantial amendment to a protocol previously agreed in November 2019 (PSP/S/0066.3) for registry study CCTL019B2401 to assess the long-term safety of patients with B lymphocyte malignancies treated with tisagenlecleucel] as per the request for supplementary information (RSI) adopted in January 2022

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

#### 7.1.2. Valproate (NAP) - EMEA/H/N/PSP/J/0075.7

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Applicant: Sanofi-Aventis Recherche & Développement (on behalf of a consortium)

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<sup>19</sup> Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC

<sup>20</sup> In accordance with Article 107n of Directive 2001/83/EC

<sup>21</sup> Advanced therapy medicinal product

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of the third interim report for drug utilisation study (DUS) extension (DUS ext.) to assess the effectiveness of the new risk minimisation measures and to further characterise the prescribing patterns for valproate and related substances, in Europe, using databases in Germany, France, Netherlands, Spain, Sweden and United Kingdom; together with an updated protocol (version 8) as a MAH's response to PSP/J/0075.6 [second interim report for a 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)]

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

## 7.2. Protocols of PASS non-imposed in the marketing authorisation(s)<sup>22</sup>

### 7.2.1. Botulinum toxin type A - NUCEIVA (CAP) - EMA/H/C/004587/MEA 002.3

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Applicant: Evolus Pharma B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Amendment to a previously agreed protocol for study EV-010: a non-interventional PASS for Nuceiva (botulinum toxin type A) in the treatment of moderate-to-severe glabellar lines

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

### 7.2.2. Brexucabtagene autoleucel - TECARTUS (CAP) - EMA/H/C/005102/MEA 005.2

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Applicant: Kite Pharma EU B.V., ATMP<sup>23</sup>

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 005.1 [protocol for study KT-EU-472-5966: a prescriber survey to assess prescribers' understanding of the risks of Tecartus (KTE-X19) to evaluate the effectiveness of risk minimisation activities, namely healthcare professional (HCP) educational materials and patient alert card (PAC) [final study report expected in September 2023] (from initial opinion/marketing authorisation(s) (MA))] as per the request for supplementary information (RSI) adopted in December 2021

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

### 7.2.3. Canagliflozin - INVOKANA (CAP) - EMA/H/C/002649/MEA 009.5

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 009.4 [amendment to a previously agreed protocol for a drug utilisation study (DUS) to evaluate the drug utilisation patterns of canagliflozin-

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<sup>22</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>23</sup> Advanced therapy medicinal product

containing medicines including off-label usage in type 1 diabetes mellitus (T1DM) and the risk of diabetic ketoacidosis (DKA) using EU databases on market uptake and exposure within the European Union] as per the request for supplementary information (RSI) adopted in December 2021

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

#### 7.2.4. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 008.5

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 008.4 [amendment to a previously agreed protocol for a drug utilisation study (DUS) to evaluate the drug utilisation patterns of canagliflozin-containing medicines including off-label usage in type 1 diabetes mellitus (T1DM) and the risk of diabetic ketoacidosis (DKA) using EU databases on market uptake and exposure within the European Union] as per the request for supplementary information (RSI) adopted in December 2021

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

#### 7.2.5. Darbepoetin alfa - ARANESP (CAP) - EMEA/H/C/000332/MEA 092.3

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Amendment to a previously agreed protocol for study 20190404 (listed as a category 3 study in the RMP): a retrospective cohort study to assess the use of erythropoiesis stimulating agents (ESAs) in subjects receiving myelosuppressive chemotherapy in Europe

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

#### 7.2.6. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/MEA 007.4

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 007.3 [amendment to a protocol previously agreed in November 2017 for study 109MS401 (ESTEEM): a multicentre, global, observational study to collect information on safety and to document the drug utilisation of Tecfidera (dimethyl fumarate) when used in routine medical practice in the treatment of relapsing multiple sclerosis] as per the request for supplementary information (RSI) adopted in September 2021

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

#### 7.2.7. Diroximel fumarate - VUMERITY (CAP) - EMEA/H/C/005437/MEA 002

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Protocol for study SE-VUM-12146 (listed as category 3 study in the RMP): an observational study utilising data from 'big data' multiple sclerosis registries to evaluate the long-term safety of Vumerity (diroximel fumarate) and Tecfidera (dimethyl fumarate) (from initial opinion/marketing authorisation(s) (MA))

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

#### 7.2.8. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 004.5

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Amendment to a previously agreed protocol as a response to MEA 010.4 [fifth monitoring interim report for study 1245.97: a non-interventional PASS assessing the risk of urinary tract malignancies in relation to empagliflozin exposure in patients with type 2 diabetes mellitus (T2DM): a multi-database European study [final clinical study report (CSR) expected in June 2021]] as per the request for supplementary information (RSI) adopted in October 2021

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

#### 7.2.9. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 006.7

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Amendment to a previously agreed protocol as a response to MEA 006.6 [fifth monitoring interim report for study 1245.97: a non-interventional PASS assessing the risk of urinary tract malignancies in relation to empagliflozin exposure in patients with type 2 diabetes mellitus (T2DM): a multi-database European study (final clinical study report (CSR) expected in June 2021)] as per the request for supplementary information (RSI) adopted in October 2021

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

#### 7.2.10. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 016

Applicant: Galapagos N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study GLPG0634-CL-413: a non-interventional, PASS of filgotinib in patients with moderately to severely active ulcerative colitis (a European multi registry-based study)

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

#### 7.2.11. Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/MEA 015

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Protocol for study 218065: a PASS to describe real-world safety and effectiveness of mepolizumab in paediatric eosinophilic granulomatosis with polyangiitis (EGPA) patients in Europe

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

#### 7.2.12. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/MEA 064.2

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Amendment to a previously agreed protocol for study 101MS411 (listed as a category 3 study in the RMP): an observational study utilising data from the US Tysabri outreach unified commitment to health (TOUCH) prescribing programme and selected EU multiple sclerosis (MS) registries to estimate the risk of progressive multifocal leukoencephalopathy (PML) and other serious opportunistic infections among patients who were exposed to a MS disease modifying treatment prior to treatment with Tysabri (natalizumab)

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

#### 7.2.13. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/MEA 002.4

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Menno van der Elst

Scope: Amendment to a previously agreed protocol for study PUMA-NER-6202: a randomised study to characterise the incidence and severity of diarrhoea in patients with early stage epidermal growth factor receptor 2 + (HER2+) breast cancer treated with neratinib and intensive loperamide prophylaxis versus neratinib and intensive loperamide prophylaxis plus a bile acid sequestrant in the first month of treatment

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

#### 7.2.14. Ofatumumab - KESIMPTA (CAP) - EMEA/H/C/005410/MEA 002.1

Applicant: Novartis Ireland Limited

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to MEA 002 [protocol for study OMB157G2407 (listed as category 3 study in the RMP): pregnancy outcomes intensive monitoring (PRIM) to evaluate pregnancy and infant outcomes in patients taking Kesimpta (ofatumumab)] as per the request for supplementary information (RSI) adopted in December 2021

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

#### 7.2.15. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/MEA 001.5

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Amendment to a previously agreed protocol for study P19-633: a post-marketing registry-based prospective cohort study of long-term safety of risankizumab in real world setting in Denmark and Sweden [final study report expected in December 2031] together with a statistical analysis plan (SAP)

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

#### 7.2.16. Risdiplam - EVRYSDI (CAP) - EMEA/H/C/005145/MEA 007.2

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: MAH's response to MEA 007.1 [protocol for study BN42833 - Risdiplam pregnancy surveillance study: a phase 4, non-interventional surveillance study [final study report expected in Q4/2031] (from initial opinion/marketing authorisation (MA))] as per the request for supplementary information (RSI) adopted in February 2022

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

#### 7.2.17. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 008.5

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 008.4 [updated protocol for study A3921312 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other safety events of interest among patients treated with tofacitinib for moderately to severely active rheumatoid arthritis (RA) within the British Society for Rheumatology Biologics Register-Rheumatoid Arthritis (BSRBR-RA) following on the recommendation of the signal on major adverse cardiovascular events (MACE) and malignancies excluding non-melanoma skin cancer (NMSC) (EPITT 19382) finalised in June 2021] as per the request for supplementary information adopted in December 2021

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

#### 7.2.18. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 009.5

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 009.4 [updated protocol for study A3921314 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other safety events of interest among patients treated with tofacitinib for moderately to severely active rheumatoid arthritis (RA) within the Swedish (ARTIS) register following on the recommendation of the signal on major adverse cardiovascular events (MACE) and malignancies excluding non-melanoma skin cancer (NMSC) (EPITT 19382) finalised in June 2021] as per the request for supplementary information adopted in December 2021

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



#### 7.2.19. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 010.5

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 010.4 [updated protocol for study A3921316 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other safety events of interest among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the Spanish registry of adverse events of biological therapies and biosimilars in rheumatoid diseases (BIOBADASER) following on the recommendation of the signal on major adverse cardiovascular events (MACE) and malignancies excluding non-melanoma skin cancer (NMSC) (EPITT 19382) finalised in June 2021] as per the request for supplementary information adopted in December 2021

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

#### 7.2.20. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 011.5

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 011.4 [updated protocol for study A3921317 (listed as a category 3 study in the RMP): a prospective non-interventional comparative active surveillance PASS of serious infection, malignancy, cardiovascular and other safety events of interest among patients treated with Xeljanz (tofacitinib) for moderately to severely active rheumatoid arthritis (RA) within the German registry Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT) following on the recommendation of the signal on major adverse cardiovascular events (MACE) and malignancies excluding non-melanoma skin cancer (NMSC) (EPITT 19382) finalised in June 2021] as per the request for supplementary information adopted in December 2021

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

#### 7.2.21. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 013.4

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 013.3 [protocol for study A3921344 (listed as a category 3 study in the RMP): an active surveillance, post-authorisation study to characterise the safety of tofacitinib in patients with moderately to severely active ulcerative colitis (UC) in the real-world setting using data from the Swedish Quality Register for Inflammatory Bowel Disease (SWIBREG) registry] as per the request for supplementary information (RSI) adopted in December 2021

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

#### 7.2.22. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 018

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study A3921407: a PASS surveillance programme among patients treated with tofacitinib for polyarticular course juvenile idiopathic arthritis and juvenile psoriatic arthritis (PsA) within the German Biologics in Paediatric Rheumatology Registry (BIKER) and within the Juvenile Arthritis Methotrexate/Biologics long-term Observation (JuMBO) biological register (from X/0024/G)

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

#### 7.2.23. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 019

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study A3921408: a PASS surveillance programme among patients treated with tofacitinib for polyarticular course juvenile idiopathic arthritis and juvenile psoriatic arthritis (PsA) within the Swedish juvenile idiopathic arthritis (JIA) clinical registry (from X/0024/G)

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

#### 7.2.24. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 020

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study A3921409: a PASS surveillance programme among patients treated with tofacitinib for polyarticular course juvenile idiopathic arthritis and juvenile psoriatic arthritis (PsA) within the UK juvenile idiopathic arthritis (JIA) biologics register (from X/0024/G)

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

#### 7.2.25. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 047

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study C4591038 (listed as a category 3 study in the RMP): a post conditional approval active surveillance study among individuals in Europe receiving the Pfizer BioNTech coronavirus disease 2019 (COVID-19) vaccine to investigate natural history of post-vaccination myocarditis and pericarditis

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

### 7.3. Results of PASS imposed in the marketing authorisation(s)<sup>24</sup>

#### 7.3.1. Lumacaftor, ivacaftor– ORKAMBI (CAP) - EMEA/H/C/PSR/S/0039

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Applicant: Vertex Pharmaceuticals

PRAC Rapporteur: Rhea Fitzgerald

Scope: Final report for study VX-14 809-108: an observational PASS to evaluate the utilisation patterns and long-term effects of lumacaftor and ivacaftor combination therapy in patients with cystic fibrosis

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

#### 7.3.2. Rivaroxaban – XARELTO (CAP) - EMEA/H/C/PSR/S/0027

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Applicant: Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Final study report comprising the pharmaco-epidemiological study programme of rivaroxaban use and potential adverse outcomes in routine clinical practice in the United Kingdom, Germany, the Netherlands and Sweden

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

### 7.4. Results of PASS non-imposed in the marketing authorisation(s)<sup>25</sup>

#### 7.4.1. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/II/0090

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Applicant: Genzyme Europe BV

PRAC Rapporteur: Nathalie Gault

Scope: Submission of the final report from non-interventional study AGLU06909/LTS13930: a prospective safety sub-registry to assess anaphylaxis and severe allergic reactions, and severe cutaneous and systemic immune complex mediated reactions with alglucosidase alfa treatment (Pompe registry report 2020 (in fulfillment of MEA024.15 and MEA025.15))

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

#### 7.4.2. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/II/0038

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Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Submission of the final study report (CSR) from PsOBest registry (listed as a category 3 study in the RMP): an observational study to assess the long-term safety and

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<sup>24</sup> In accordance with Article 107p-q of Directive 2001/83/EC

<sup>25</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

effectiveness of apremilast in routine clinical practice in Germany. The RMP (version 14.0) is updated accordingly

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

#### 7.4.3. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/II/0244

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Eva Segovia

Scope: Submission of the final report from study B1801310 (BIKER) (listed as a category 3 study in the RMP): an observational PASS of etanercept and methotrexate in the treatment of juvenile idiopathic arthritis (JIA) using data obtained from participants in the German Biologics JIA registry (BIKER) to monitor long-term safety and effectiveness of etanercept in the treatment of JIA in regular clinical practice

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

#### 7.4.4. Hepatitis B surface antigen - HEPLISAV B (CAP) - EMEA/H/C/005063/II/0014

Applicant: Dynavax GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report from study HBV25 (listed as a category 3 study in the RMP): a post-marketing observational surveillance study comparing the occurrence of acute myocardial infarction (AMI) in recipients of Heplisav B (hepatitis B surface antigen) with recipients of another hepatitis B vaccine. As a consequence, the MAH proposed the removal of AMI as an important potential risk from the list of safety concerns. The RMP (version 1.2) is updated accordingly

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

#### 7.4.5. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/II/0231

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report of the Remicade (infliximab) Anti-Rheumatic Therapy in Sweden (ARTIS) register study. The RMP (version 20.1) is updated accordingly and with revisions agreed in previous procedures

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

#### 7.4.6. Loxapine - ADASUVE (CAP) - EMEA/H/C/002400/II/0033

Applicant: Ferrer Internacional s.a.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update safety information on bronchospasm based on final results from study AMDC-204-401 EU PASS (listed as a category 3 study in the RMP): a post-authorisation observational study to

evaluate the safety of Adasuve (loxapine for inhalation) in agitated persons in routine clinical care (assessed in variation II/0032 finalised in May 2021). The package leaflet and labelling 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 Assessment Report

#### 7.4.7. Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/II/0051

Applicant: Amgen Europe B.V., ATMP<sup>26</sup>

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report from study 20180062 (listed as a category 3 study in the RMP) - an observational research study report (ORSR): a multinational, non-interventional, cross-sectional survey study for patients aged  $\geq 18$  years who have received Imlygic (talimogene laherparepvec) at least once in the 3 months prior to completing the survey to evaluate the effectiveness of patient-directed additional risk minimisation measures

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

#### 7.4.8. Velaglucerase alfa - VPRIV (CAP) - EMEA/H/C/001249/II/0049, Orphan

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Martin Huber

Scope: Submission of final physician data study results for study EUPASS 14255: an evaluation of the effectiveness of risk minimisation measures - a survey among healthcare professionals (HCPs) and patient/caregivers to assess their knowledge and attitudes on prescribing and home administration conditions of velaglucerase alfa (Vpriv) in 6 European countries

**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. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/MEA 002.4

Applicant: Merck Europe B.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Third yearly progress update report for study MS100070-0031 (listed as a category 3 study in the RMP): a non-interventional cohort study to assess characteristics and management of patients with Merkel cell carcinoma (MCC) in Germany [final study report expected in Q1/2024]

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

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<sup>26</sup> Advanced therapy medicinal product

### 7.5.2. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 006.4

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Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Semi-annual report (period covered 01 June 2021 to 30 November 2021) for study COVID-19 vaccines International Pregnancy Exposure Registry (C-VIPER) (listed as a category 3 study in the RMP): a pregnancy registry of women exposed to Vaxzevria (AZD1222 – COVID-19 vaccine) immediately before or during pregnancy (from initial opinion/marketing authorisation(s) (MA))

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

### 7.5.3. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/004054/MEA 003.3

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Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

Scope: Twelfth annual European Haemophilia Safety Surveillance (EUHASS) report for study 14149 (listed as a category 3 study in the RMP): evaluation of cases with adverse events (AEs) of special interest in the EUHASS registry

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

### 7.5.4. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 003.5

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Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Fourth interim report for a study (listed as a category 3 study in the RMP): a post authorisation safety of Spikevax (elasomeran) in the US - an enhanced pharmacovigilance study to provide additional evaluation of adverse events of special interest (AESI) and emerging validated safety signals [final clinical study report (CSR) expected in June 2023] (from initial opinion/marketing authorisation (MA)) and MAH's response to MEA 003.3 as per the response for supplementary information (RSI) adopted in November 2021

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

### 7.5.5. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 005.3

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Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Interim report for a study (listed as a category 3 study in the RMP): Moderna mRNA-1273 observational pregnancy outcome study to evaluate outcomes of pregnancies in females exposed to Spikevax (elasomeran) during pregnancy [final clinical study report (CSR) expected in June 2024]

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

#### 7.5.6. Lenvatinib - LENVIMA (CAP) - EMEA/H/C/003727/MEA 014.4

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Applicant: Eisai GmbH

PRAC Rapporteur: Annika Folin

Scope: First annual study progress report for study E7080-M000-508: an observational study to characterise hepatic related toxicity and overall safety profile in real-life conditions in the EU (Western population) in hepatocellular carcinoma (HCC) patients, including patients with Child-Pugh B

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

#### 7.5.7. Levofloxacin - QUINSAIR (CAP) - EMEA/H/C/002789/ANX 004.6

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Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Fourth annual interim report for a post-marketing, open-label, observational safety study of Quinsair (nebulised levofloxacin hemihydrate) in patients with cystic fibrosis and chronic *Pseudomonas aeruginosa* infection, using data collected through European cystic fibrosis registries [final clinical study report (CSR) expected in June 2022]

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

### 7.6. Others

#### 7.6.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/ANX 010.3

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Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to ANX 010.1 [feasibility report for a drug utilisation study (DUS) to assess compliance with the therapeutic indication and effectiveness of measures to minimise the risk of cardiovascular and cerebrovascular adverse events in close temporal association with Lemtrada (alemtuzumab) infusion and immune-mediated adverse reactions, as requested in the conclusions of the referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMEA/H/A-20/1483) finalised in 2019] as per the request for supplementary information (RSI) adopted in December 2021

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

#### 7.6.2. Avatrombopag - DOPTelet (CAP) - EMEA/H/C/004722/MEA 002.4

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Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 002.3 [feasibility assessment for study AVA-CLD-402: evaluation of the feasibility of conducting a PASS of Doptelet (avatrombopag) in patients with severe chronic liver disease (CLD) and of the use of potential European electronic health care databases] as per the request for supplementary information (RSI) adopted in

June 2021

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

### 7.6.3. Avatrombopag - DOPTLET (CAP) - EMEA/H/C/004722/MEA 003.1

---

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Eva Segovia

Scope: MAH's response to MEA 003 [feasibility assessment for a study to further characterise the long-term safety profile of avatrombopag in patients with primary chronic immune thrombocytopenia in European patient registers and electronic healthcare databases as requested in the conclusions of variation II/0004/G finalised in December 2020] as per the request for supplementary information (RSI) adopted in July 2021

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

### 7.6.4. Zanubrutinib - BRUKINSA (CAP) - EMEA/H/C/004978/MEA 002

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Applicant: BeiGene Ireland Ltd

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study LTE1 (listed as a category 3 study in the RMP): a phase 3, open-label study to evaluate the long-term safety and efficacy of zanubrutinib, as monotherapy or in combination, in patients with B-cell malignancies who are or were previously enrolled in a BeiGene parent study and who are still benefiting or may benefit from treatment with zanubrutinib, or who are willing to have long-term survival follow-up

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

## 7.7. Scientific Advice

None

## 7.8. Ongoing Scientific Advice

None

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

None



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

### 8.1. Annual reassessments of the marketing authorisation

#### 8.1.1. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/S/0029 (with RMP)

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Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

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. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/005208/R/0017 (with RMP)

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Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

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

#### 8.2.2. Imlifidase - IDEFIRIX (CAP) - EMEA/H/C/004849/R/0007 (without RMP)

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Applicant: Hansa Biopharma AB

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

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

#### 8.2.3. Larotrectinib - VITRAKVI (CAP) - EMEA/H/C/004919/R/0024 (without RMP)

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Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Conditional renewal of the marketing authorisation

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

#### 8.2.4. Tafasitamab - MINJUVI (CAP) - EMEA/H/C/005436/R/0003 (without RMP)

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Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

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

### 8.3. Renewals of the marketing authorisation

#### 8.3.1. Alectinib - ALECENSA (CAP) - EMEA/H/C/004164/R/0039 (without RMP)

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: 5-year renewal of the marketing authorisation

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

#### 8.3.2. Buprenorphine, naloxone - ZUBSOLV (CAP) - EMEA/H/C/004407/R/0019 (without RMP)

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Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

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

#### 8.3.3. Fluticasone furoate, umeclidinium, vilanterol - ELEBRATO ELLIPTA (CAP) - EMEA/H/C/004781/R/0026 (with RMP)

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Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Annika Folin

Scope: 5-year renewal of the marketing authorisation

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

#### 8.3.4. Fluticasone furoate, umeclidinium, vilanterol - TRELEGY ELLIPTA (CAP) - EMEA/H/C/004363/R/0023 (with RMP)

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Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Annika Folin

Scope: 5-year renewal of the marketing authorisation

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

#### 8.3.5. Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/R/0033 (without RMP)

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

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

**8.3.6. Human fibrinogen, human thrombin - VERASEAL (CAP) - EMEA/H/C/004446/R/0018 (without RMP)**

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Applicant: Instituto Grifols, S.A.

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

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

**8.3.7. Lutetium (<sup>177</sup>Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/R/0032 (without RMP)**

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Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

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

**8.3.8. Naloxone - NYXOID (CAP) - EMEA/H/C/004325/R/0014 (without RMP)**

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Applicant: Mundipharma Corporation (Ireland) Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

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

**8.3.9. Niraparib - ZEJULA (CAP) - EMEA/H/C/004249/R/0034 (without RMP)**

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Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

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

**8.3.10. Ritonavir - RITONAVIR MYLAN (CAP) - EMEA/H/C/004549/R/0015 (without RMP)**

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Applicant: Mylan Pharmaceuticals Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

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

**8.3.11. Tacrolimus - TACFORIUS (CAP) - EMEA/H/C/004435/R/0010 (without RMP)**

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Applicant: Teva B.V.

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PRAC Rapporteur: Ronan Grimes

Scope: 5-year renewal of the marketing authorisation

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

#### 8.3.12. Tivozanib - FOTIVDA (CAP) - EMEA/H/C/004131/R/0021 (without RMP)

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Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: 5-year renewal of the marketing authorisation

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

#### 8.3.13. Trastuzumab - ONTRUZANT (CAP) - EMEA/H/C/004323/R/0040 (with RMP)

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Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

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 CHMP or EMA

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

#### 10.1.1. Cholic acid – ORPHACOL (CAP) - EMEA/H/C/001250/II/0044

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Applicant: Laboratoires CTRS

PRAC Rapporteur: Sofia Trantza

Scope: PRAC consultation on a variation to update sections 4.3 and 4.5 of the SmPC in order to extend the currently existing contra-indication with phenobarbital in order to include primidone based on scientific literature. The package leaflet is updated accordingly. The MAH took the opportunity to submit a combined SmPC for both dosages, 50 mg and 250 mg, to introduce editorial changes and to update the contact details of the local representatives in the package leaflet

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

#### 10.1.2. [Cholic acid – ORPHACOL \(CAP\) - EMEA/H/C/001250/II/0045](#)

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Applicant: Laboratoires CTRS

PRAC Rapporteur: Sofia Trantza

Scope: PRAC consultation on a variation to update section 4.5 of the SmPC in order update the existing information regarding concomitant use of cholic acid (the active substance of Orphacol) and ursodeoxycholic acid based on scientific literature. The package leaflet is updated accordingly

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

#### 10.1.3. [Vildagliptin - GALVUS \(CAP\), JALRA \(CAP\), XILARX \(CAP\); vildagliptin, metformin - EUCREAS \(CAP\), ICANDRA \(CAP\), ZOMARIST \(CAP\)- EMA/H/C/WS2253](#)

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: PRAC consultation on a variation to update section 4.8 of the SmPC in order to add 'cutaneous vasculitis' as a new adverse drug reaction (ADR)

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

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

None

### 10.3. **Other requests**

None

### 10.4. **Scientific Advice**

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

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

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

None

### 11.2. Other requests

#### 11.2.1. Canagliflozin - CZ/H/1139/001-002/DC

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PRAC Lead: Eva Jirsová

Scope: PRAC consultation on the evaluation of an initial marketing authorisation application under the decentralised procedure for a generic canagliflozin-containing medicinal product, on request of Czechia

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

## 12. Organisational, regulatory and methodological matters

### 12.1. Mandate and organisation of the PRAC

#### 12.1.1. PRAC membership

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**Action:** For information

#### 12.1.2. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q1 2022

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**Action:** For discussion

#### 12.1.3. Vote by proxy

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None

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

#### 12.2.1. Joint PRAC/CAT recommendation on long-term safety and efficacy follow-up for patients using chimeric antigen receptor (CAR) T-cell therapy using European Society for Blood and Marrow Transplantation (EBMT) registry as data source

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**Action:** for adoption

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

None

### **12.4. Cooperation within the EU regulatory network**

#### **12.4.1. Coronavirus (COVID-19) pandemic - update**

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**Action:** For discussion

### **12.5. Cooperation with International Regulators**

None

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

None

### **12.7. PRAC work plan**

None

### **12.8. Planning and reporting**

#### **12.8.1. EU Pharmacovigilance system - quarterly workload measures and performance indicators – Q1 2022 and predictions**

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**Action:** For discussion

#### **12.8.2. Marketing authorisation applications (MAA) three-year forecast report**

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**Action:** For discussion

#### **12.8.3. PRAC workload statistics – Q1 2022**

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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 reporting

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

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None



#### 12.12.2. Additional monitoring

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None

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

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**Action:** For adoption

### 12.13. EudraVigilance database

#### 12.13.1. Activities related to the confirmation of full functionality

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None

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

#### 12.14.1. Risk management systems

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None

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

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None

#### 12.14.3. Risk management plan (RMP) of medicinal product(s) containing new active substance(s) - publications

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**Action:** For discussion

### 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. Impact of pharmacovigilance activities**

None

## **12.21. Others**

None

## **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/)