29 November 2021
EMA/PRAC/611142/2021
Human Medicines Division

# Pharmacovigilance Risk Assessment Committee (PRAC)

## Draft agenda for the meeting on 29 November-02 December 2021

Chair: Sabine Straus – Vice-Chair: Martin Huber

29 November 2021, 10:30 – 19:30, via teleconference

30 November 2021, 08:30 – 19:30, via teleconference

01 December 2021, 08:30 – 19:30, via teleconference

02 December 2021, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

13 December 2021, 09:00 – 12:00, via teleconference

**Disclaimers**

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

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

**Note on access to documents**

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

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# 1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 29 November – 02 December 2021. See December 2021 PRAC minutes (to be published post January 2022 PRAC meeting).

## 1.2. Agenda of the meeting on 29 November - 02 December 2021

**Action:** For adoption

## 1.3. Minutes of the previous meeting on 25-28 October 2021

**Action:** For adoption

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

## 2.1. Newly triggered procedures

None

## 2.2. Ongoing procedures

None

## 2.3. Procedures for finalisation

None

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

## 3.1. Newly triggered procedures

None

## 3.2. Ongoing procedures

None

### 3.2.1. Amfepramone (NAP) - EMEA/H/A-31/1501

Applicant(s): Artegodan GmbH, Temmler Pharma GmbH

PRAC Rapporteur: Anette Kirstine Stark; PRAC Co-rapporteur: Eva Jirsová

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

**Action:** For adoption of a revised timetable

## 3.3. Procedures for finalisation

None

## 3.4. Re-examination procedures[1]

None

## 3.5. Others

None

# 4. Signals assessment and prioritisation[2]

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

### 4.1.1. Canakinumab – ILARIS (CAP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of interstitial lung disease (ILD) and alveolar proteinosis

**Action:** For adoption of PRAC recommendation

EPITT 19736 – New signal

Lead Member State(s): DE

[1] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC
[2] 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. Dabigatran etexilate – PRADAXA (CAP)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of autoimmune haemolytic anaemia

**Action:** For adoption of PRAC recommendation

EPITT 19745 – New signal

Lead Member State(s): DK

### 4.1.3. Vildagliptin - GALVUS (CAP), JALRA (CAP), XILIARX (CAP); vildagliptin, metformin - EUCREAS (CAP), ICANDRA (CAP), ZOMARIST (CAP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Signal of cutaneous vasculitis

**Action:** For adoption of PRAC recommendation

EPITT 19742 – New signal

Lead Member State(s): SE

## 4.2. New signals detected from other sources

### 4.2.1. Abatacept – ORENCIA (CAP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Signal of acute respiratory distress syndrome (ARDS)

**Action:** For adoption of PRAC recommendation

EPITT 19751 – New signal

Lead Member State(s): FI

### 4.2.2. Atezolizumab - TECENTRIQ (CAP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Signal of optic neuritis

**Action:** For adoption of PRAC recommendation

EPITT 19747 – New signal

Lead Member State(s): PT

### 4.2.3. Coronavirus (COVID-19) mRNA[3] vaccine (nucleoside-modified) - SPIKEVAX (CAP)

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Signal of autoimmune hepatitis

**Action:** For adoption of PRAC recommendation

EPITT 19750 – New signal

Lead Member State(s): DK

### 4.2.4. Liraglutide – SAXENDA (CAP), VICTOZA (CAP)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Signal of cutaneous amyloidosis

**Action:** For adoption of PRAC recommendation

EPITT 19740 – New signal

Lead Member State(s): NL

### 4.2.5. Tozinameran (previously COVID-19 mRNA[4] vaccine (nucleoside modified)) - COMIRNATY (CAP)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of autoimmune hepatitis

**Action:** For adoption of PRAC recommendation

EPITT 19749 – New signal

Lead Member State(s): NL

## 4.3. Signals follow-up and prioritisation

### 4.3.1. Coronavirus (COVID-19) mRNA[5] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/SDA/033.2

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Signal of myocarditis and pericarditis

**Action:** For adoption of PRAC recommendation

[3] Messenger ribonucleic acid
[4] Messenger ribonucleic acid
[5] Messenger ribonucleic acid

EPITT 19713 – Follow-up to November 2021[6]

### 4.3.2. Olmesartan (NAP); olmesartan, amlodipine (NAP); olmesartan, hydrochlorothiazide (NAP); olmesartan medoxomil, amlodipine besilate, hydrochlorothiazide (NAP)

Applicant(s): various

PRAC Rapporteur: Martin Huber

Scope: Signal of autoimmune hepatitis

**Action:** For adoption of PRAC recommendation

EPITT 19258 – Follow-up to November 2021[7]

### 4.3.3. Tozinameran (previously COVID-19 mRNA[8] vaccine (nucleoside modified)) - COMIRNATY (CAP) - EMEA/H/C/005735/SDA/032.2

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of myocarditis and pericarditis

**Action:** For adoption of PRAC recommendation

EPITT 19712 – Follow-up to November 2021[9]

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

### 4.4.1. Coronavirus (COVID-19) mRNA[10] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0028

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of an updated RMP (version 2.1) to include myocarditis and pericarditis in the list of the safety concerns as an important identified risk, as requested in the outcome of the signal procedure on myocarditis and pericarditis (EPITT 19713) adopted in July 2021 (SDA 033)

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

### 4.4.2. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0044

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.4, 4.8 and 5.1 to add warnings and safety data on serious

[6] Held 25-28 October 2021
[7] Held 25-28 October 2021
[8] Messenger ribonucleic acid
[9] Held 25-28 October 2021
[10] Messenger ribonucleic acid

infections, viral reactivation, non-melanoma skin cancer and fractures. This is based on the final results from study A3921133 (listed as a category 3 study in the RMP): a PASS conducted to evaluate the safety of tofacitinib 5 mg and 10 mg compared to tumour necrosis factor inhibitor (TNFi) in adult subjects aged ≥50 years with moderately or severely active rheumatoid arthritis (RA) and with at least 1 additional cardiovascular (CV) risk factor, as requested in the outcome of the signal procedure (EPITT 19382) adopted in June 2021 (SDA 016). The package leaflet is updated accordingly. The RMP (version 21.1) is also updated in accordance. In addition, the MAH took the opportunity to update the outer carton (section 4 for oral solution) to include a total volume of 240 mL as requested in the conclusions of procedure X/0024/G adopted in June 2021

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

# 5. Risk management plans (RMPs)

## 5.1. Medicines in the pre-authorisation phase

### 5.1.1. Betaine anhydrous - EMEA/H/C/005637

Scope: Treatment of homocystinuria

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

### 5.1.2. Ciltacabtagene autoleucel - EMEA/H/C/005095, Orphan

Applicant: Janssen-Cilag International NV, ATMP[11]

Scope: Treatment of multiple myeloma

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

### 5.1.3. Daridorexant - EMEA/H/C/005634

Scope: Treatment of insomnia

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

### 5.1.4. Difelikefalin - EMEA/H/C/005612

Scope: Treatment of pruritus

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

### 5.1.5. Enfortumab vedotin - EMEA/H/C/005392

Scope: Treatment of locally advanced (LA) or metastatic urothelial cancer (mUC)

[11] Advanced therapy medicinal product

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

### 5.1.6. Gefapixant - EMEA/H/C/005476

Scope: Treatment of refractory or unexplained chronic cough

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

### 5.1.7. Gefapixant - EMEA/H/C/005884

Scope: Treatment of refractory or unexplained chronic cough

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

### 5.1.8. Molnupiravir - EMEA/H/C/005789

Scope: Treatment of coronavirus disease 2019 (COVID-19)

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

### 5.1.9. Opicapone - EMEA/H/C/005782

Scope: Treatment of Parkinson's disease and motor fluctuations

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

### 5.1.10. Relugolix - EMEA/H/C/005353

Scope: Treatment of adult patients with advanced prostate cancer

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

### 5.1.11. Sotrovimab – EMEA/H/C/005676

Scope: Treatment of coronavirus disease 2019 (COVID-19)

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

### 5.1.12. Teriparatide - EMEA/H/C/004932

Scope: Treatment of osteoporosis in postmenopausal women and in men at increased risk of fracture

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

### 5.1.13. Teriparatide - EMEA/H/C/005827

Scope : Treatment of osteoporosis

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

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

### 5.2.1. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP)- EMEA/H/C/005737/II/0018

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 2.2) in order to include thrombocytopenia as an important potential risk as per the outcome of the signal procedure on embolic and thrombotic events (SDA/018.1 - EPITT 19689) in May 2021 and the outcome of variation II/0006/G dated July 2021, to propose studies aimed at further characterisation of thrombosis with thrombocytopenia syndrome (TTS) and thrombocytopenia, following the outcome of the signal procedure on embolic and thrombotic events (SDA/018.1 - EPITT 19689) in May 2021, to include Guillain-Barré syndrome as an important identified risk as per the outcome of variation II/0012 dated July 2021. In addition, the MAH took the opportunity to update in the RMP to include the submission milestone dates for study VAC31518COV4001: a post-authorisation, observational study to assess the safety of Ad26.COV2.S (COVID-19 Vaccine Janssen) using health insurance claims and/or electronic health record (EHR) database(s) in the United States, and study VAC31518COV4002: a post-authorisation, observational study to assess the effectiveness of Ad26.COV2.S (COVID-19 Vaccine Janssen) using health insurance claims and/or electronic health record (EHR) database(s) in the United States

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

### 5.2.2. Coronavirus (COVID-19) mRNA[12] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0022

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of an updated RMP (version 2.0) to include clinical safety data from study mRNA-1273 P203 (NCT04649151): a phase 2/3, randomised, observer-blind, placebo-controlled study evaluating the safety, reactogenicity and effectiveness of the mRNA-1273 vaccine in healthy adolescents aged ≥ 12 to < 18 years

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

### 5.2.3. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/II/0040

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of an updated RMP (version 4.1) in order to add 'thrombosis in combination with thrombocytopenia' as an important potential risk as requested in the outcome of the signal procedure on immune thrombocytopenia (ITP) (EPITT 19678) adopted in July 2021 (SDA/034.1), to add acute macular neuroretinopathy, acute macular outer

[12] Messenger ribonucleic acid

retinopathy, paracentral acute middle maculopathy, paresthesia and dysaesthesia in the list of adverse events of special interest (AESI) as requested in the outcome of the signal procedure on acute macular outer retinopathy (EPITT 19703) adopted in July 2021 (SDA/065). In addition, the updated RMP include the removal of the enhanced active surveillance (EAS) studies D8111R00003 [EU], D8110R00001 [US], D8111C00004 [UK], the update of the important potential risk of 'nervous system disorders, including immune-mediated neurological conditions' to reflect the recent product information on Guillain-Barré syndrome (IB/0034) as requested in the outcome of fourth monthly summary safety update (MSSR) (MEA 027.3) adopted in July 2021. Finally, the updated RMP includes the addition of the UK effectiveness study D8111R00007 as per the CHMP conclusion (MEA 010.1) dated June 2021 and the addition of study D8111R00010 to assess the relationship between the exposure to COVID-19 vaccines and the risk of thrombotic thrombocytopenia syndrome

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

### 5.2.4. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/WS2158/0051; ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/WS2158/0063

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' regarding study B20-146 on the hepatocellular carcinoma (HCC) recurrence PASS to change its milestone due date from 'Q3 2021' to 'Q4 2021', following EMA's recommendation dated July 2021. In addition, the MAH took the opportunity to introduce few minor linguistic and typographical corrections in the product information of Exviera (dasabuvir) for the Hungarian, Latvian and Romanian translations

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

### 5.2.5. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0091/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of the submission of an updated RMP (version 28.0) in order to: 1) remove osteonecrosis outside the jaw (OOJ) including external auditory canal (OEAC) as an important potential risk; 2) remove immunogenicity following a significant change to the manufacturing process as missing information; 3) introduce changes study 20190038 (listed as a category 3 study/PASS in the RMP): a retrospective cohort database study to assess the potential increased risk of cardiovascular and cerebrovascular events among women with postmenopausal osteoporosis (PMO) and men with osteoporosis by adding the study objectives. In addition, the MAH took the opportunity to update the RMP in order to provide the date for the provision of the final study report for study 20190038 and to include the post-marketing exposure data from the last submitted PSUR (#13)

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

### 5.2.6. Romosozumab - EVENITY (CAP) - EMEA/H/C/004465/II/0010

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of an updated RMP (version 2.0) in order to remove 'immunogenicity' as an important identified risk revision 2 of GVP module V on 'Risk management systems', EMA guidance on immunogenicity assessment, and the available non-clinical, clinical and post-marketing data. In addition, the MAH took the opportunity to add 'cardiac arrythmia' as an important potential risk to the RMP and to update the protocol for the ongoing study OP0004: a European non-interventional PASS related to serious cardiovascular events of myocardial infarction and stroke, and all-cause mortality for romosozumab by the EU-ADR Alliance to include cardiac arrhythmias as specific events to monitor, and include a targeted follow-up questionnaire (FUQ) related to cardiac arrhythmias, in line with the outcome of the signal procedure on cardiac arrhythmia (EPITT 19629) adopted in May 2021. The MAH took also the opportunity to introduce minor changes in the PASS protocols of studies OP0004, OP0005: a European non-interventional PASS related to adherence to the risk minimization measures for romosozumab by the EU-ADR Alliance, and OP0006: European non-interventional PASS related to serious infections for romosozumab by the EU-ADR Alliance

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

### 5.2.7. Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/WS2064/0043; VIHUMA (CAP) - EMEA/H/C/004459/WS2064/0024

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 11) to remove the following completed studies: 1) study GENA-05: immunogenicity, efficacy and safety of treatment with simoctocog alfa in previously untreated patients with severe haemophilia A; 2) study GENA-15: extension study for patients who completed GENA-05 (NuProtect)- to investigate immunogenicity, efficacy and safety of treatment with simoctocog alfa. As a consequence, 'safety in previously untreated patients', 'children < 2 years' and 'immune tolerance induction' are removed as missing information in the list of safety concerns. Finally, the RMP is brought in line with revision 2 of GVP module V on 'Risk management systems'

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

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

### 5.3.1. Adalimumab - IMRALDI (CAP) - EMEA/H/C/004279/II/0048/G

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) introduction of an additional concentration of 40 mg/0.4 mL (same 40 mg strength) for the solution for subcutaneous injection in pre-filled syringe (PFS) and pre-filled pen (PFP) with a shelf life for the active substance of 24 months when stored at or below -60°C and a shelf life and storage conditions for the finished product of 12 months when stored at 5 ± 3°C and up to 31 days at 25°C; 2) change of the composition in excipients for the proposed 40 mg/0.4 mL solution for injection in PFS and

PFP; 3) addition of 2 presentations: 1 PFS and 1 PFP with 2 alcohol pads each for the proposed 40 mg/0.4 mL solution for injection; 4) addition of 2 presentations: 2 PFSs and 2 PFPs with 2 alcohol pads each for the proposed 40 mg/0.4 mL solution for injection; 5) addition of 2 presentations: 4 PFSs and 4 PFPs with 4 alcohol pads each for the proposed 40 mg/0.4 mL solution for injection; 6) addition of 2 presentations: 6 PFSs and 6 PFPs with 6 alcohol pads each for the proposed 40 mg/0.4 mL solution for injection. The RMP (version 7.0) is updated accordingly. The MAH took the opportunity to introduce minor updated throughout the product information and implement various editorial changes in Module 3

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

### 5.3.2. Adalimumab - YUFLYMA (CAP) - EMEA/H/C/005188/X/0005

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application to introduce a new strength of 80 mg solution for injection. The RMP (version 1.1) is updated accordingly

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

### 5.3.3. Anakinra - KINERET (CAP) - EMEA/H/C/000363/II/0086

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Anette Kirstine Stark

Scope: Extension of indication to include treatment of coronavirus disease 2019 (COVID-19) in adult patients with pneumonia who are at risk of developing severe respiratory failure. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 5.7) are updated in accordance

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

### 5.3.4. Apalutamide - ERLEADA (CAP) - EMEA/H/C/004452/II/0017

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section 5.3 of the SmPC in order to update non-clinical information based on final results from study TOX11338 (in completion of MEA 006): a 2-year study to better characterize the carcinogenic potential of JNJ-56021927-AAA (apalutamide) by oral gavage in rats. The RMP (version 4.1) is updated accordingly. In addition, the MAH took the opportunity to include general information in the RMP regarding study TITAN (PCR3002): a phase 3 randomized, placebo-controlled, double-blind study of apalutamide plus androgen deprivation therapy (ADT) versus ADT in subjects with metastatic hormone-sensitive prostate cancer (mHSPC)

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

### 5.3.5. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0066

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Submission of the final report for study WO29635 (listed as a category 3 study activity): a phase 1B/2 study of the safety and pharmacology of atezolizumab administered with or without bacille Calmette-Guérin (BCG) in patients with high risk non muscle-invasive bladder cancer. The RMP (version 22.0) is updated accordingly. The RMP also includes a revision of the due date for the submission of the final clinical study report (CSR) for study MO39171 (TAIL): a phase 3/4, single arm, multicentre study of atezolizumab to investigate long-term safety and efficacy in previously-treated patients with locally advanced or metastatic non-small cell lung cancer (TAIL)

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

### 5.3.6. Autologous peripheral blood T cells CD[13]4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - TECARTUS (CAP) - EMEA/H/C/005102/WS2206/0015; axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/WS2206/0045

Applicant: Kite Pharma EU B.V., ATMP[14]

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2 and 4.4 of the SmPC and Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' in order to add statements for the use of Tecartus (autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured) and Yescarta (axicabtagene ciloleucel) exceptionally during shortage of tocilizumab following the 'CAT recommendation for the use of chimeric antigen receptor (CAR)-T cell-based therapies in EU during shortages of tocilizumab'. The RMP for both products are updated accordingly (version 1.2 for Tecartus and version 5.2 for Yescarta)

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

### 5.3.7. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/II/0029/G

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Grouped variations consisting of: 1) extension of indication to include treatment of severe alopecia areata in adult patients. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 12.1) are updated in accordance; 2) update of the RMP (version 12.1) regarding study I4V-MC-B011 (listed as a category 3 study in the RMP): a retrospective cohort study to assess the safety of baricitinib compared with other therapies used in the treatment of rheumatoid arthritis in

[13] Cluster of differentiation
[14] Advanced therapy medicinal product

Nordic countries to change the end of data collection for the atopic dermatitis cohort from 'December 2026' to 'December 2027' and the subsequent final study report milestone from 'December 2027' to 'December 2028'

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

### 5.3.8. Bosutinib - BOSULIF (CAP) - EMEA/H/C/002373/II/0050/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of an update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to reflect results from: 1) study B1871039 (listed as a specific obligation (SOB) in Annex II): a phase 4 safety and efficacy study of bosutinib in patients with Philadelphia chromosome positive chronic myeloid leukaemia (CML) previously treated with one or more tyrosine kinase inhibitors. As a consequence, the study is removed from Annex II-E on 'Specific obligations to complete post-authorisation measures for the conditional marketing authorisation' of the product information and the MAH requested a switch from the conditional marketing authorisation to a full marketing authorisation; 2) study B1871040 (listed a category 3 study in the RMP): an open-label bosutinib treatment extension study for subjects with CML who have previously participated in bosutinib studies B1871006 or B1871008. The package leaflet is updated accordingly. The RMP (version 6.0) is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives for Belgium, Luxemburg, Germany and Northern Ireland in the package leaflet. The MAH also requested the deletion of the medicinal product from the additional monitoring list

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

### 5.3.9. 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

### 5.3.10. Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/II/0023, Orphan

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of fibroblast growth factor 23 (FGF23)-related hypophosphataemia in tumour-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumours that cannot be curatively resected or localised in patients aged 1 year and over, based on data from two ongoing open-label clinical studies, namely: 1) study UX023T-CL201: a phase 2 open-label trial to assess the efficacy and

safety of burosumab in subjects with TIO or epidermal nevus syndrome (ENS)-associated osteomalacia, 2) study KRN23-002: a phase 2 open-label trial to assess the efficacy and safety of burosumab in patients with TIO or ENS (144-week data and 88-week data respectively). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 4.0) are updated accordingly. The MAH also applied for one additional year of market protection

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

### 5.3.11. Dengue tetravalent vaccine (live, attenuated) - DENGVAXIA (CAP) - EMEA/H/C/004171/II/0016/G

Applicant: Sanofi Pasteur

PRAC Rapporteur: Sonja Hrabcik

Scope: Grouped variations consisting of an update of section 4.5 of the SmPC to include co-administration data on Gardasil/Cervarix (human papillomavirus vaccine) and Adacel (tetanus toxoid/reduced diphtheria toxoid and acellular/pertussis vaccine (adsorbed)) based on the final results of studies (listed as category 3 studies in the RMP) dedicated to immunogenicity and safety of the concomitant administration, namely: 1) study CYD66: a phase 3b, randomised, multicentre, open-label study in 688 subjects aged from 9 to 60 years in the Philippines; 2) study CYD67: a phase 3b, randomised, open-label, multicentre study in 528 subjects aged 9 to 13 years in Malaysia; 3) study CD71: a phase 3b, randomised, open-label, multicentre study in 480 female subjects aged 9 to 14 years in Mexico. The package leaflet and the RMP (version 6.1) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

### 5.3.12. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0073

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include treatment of relapsing remitting multiple sclerosis (RRMS) in paediatrics patients from 10 years of age and over based on results from study 109MS306: an open-label, randomized, multicentre, multiple-dose, active-controlled, parallel-group, efficacy and safety study of dimethyl fumarate in children from 10 to less than 18 years of age with RRMS with optional open-label extension. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 11.4) is updated in accordance. The MAH requested an extension of the market protection of one additional year in line with the guidance on elements required to support the significant clinical benefit in comparison with existing therapies of a new therapeutic indication in accordance with Article 14(11) of Regulation (EC) 726/2004

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

### 5.3.13. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/II/0060

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to add the treatment of patients with heart failure with preserved ejection fraction (HFpEF) based on the results from clinical study 1245.110 (EMPEROR-Preserved): a phase 3 randomised, double-blind trial to evaluate efficacy and safety of once daily empagliflozin 10 mg compared to placebo, in patients with chronic HFpEF. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 16.0) are updated accordingly. In addition, the statement 'sodium free' was moved from section 2 of the SmPC to section 4.4 in line with the latest quality review of documents (QRD) template (version 10.2 Rev.1). The MAH took the opportunity to include minor linguistic changes to the national translations of the product information. Further, the MAH applied for an additional year of market protection

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

### 5.3.14. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0068

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of section 4.4 of the SmPC in order to add baseline monitoring in addition to the current warnings for periodic monitoring of cardiac failure and cardiac arrhythmias in patients receiving ibrutinib. The package leaflet and the RMP (version 18.1) are updated accordingly

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

### 5.3.15. Insulin degludec - TRESIBA (CAP) - EMEA/H/C/002498/II/0054

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.6 and 5.1 of the SmPC in order to include new clinical data from the pregnancy trial EXPECT: a trial comparing the effect and safety of insulin degludec versus insulin detemir, both in combination with insulin aspart, in the treatment of pregnant women with type 1 diabetes (T1DM). The package leaflet is updated in accordance. The RMP (version 9.0) is also updated accordingly

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

### 5.3.16. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/II/0033, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Annika Folin

Scope: Submission of the final report for the final analysis of overall survival (OS) for study C16010 (listed as an obligation in Annex II): a phase 3, randomised, double-blind multicentre study comparing ixazomib in combination with lenalidomide and dexamethasone (LenDex) versus placebo plus LenDex in adult patients with relapsed and/or refractory multiple myeloma. Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' and the RMP (version 7.0) are updated accordingly

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

## 5.3.17. Lanadelumab - TAKHZYRO (CAP) - EMEA/H/C/004806/II/0022, Orphan

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.8 and 5.1 of the SmPC to reflect the result of study DX-2930-04 (HELP study extension): an open-label study to evaluate the long-term safety and efficacy of lanadelumab (DX-2930) for prevention against acute attacks of hereditary angioedema (HAE). The RMP (version 2.0) is updated accordingly and in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template). In addition, the MAH took the opportunity to include a refrigeration statement for the multi-pack pre-filled syringe in the product information

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

## 5.3.18. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/II/0046

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an alternative study: an evaluation of the effect of lomitapide treatment on major adverse cardiovascular events (MACE) in patients with homozygous familial hypercholesterolemia (LILITH) to the currently agreed protocol for study on the effects of lomitapide on carotid and aortic atherosclerosis in patients treated with lomitapide in usual care (CAPTURE) in order to propose an evaluation of the effect of lomitapide treatment on MACE in patients with homozygous familial hypercholesterolemia. As a consequence, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' and the RMP (version 6.4) are updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.2)

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

## 5.3.19. Lorlatinib - LORVIQUA (CAP) - EMEA/H/C/004646/II/0015

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to include the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously not treated with an ALK inhibitor based on results from study 1006 (CROWN) (listed as a specific obligation (SOB) in Annex II): a phase 3 randomised open-label study of lorlatinib monotherapy versus crizotinib monotherapy in the first-line treatment of patients with advanced ALK-positive NSCLC. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 3.0) are updated accordingly. In addition, the applicant proposed to downgrade the SOB to conduct a single arm study in patients who progressed after alectinib or ceritinib to a recommendation and convert the conditional marketing authorisation to a full marketing authorisation (MA)

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

## 5.3.20. Lutetium ($^{177}$Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/II/0030, Orphan

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC based on pivotal study NETTER-1: a multicentre, stratified, open, randomized, comparator-controlled, parallel-group phase 3 study comparing treatment with Luthatera (($^{177}$Lu) oxodotreotide) to octreotide long acting release (LAR) in patients with inoperable, progressive, somatostatin receptor positive midgut carcinoid tumours. Additionally, updates are proposed in the product information to correct some information based on currently approved data. The package leaflet and the RMP (version 2.0) are updated accordingly. The MAH took the opportunity to update the details of local representatives in the package leaflet

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

## 5.3.21. Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/X/0042

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension application to introduce a new strength of 40 mg for Nucala (mepolizumab) solution for injection in a pre-filled syringe for subcutaneous use to be used in children aged 6 to 11 years. The RMP (version 8.0) is updated accordingly

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

## 5.3.22. Octocog alfa - KOVALTRY (CAP) - EMEA/H/C/003825/II/0038

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.8 and 5.1 of the SmPC to include data from LEOPOLD kids part B: a long term efficacy open-label programme in severe haemophilia A disease (previously submitted as Art 46; an addendum on biomarker data is included in this submission) and extension study results. In addition, an editorial revision in section 4.2 and a clarification in section 6.5 of the SmPC are proposed. The package leaflet is updated accordingly. The MAH took the opportunity to correct a typo in the Greek product information. The RMP (version 4.1) is updated and brought in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template)

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

## 5.3.23. Padeliporfin - TOOKAD (CAP) - EMEA/H/C/004182/II/0013

Applicant: STEBA Biotech S.A

PRAC Rapporteur: Maia Uusküla

Scope: Extension of indication to modify the wording of the existing indication to treatment of adult patients with previously untreated, unilateral, low-risk, adenocarcinoma of the prostate with a life expectancy ≥ 10 years and clinical stage T1c or T2a, International Society of Urological Pathology (ISUP) grade group ≤ 2, based on high-resolution biopsy strategies, prostate-specific antigen (PSA) ≤ 10 ng/mL, low core positivity. As a consequence, section 4.1 of the SmPC is updated. The RMP (version 6.0) is updated accordingly

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

## 5.3.24. Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - ADJUPANRIX (CAP) - EMEA/H/C/001206/II/0074

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include use in children from 6 months to <18 years for Adjupanrix (pandemic influenza vaccine (H5N1)) based on the results of the following studies: 1) study H5N1-013: a phase 2, non-randomised, open-label study to evaluate the safety and immunogenicity in children aged 6 to 35 months; 2) study H5N1-032: a phase 3, randomised, open, active-controlled study to evaluate the safety and immunogenicity in children aged 3 to 17 years. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 13) are updated in accordance. Further, the MAH proposed to update section 4.4 with information on sodium and potassium content in line with the excipient guideline, as well as to add some wording on traceability. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.2). Finally, the MAH introduced minor editorial changes throughout the product information

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

## 5.3.25. Patisiran - ONPATTRO (CAP) - EMEA/H/C/004699/II/0022, Orphan

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC to confirm that the safety profile of pasitiran in liver transplant recipients is comparable to data in patients without liver transplant, based on final results from study ALN-TTR02-008: a global phase 3b, open-label, extension study to evaluate safety, efficacy and pharmacokinetics of patisiran in patients with hereditary transthyretin-mediated amyloidosis (HATTR amyloidosis) with disease progression post-orthotopic liver transplant (OLT). The package leaflet and the RMP (version 1.1) are updated accordingly. In addition, the MAH took the opportunity to make some minor changes to the English product information and to update to local representatives in Cyprus, Malta, and United Kingdom changed to 'United Kingdom [Northern Ireland]' in line with the latest quality review of documents (QRD) template (version 10.2 Rev. 1). Finally, the MAH implemented minor linguistic changes and typographical error corrections in the Italian product information translation

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

## 5.3.26. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0108

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include the adjuvant treatment in monotherapy of adults with renal cell carcinoma (RCC) at intermediate-high or high risk of recurrence following nephrectomy or following nephrectomy and resection of metastatic lesions. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 35.1) are updated accordingly

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

## 5.3.27. Pyronaridine, artesunate - PYRAMAX (Art 58[15]) - EMEA/H/W/002319/II/0023/G

Applicant: Shin Poong Pharmaceutical Co., Ltd.

PRAC Rapporteur: Nathalie Gault

Scope: Grouped variations consisting of the submission of the final clinical study reports (CSR) of two completed studies: 1) study SP-C-021-15 (listed as a category 3 study in the RMP): a phase 3b/4 cohort event monitoring study conducted in Central Africa to evaluate the safety in patients after the local registration of Pyramax (pyronaridine/artesunate) (CANTAM study); 2) study SP-C-026-18: a randomized open-label exploratory study to determine the efficacy of different treatment regimens of Pyramax (pyronaridine/artesunate) in asymptomatic carriers of Plasmodium falciparum mono-infections. This non-imposed study was conducted in Gambia and Zambia and compared asymptomatic subjects with parasitaemia dosed according to the approved label of 3-day dosing with 2-day and 1-day dosing. As a consequence, sections 4.2, 4.4, 4.6, 4.8 and 5.1 are updated. The package leaflet is updated in accordance. The RMP (version 17) is also updated accordingly and in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template)

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

## 5.3.28. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/II/0016

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include treatment of adults with pneumonia not requiring supplemental oxygen (moderate coronavirus-19 (COVID-19)) based on: 1) part A of study GS-US-540-5774: a phase 3, randomized, open-label, multicentre study comparing 2 remdesivir (RDV) regimens (5 days and 10 days) versus standard of care in 584 participants with moderate COVID 19; 2) study CO-US-540-5776 (adaptive COVID-19 treatment trial (ACTT)): a National Institute of Allergy and Infectious Diseases (NIAID)-sponsored phase 3, multicentre, adaptive, randomized, double blind, placebo controlled trial on the safety and efficacy study of investigational therapeutics for the treatment of COVID-19. As a consequence, sections 4.1 and 5.1 of the SmPC are updated. The package leaflet and the

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

RMP (version 1.2) are updated in accordance

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

## 5.3.29. Ruxolitinib - JAKAVI (CAP) - EMEA/H/C/002464/II/0053

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to include treatment of patients with graft versus host disease (GvHD) aged 12 years and older who have inadequate response to corticosteroids or other systemic therapies. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8. 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 13.0) are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives for the Netherlands in the package leaflet

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

## 5.3.30. Saxagliptin - ONGLYZA (CAP) - EMEA/H/C/001039/WS2098/0053; saxagliptin, metformin hydrochloride - KOMBOGLYZE (CAP) - EMEA/H/C/002059/WS2098/0051

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study D1680C00016 (MEASURE HF) (listed as a category 3 study in the RMP): a 24-week, multicentre, randomised, double-blind, parallel group, placebo-controlled study to investigate the effects of saxagliptin and sitagliptin on cardiac dimensions and function in patients with type 2 diabetes mellitus (T2DM) and heart failure. The RMP (version 16) is updated accordingly

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

## 5.3.31. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/II/0076

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to introduce a new posology regimen for adult plaque psoriasis patients and psoriatic arthritis patients with concomitant moderate to severe plaque psoriasis based on the final results of study CAIN457A2324 (and exposure-response modelling): a randomised, double-blind, multicentre study assessing short (16 weeks) and long-term efficacy (up to 1 year), safety, and tolerability of sub-cutaneous secukinumab in subjects of body weight 90 kg or higher with moderate to severe chronic plaque-type psoriasis. The package leaflet and the RMP (version 9.0) are updated accordingly

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

## 5.3.32. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/II/0034

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nathalie Gault

Scope: Update of section 4.8 of the SmPC to add 'dyspepsia' as a new adverse drug reaction (ADR) and to include further information on the frequency of 'dyspepsia' and 'anaemia' specific to initial 2-step triple combination therapy, based on: 1) study AC-065A308 (TRITON) : a randomised, double-blind, placebo-controlled, parallel-group, phase 3b, efficacy and safety study comparing triple oral combination therapy (selexipag, macitentan, tadalafil) with double oral combination therapy (placebo, macitentan, tadalafil) in newly diagnosed, treatment-naïve participants with pulmonary arterial hypertension (PAH); 2) study AC-065A404 (TRACE): a randomised, double-blind, placebo-controlled, parallel-group, exploratory phase 4 study in participants with PAH to assess the effect of selexipag on daily life physical activity and participant's self-reported symptoms and their impacts. The package leaflet and the RMP (version 9.2) are updated accordingly

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

## 5.3.33. Selinexor - NEXPOVIO (CAP) - EMEA/H/C/005127/II/0001/G

Applicant: Karyopharm Europe GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations consisting of: 1) extension of indication for Nexpovio (selinexor) in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy; 2) addition of a new pack size (8 tablets) to align with the dose modification guidance for the new indication. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 6.5 of the SmPC are updated accordingly. Annex II is updated to reflect the completion of the specific obligation. The labelling, package leaflet and RMP (version 1.1) are updated in accordance

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

## 5.3.34. Siponimod - MAYZENT (CAP) - EMEA/H/C/004712/X/0007

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension application to add a new strength of 1 mg film-coated tablet. The RMP (version 3.0) is updated in accordance

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

## 5.3.35. Sugammadex - BRIDION (CAP) - EMEA/H/C/000885/II/0042

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to change posology recommendations and update safety, efficacy and pharmacokinetic information in children and adolescents (2-17 years) following P46/025 and based on final results from study P089MK8616: a phase 4 double-blind, randomised, active comparator-controlled clinical trial to study the efficacy, safety and pharmacokinetics of sugammadex (MK-8616) for reversal

of neuromuscular blockade in paediatric participants. In addition, the MAH took the opportunity to implement some minor editorial changes throughout the product information. The package leaflet is updated in accordance and the MAH took the opportunity to update the list of local representatives. The RMP (version 7.2) is also updated accordingly and in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template)

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

## 5.3.36. Ticagrelor - BRILIQUE (CAP) - EMEA/H/C/001241/II/0049

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include, in co-administration with acetylsalicylic acid (ASA), the prevention of stroke in adult patients with acute ischaemic stroke or transient ischaemic attack (TIA), based on the final results of study D5134C00003 (THALES): a phase 3, international, multicentre, randomised, double-blind, placebo-controlled study to investigate the efficacy and safety of ticagrelor and ASA compared with ASA in the prevention of stroke and death in patients with acute ischaemic stroke or transient ischaemic attack. 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 13.0) are updated in accordance

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

## 5.3.37. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/II/0044, Orphan

Applicant: Novartis Europharm Limited, ATMP[16]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of adult patients with follicular lymphoma (FL) after two or more lines of therapy who are refractory, or relapsed during or within 6 months after completion of anti-CD[17]20 antibody maintenance, or relapsed after autologous haematopoietic stem cell transplantation (HSCT). 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 4.0) are updated accordingly. The MAH took the opportunity to introduce minor editorial corrections throughout the product information to bring in line with the latest quality review of documents (QRD) template (version 10.2). Module 3 is also updated to include the incoming FL material characterisation, final product characterisation and FL batch analyses data

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

## 5.3.38. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/II/0101

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment of coronavirus disease 2019

[16] Advanced therapy medicinal product
[17] Cluster of differentiation

(COVID-19) in hospitalised adults who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation. As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.8, 5.1 and 5.2 of the SmPC for RoActemra (tocilizumab) 20 mg/mL concentrate for solution for infusion are updated. The package leaflet and the RMP (version 27.0) are updated in accordance. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.2 Rev. 1)

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

### 5.3.39. 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

### 5.3.40. Trametinib - MEKINIST (CAP) - EMEA/H/C/002643/II/0051

Applicant: Novartis Europharm Limited

PRAC Rapporteur: David Olsen

Scope: Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations in hepatic impairment and update pharmacokinetic information based on final results from study MEC116354 (listed as a category 3 study in the RMP): a phase 1 trial of single agent trametinib (GSK1120212) in advanced cancer patients with hepatic dysfunction. The RMP (version 18) is updated accordingly

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

# 6. Periodic safety update reports (PSURs)

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

### 6.1.1. Abiraterone - ZYTIGA (CAP) - PSUSA/00000015/202104

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

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

### 6.1.2. Acalabrutinib - CALQUENCE (CAP) - PSUSA/00010887/202104

Applicant: AstraZeneca AB

PRAC Rapporteur: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

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

### 6.1.3. Andexanet alfa - ONDEXXYA (CAP) - PSUSA/00010764/202104

Applicant: Alexion Europe SAS

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

### 6.1.4. Apixaban - ELIQUIS (CAP) - PSUSA/00000226/202105

Applicants: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

### 6.1.5. Atezolizumab - TECENTRIQ (CAP) - PSUSA/00010644/202105

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

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

### 6.1.6. Avatrombopag - DOPTELET (CAP) - PSUSA/00010779/202105

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

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

### 6.1.7. Axicabtagene ciloleucel - YESCARTA (CAP) - PSUSA/00010703/202104

Applicant: Kite Pharma EU B.V. ATMP[18]

PRAC Rapporteur: Anette Kirstine Stark

[18] Advanced therapy medicinal product

Scope: Evaluation of a PSUSA procedure

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

### 6.1.8. Basiliximab - SIMULECT (CAP) - PSUSA/00000301/202104

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

### 6.1.9. Brigatinib - ALUNBRIG (CAP) - PSUSA/00010728/202104

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

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

### 6.1.10. Cefiderocol - FETCROJA (CAP) - PSUSA/00010849/202105

Applicant: Shionogi B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

### 6.1.11. Cerliponase alfa - BRINEURA (CAP) - PSUSA/00010596/202104

Applicant: BioMarin International Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

### 6.1.12. Conestat alfa - RUCONEST (CAP) - PSUSA/00000873/202104

Applicant: Pharming Group N.V

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

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

### 6.1.13. Crizanlizumab - ADAKVEO (CAP) - PSUSA/00010888/202105

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

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

### 6.1.14. Delamanid - DELTYBA (CAP) - PSUSA/00010213/202104

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

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

### 6.1.15. Dolutegravir, rilpivirine - JULUCA (CAP) - PSUSA/00010689/202105

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

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

### 6.1.16. Durvalumab - IMFINZI (CAP) - PSUSA/00010723/202104

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

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

### 6.1.17. Ebola Zaire vaccine (live, attenuated) - ERVEBO (CAP) - PSUSA/00010834/202105

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

### 6.1.18. Empagliflozin - JARDIANCE (CAP); empagliflozin, metformin - SYNJARDY (CAP) – PSUSA/00010388/202104

Applicant(s): Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

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

### 6.1.19. Epoetin theta - BIOPOIN (CAP); EPORATIO (CAP) - PSUSA/00001240/202104

Applicant(s): ratiopharm GmbH (Eporatio), Teva GmbH (Biopoin)

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

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

### 6.1.20. Erenumab - AIMOVIG (CAP) - PSUSA/00010699/202105

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

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

### 6.1.21. Eslicarbazepine acetate - ZEBINIX (CAP) - PSUSA/00001267/202104

Applicant: Bial - Portela & Cª, S.A.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

### 6.1.22. Everolimus[19] - AFINITOR (CAP) - PSUSA/00010268/202103

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

### 6.1.23. Everolimus[20] - VOTUBIA (CAP) - PSUSA/00001343/202103

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

### 6.1.24. Febuxostat - ADENURIC (CAP) - PSUSA/00001353/202104

Applicant: Menarini International Operations Luxembourg S.A.

[19] Indicated for advanced renal cell carcinoma, advanced breast cancer, advanced neuroendocrine tumours (gastrointestinal, lung, pancreatic cancers) (NET)
[20] Indicated for subependymal giant cell astrocytoma (SEGA), renal angiomyolipoma, refractory seizures

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

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

### 6.1.25. Fenofibrate, pravastatin - PRAVAFENIX (CAP) - PSUSA/00001363/202104

Applicant: Laboratoires SMB s.a.

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

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

### 6.1.26. Fexinidazole - FEXINIDAZOLE WINTHROP (Art 58[21]) - EMEA/H/W/002320/PSUV/0008

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUR procedure

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

### 6.1.27. Fluticasone furoate - AVAMYS (CAP) - PSUSA/00009154/202104

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

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

### 6.1.28. Fostamatinib - TAVLESSE (CAP) - PSUSA/00010819/202104

Applicant: Instituto Grifols, S.A.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

### 6.1.29. Gemtuzumab ozogamicin - MYLOTARG (CAP) - PSUSA/00010688/202105

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

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

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

### 6.1.30. Givosiran - GIVLAARI (CAP) - PSUSA/00010839/202105

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

### 6.1.31. Glasdegib - DAURISMO (CAP) - PSUSA/00010859/202105

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

### 6.1.32. Glycopyrronium bromide, formoterol - BEVESPI AEROSPHERE (CAP) - PSUSA/00010739/202104

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

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

### 6.1.33. Hepatitis B surface antigen - HEPLISAV B (CAP) - PSUSA/00010919/202105

Applicant: Dynavax GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

### 6.1.34. Insulin lispro - HUMALOG (CAP); INSULIN LISPRO SANOFI (CAP); LIPROLOG (CAP); LYUMJEV (CAP) - PSUSA/00001755/202104

Applicant(s): Eli Lilly Nederland B.V. (Humalog, Liprolog, Lyumjev), Sanofi-aventis groupe (Insulin lispro Sanofi)

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

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

### 6.1.35. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - PSUSA/00010868/202104

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

### 6.1.36. Laronidase - ALDURAZYME (CAP) - PSUSA/00001830/202104

Applicant: Genzyme Europe BV

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

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

### 6.1.37. Lumacaftor, ivacaftor - ORKAMBI (CAP) - PSUSA/00010455/202105

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

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

### 6.1.38. Lumasiran - OXLUMO (CAP) - PSUSA/00010884/202105

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

### 6.1.39. Meningococcal group a, c, w135, y conjugate vaccine[22] - MENQUADFI (CAP); NIMENRIX (CAP) - PSUSA/00010044/202104

Applicant(s): Sanofi Pasteur (MenQuadfi), Pfizer Europe MA EEIG (Nimenrix)

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

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

### 6.1.40. Ozanimod - ZEPOSIA (CAP) - PSUSA/00010852/202105

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

[22] Conjugated to tetanus toxoid carrier protein

Scope: Evaluation of a PSUSA procedure

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

### 6.1.41. Padeliporfin - TOOKAD (CAP) - PSUSA/00010654/202105

Applicant: STEBA Biotech S.A

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

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

### 6.1.42. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) - PSUSA/00010501/202105

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

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

### 6.1.43. Parathyroid hormone - NATPAR (CAP) - PSUSA/00010591/202104

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

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

### 6.1.44. Pemigatinib - PEMAZYRE (CAP) - PSUSA/00010923/202104

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

### 6.1.45. Prasterone[23] - INTRAROSA (CAP) - PSUSA/00010672/202105

Applicant: Endoceutics S.A.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

[23] Pessary, vaginal use only

### 6.1.46. Radium ($Ra^{223}$) dichloride - XOFIGO (CAP) - PSUSA/00010132/202105

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

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

### 6.1.47. Regadenoson - RAPISCAN (CAP) - PSUSA/00002616/202104

Applicant: GE Healthcare AS

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

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

### 6.1.48. Remdesivir - VEKLURY (CAP) - PSUSA/00010840/202105

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

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

### 6.1.49. Rurioctocog alfa pegol - ADYNOVI (CAP) - PSUSA/00010663/202105

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

### 6.1.50. Selpercatinib - RETSEVMO (CAP) - PSUSA/00010917/202105

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

### 6.1.51. Sotagliflozin - ZYNQUISTA (CAP) - PSUSA/00010766/202104

Applicant: Guidehouse Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

### 6.1.52. Susoctocog alfa - OBIZUR (CAP) - PSUSA/00010458/202105

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

### 6.1.53. Tafamidis - VYNDAQEL (CAP) - PSUSA/00002842/202105

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

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

### 6.1.54. Temsirolimus - TORISEL (CAP) - PSUSA/00002887/202103

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

### 6.1.55. Thiotepa[24] - TEPADINA (CAP); THIOTEPA RIEMSER (CAP) - PSUSA/00002932/202103

Applicant(s): Adienne S.r.l. S.U. (Tepadina), Riemser Pharma GmbH (Thiotepa Riemser)

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

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

### 6.1.56. Tolvaptan[25] - JINARC (CAP) - PSUSA/00010395/202105

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

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

[24] Centrally authorised product(s) only
[25] Indicated for adults with autosomal dominant polycystic kidney disease (ADPKD)

### 6.1.57. Tolvaptan[26] - SAMSCA (CAP) - PSUSA/00002994/202105

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

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

### 6.1.58. Vedolizumab - ENTYVIO (CAP) - PSUSA/00010186/202105

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

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

### 6.1.59. Volanesorsen - WAYLIVRA (CAP) - PSUSA/00010762/202105

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

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. Capecitabine - CAPECITABINE ACCORD (CAP); CAPECITABINE MEDAC (CAP); ECANSYA (CAP); XELODA (CAP); NAP - PSUSA/00000531/202104

Applicants: Accord Healthcare S.L.U. (Capecitabine Accord), KRKA, d.d., Novo mesto (Ecansya), medac Gesellschaft fur klinische Spezialpraparate mbH (Capecitabine medac), Roche Registration GmbH (Xeloda), various

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

### 6.2.2. Mycophenolate mofetil - CELLCEPT (CAP); MYCLAUSEN (CAP); MYCOPHENOLATE MOFETIL TEVA (CAP); MYFENAX (CAP); NAP - mycophenolic acid (NAP) - PSUSA/00010550/202105

Applicants: Passauer Pharma GmbH (Myclausen), Roche Registration GmbH (CellCept), Teva B.V. (Mycophenolate mofetil Teva, Myfenax), various

[26] Indicated for adults with hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH)

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

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

### 6.2.3. Olopatadine - OPATANOL (CAP); NAP - PSUSA/00002211/202104

Applicants: Novartis Europharm Limited (Opatanol), various

PRAC Rapporteur: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

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

### 6.2.4. Tacrolimus[27] - ADVAGRAF (CAP); ENVARSUS (CAP); MODIGRAF (CAP); NAP - PSUSA/00002839/202103

Applicants: Astellas Pharma Europe B.V. (Advagraf, Modigraf), Chiesi Farmaceutici S.p.A. (Envarsus), various

PRAC Rapporteur: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

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

### 6.2.5. Tacrolimus[28] - PROTOPIC (CAP); NAP - PSUSA/00002840/202103

Applicants: LEO Pharma A/S (Protopic), various

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

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

### 6.2.6. Ulipristal acetate[29] - ELLAONE (CAP); NAP - PSUSA/00003074/202105

Applicants: Laboratoire HRA Pharma (ellaOne), various

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

[27] Systemic formulation(s) only
[28] Topical formulation(s) only
[29] Indicated for female emergency contraception only

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

### 6.3.1. Amlodipine besilate, ramipril (NAP); amlodipine, hydrochlorothiazide, ramipril (NAP); hydrochlorothiazide, ramipril (NAP) - PSUSA/00010774/202103

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

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

### 6.3.2. Argipressin (NAP) - PSUSA/00010749/202103

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

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

### 6.3.3. Bacterial lysate of haemophilus influenzae, klebsiella pneumoniae, moraxella catarrhalis, staphylococcus aureus, streptococcus mitis, streptococcus pneumoniae, streptococcus pyogenes (NAP); bacterial lysate of haemophilus influenzae, klebsiella pneumoniae, moraxella catarrhalis, staphylococcus aureus, streptococcus pneumoniae, streptococcus pyogenes (NAP); streptococcus pneumoniae, streptococcus agalactiae, staphylococcus aureus, haemophilus influenzae (NAP) - PSUSA/00002786/202103

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

### 6.3.4. Budesonide[30] (NAP) - PSUSA/00000449/202104

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

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

### 6.3.5. Captopril, hydrochlorothiazide (NAP) - PSUSA/00000536/202104

Applicant(s): various

[30] Nationally authorised product(s) only

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

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

### 6.3.6. Carmustine[31] (NAP) - PSUSA/00010349/202104

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

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

### 6.3.7. Chloroquine (NAP) - PSUSA/00000685/202104

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

### 6.3.8. Chlorprothixene (NAP) - PSUSA/00000717/202103

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

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

### 6.3.9. Cytarabine (NAP) - PSUSA/00000911/202103

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

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

### 6.3.10. Deoxycholic acid (NAP) - PSUSA/00010525/202104

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

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

[31] Powder and solvent for solution for infusion only

### 6.3.11. Dexamethasone, netilmicin (NAP) - PSUSA/00010854/202104

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

### 6.3.12. Dexamethasone, tobramycin[32] (NAP) - PSUSA/00000979/202103

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

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

### 6.3.13. Dihydroergotamine (NAP) - PSUSA/00001075/202104

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

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

### 6.3.14. Docosanol (NAP) - PSUSA/00010092/202104

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

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

### 6.3.15. Fentanyl[33] [34] (NAP) - PSUSA/00001370/202104

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

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

### 6.3.16. Human anti-d immunoglobulin (NAP) - PSUSA/00001614/202103

Applicant(s): various

[32] Ophthalmic and otic use only
[33] Transdermal patches and solution for injection only
[34] Nationally authorised product(s) only

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

### 6.3.17. Human prothrombin complex (NAP) - PSUSA/00001638/202104

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

### 6.3.18. Hydroxychloroquine (NAP) - PSUSA/00001693/202104

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

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

### 6.3.19. Hydrochlorothiazide, quinapril (NAP) - PSUSA/00002592/202104

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

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

### 6.3.20. Isotretinoin[35] (NAP) - PSUSA/00010488/202105

Applicant(s): various

PRAC Lead: Krõõt Aab

Scope: Evaluation of a PSUSA procedure

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

### 6.3.21. Ivermectin[36] (NAP) - PSUSA/00010376/202104

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

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

[35] Oral formulation(s) only
[36] For topical use only

### 6.3.22. Latanoprost[37] (NAP) - PSUSA/00001832/202104

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

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

### 6.3.23. Metformin (NAP) - PSUSA/00002001/202104

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

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

### 6.3.24. Methoxyflurane (NAP) - PSUSA/00010484/202105

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

### 6.3.25. N(2)-L-alanyl-L-glutamine (NAP) - PSUSA/00003158/202103

Applicant(s): various

PRAC Lead: Alexandra Maria Spurni

Scope: Evaluation of a PSUSA procedure

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

### 6.3.26. Nadroparin (NAP) - PSUSA/00002104/202103

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

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

### 6.3.27. Nitrendipine (NAP) - PSUSA/00002171/202103

Applicant(s): various

PRAC Lead: Jan Neuhauser

[37] Except medicinal product(s) with paediatric indication(s)

Scope: Evaluation of a PSUSA procedure

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

### 6.3.28. Ofloxacin[38] (NAP) - PSUSA/00002203/202104

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

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

### 6.3.29. Ofloxacin[39] (NAP) - PSUSA/00002204/202104

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

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

### 6.3.30. Oxaliplatin (NAP) - PSUSA/00002229/202104

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

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

### 6.3.31. Oxycodone (NAP) - PSUSA/00002254/202104

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

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

### 6.3.32. Ozenoxacin (NAP) - PSUSA/00010651/202105

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

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

[38] For systemic use only
[39] For topical use only

### 6.3.33. Pholcodine (NAP) - PSUSA/0002396/202105

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

**Action:** For preliminary discussion

### 6.3.34. Pholcodine, biclotymol, chlorphenamine maleate (NAP) - PSUSA/00010437/202104

Applicant(s): various

PRAC Lead: Rugilė Pilvinienė

Scope: Evaluation of a PSUSA procedure

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

### 6.3.35. Plasma protein fraction (NAP) - PSUSA/00002449/202104

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

### 6.3.36. Praziquantel (NAP) - PSUSA/00002503/202104

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

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

### 6.3.37. Promestriene[40] (NAP) - PSUSA/00009271/202103

Applicant(s): various

PRAC Lead: Alexandra Maria Spurni

Scope: Evaluation of a PSUSA procedure

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

### 6.3.38. Quinapril (NAP) - PSUSA/00002591/202104

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

[40] Cream and vaginal capsule(s) only

Scope: Evaluation of a PSUSA procedure

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

### 6.3.39. Risedronate (NAP) - PSUSA/00002648/202103

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

### 6.3.40. Tafluprost (NAP) - PSUSA/00002843/202104

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

### 6.3.41. Terlipressin (NAP) - PSUSA/00002905/202104

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

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

### 6.3.42. Tobramycin[41] (NAP) - PSUSA/00009317/202103

Applicant(s): various

PRAC Lead: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

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

### 6.3.43. Triamcinolone[42] (NAP) - PSUSA/00010292/202103

Applicant(s): various

PRAC Lead: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

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

[41] Ophthalmic and otic use only
[42] Intraocular formulation(s) only

### 6.3.44. Valganciclovir (NAP) - PSUSA/00003089/202103

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

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

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

### 6.4.1. Arsenic trioxide - TRISENOX (CAP) - EMEA/H/C/000388/LEG 051

Applicant: Teva B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Cumulative review including all available data of cases of paresis, bone marrow necrosis, deafness, melanoma, pancreatic cancer, squamous cell carcinoma and toxic epidermal necrolysis following the addition of these adverse drug reactions (ADRs) in the US product information at the FDA's request, as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00000235/202009) adopted in June 2021

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

### 6.4.2. Leflunomide - ARAVA (CAP) - EMEA/H/C/000235/LEG 058.1

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to LEG 058 [cumulative review of cases of skin ulcer in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001837/202009) adopted in May 2021] as per the request for supplementary information (RSI) adopted in October 2021

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

### 6.4.3. Tolvaptan - JINARC (CAP) - EMEA/H/C/002788/LEG 008.1

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to LEG 008 [review of cases of rapid correction of hyponatremia and neurological sequelae as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010395/202005) adopted in January 2021] as per the request for supplementary information (RSI) adopted in June 2021

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

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

### 6.5.1. Arsenic trioxide - TRISENOX (CAP) - EMEA/H/C/000388/II/0076

Applicant: Teva B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section 4.6 of the SmPC in order to update information on pregnancy and contraception in male patients as requested in the conclusions of the last PSUR single assessment (PSUSA) procedure (PSUSA/00000235/202009) adopted in June 2021. The package leaflet is updated accordingly

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

### 6.5.2. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/II/0025

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC concerning immunogenicity and loss of efficacy due to anti-emicizumab antibodies as requested in the conclusions of the latest periodic safety update report single assessment (PSUSA) procedure (PSUSA/00010668/202011) adopted in June 2021, together with a review of haemorrhagic cases as requested in the conclusions of the PSUSA procedure (PSUSA/00010668/202005) finalised in January 2021. The RMP (version 3.0) is updated accordingly

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

### 6.5.3. Lurasidone - LATUDA (CAP) - EMEA/H/C/002713/II/0036

Applicant: Aziende Chimiche Riunite Angelini Francesco A.C.R.A.F. S.p.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.8 of the SmPC to amend the frequency of adverse drug reactions (ADRs) in adults, as well as to add 'syncope' and 'cerebrovascular accident' as reminded in the conclusions of the last PSUR single assessment (PSUSA) procedure (PSUSA/00010114/202010) adopted in June 2021. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to combine all the dosages in a single version of the product information, to update the list of local representatives in the package leaflet and to bring the product information in line with the latest quality review of documents (QRD) template (version 10.2 Rev. 1)

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

### 6.5.4. Tozinameran (previously COVID-19 mRNA[43] vaccine (nucleoside modified)) - COMIRNATY (CAP) - EMEA/H/C/005735/II/0080

Applicant: BioNTech Manufacturing GmbH

[43] Messenger ribonucleic acid

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 4.4 of the SmPC in order to amend an existing warning on anxiety-related reactions to add 'numbness' based on the outcome of the ninth monthly summary safety report (MSSR) (MEA 002.8) finalised in October 2021. In addition, the MAH took the opportunity to make minor editorial changes throughout the product information

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

## 6.6. Expedited summary safety reviews[44]

### 6.6.1. Coronavirus (COVID-19) mRNA[45] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 011.9

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Tenth expedited monthly summary safety report (MSSR) for Spikevax (COVID-19 mRNA vaccine (nucleoside-modified)) during the coronavirus disease (COVID-19) pandemic

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

### 6.6.2. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) – EMEA/H/C/005737/MEA 014.7

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Eighth expedited monthly summary safety report (MSSR) for COVID-19 Vaccine Janssen (COVID-19 vaccine (Ad26.COV2-S, recombinant)) during the coronavirus disease (COVID-19) pandemic

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

### 6.6.3. Tozinameran (previously COVID-19 mRNA[46] vaccine (nucleoside modified)) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 002.10

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Eleventh expedited monthly summary safety report (MSSR) for Comirnaty (COVID-19 mRNA vaccine (nucleoside-modified)) during the coronavirus disease (COVID-19) pandemic

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

[44] 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
[45] Messenger ribonucleic acid
[46] Messenger ribonucleic acid

# 7. Post-authorisation safety studies (PASS)

## 7.1. Protocols of PASS imposed in the marketing authorisation(s)[47]

### 7.1.1. Evinacumab – EVKEEZA (CAP) – EMEA/H/C/PSP/S/0096

Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Annika Folin

Scope: Protocol for a study to evaluate long-term effects of evinacumab treatment in patients with homozygous familial hypercholesterolemia (HoFH), including safety outcomes in patients with HoFH who are ≥12 years old, frequency and outcomes of pregnancy in female patients with HoFH, atherosclerosis process over time in patients with HoFH who undergo cardiovascular imaging and frequency of cardiovascular imaging of patients with HoFH

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

### 7.1.2. Idecabtagene vicleucel – ABECMA (CAP) - EMEA/H/C/PSP/S/0097

Applicant: Bristol-Myers Squibb Pharma EEIG , ATMP[48]

PRAC Rapporteur: Annika Folin

Scope: Protocol for a non-interventional PASS of patients treated with idecabtagene vicleucel (ide-cel, bb2121) for multiple myeloma (MM) in the post-marketing setting to characterize the incidence and severity of selected adverse drug reactions (ADRs), as outlined in the product information, in patients treated with ide-cel in the post-marketing setting and to monitor for potential clinically important adverse events (AEs) that have not yet been identified as part of the ide-cel safety profile

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

## 7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[49]

### 7.2.1. Autologous peripheral blood T cells CD[50]4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - TECARTUS (CAP) - EMEA/H/C/005102/MEA 005.1

Applicant: Kite Pharma EU B.V., ATMP[51]

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 005 [protocol for study KT-EU-472-5966: a prescriber

[47] In accordance with Article 107n of Directive 2001/83/EC
[48] Advanced therapy medicinal product
[49] 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
[50] Cluster of differentiation
[51] Advanced therapy medicinal product

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 July 2021

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

### 7.2.2. Beclometasone, formoterol, glycopyrronium bromide - TRIMBOW (CAP) - EMEA/H/C/004257/MEA 002.1

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: MAH's response to MEA 002 [protocol for study CLI-05993BA1-05 (TRIBE): a multinational database cohort study to assess adverse cardiovascular and cerebrovascular outcomes in patients with chronic obstructive pulmonary disease initiating a fixed triple therapy containing beclometasone dipropionate, formoterol fumarate and glycopyrronium administered via dry powder inhaler (DPI) compared to pressurised metered dose inhaler (pMDI)] as per the request for supplementary information (RSI) adopted in July 2021

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

### 7.2.3. Berotralstat - ORLADEYO (CAP) - EMEA/H/C/005138/MEA 002.1

Applicant: BioCryst Ireland Limited

PRAC Rapporteur: Julia Pallos

Scope: MAH's response to MEA 002 [protocol for study BCX7353-401: a non-interventional post-authorisation study to evaluate safety, tolerability and effectiveness of berotralstat for patients with hereditary angioedema in a real-world setting (from initial opinion/marketing authorisation (MA))] as per the request for supplementary information (RSI) adopted in October 2021

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

### 7.2.4. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 009.4

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 009.3 [amended 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 July 2021

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

### 7.2.5. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 008.4

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 008.3 [amended 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 July 2021

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

### 7.2.6. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) - EMEA/H/C/005737/MEA 008.1

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 008 [protocol for study VAC31518COV4003 (listed as a category 3 study in the RMP): a post-authorisation, observational study to assess the safety of Ad26.COV2.S using electronic health record (EHR) database(s) in Europe (from initial opinion/marketing authorisation(s) (MA))] as per the request for supplementary information (RSI) adopted in July 2021

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

### 7.2.7. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) - EMEA/H/C/005737/MEA 010.1

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 010 [protocol for study VAC31518COV4001 (listed as a category 3 study in the RMP): a post-authorisation, observational study to assess the safety of Ad26.COV2.S (COVID-19 Vaccine Janssen) using health insurance claims and/or electronic health record (EHR) database(s) in the United States [final study report expected in December 2024]] as per the request for supplementary information (RSI) adopted in October 2021

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

### 7.2.8. Crizanlizumab - ADAKVEO (CAP) - EMEA/H/C/004874/MEA 004

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Laurence de Fays

Scope: Protocol for study CSEG101A2405 (listed as a category 3 study in the RMP): a non-interventional PASS - Registry-based study to assess long-term safety and pregnancy outcomes in patients with Sickle cell disease (SCD) using crizanlizumab

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

### 7.2.9. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/MEA 029.2

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Tiphaine Vaillant

Scope: Updated protocol for study Instanyl-5002 (listed as a category 3 study in the RMP): a non-interventional study to assess the effectiveness of updated educational materials on prescribers' knowledge and behaviour with respect to risks associated with Instanyl (fentanyl) off-label use [final clinical study report (CSR) expected in Q3 2023]

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

### 7.2.10. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 003.1

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 003 [protocol for study GS-EU-417-9047: a non-interventional PASS of filgotinib in the treatment of patients with moderate to severe active rheumatoid arthritis within the Anti-Rheumatic Treatment in Sweden (ARTIS) register [final report expected in Q2 2030]] as per the request for supplementary information (RSI) adopted in June 2021

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

### 7.2.11. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/MEA 020.4

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: MAH's response to MEA 020.3 [protocol for study CT-P13 4.8: an observational, prospective cohort study to evaluate the safety of Remsima (infliximab) subcutaneous in patients with rheumatoid arthritis (RA)] as per the request for supplementary information (RSI) adopted in June 2021

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

### 7.2.12. Lutetium ($^{177}$Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/MEA 001.8

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Substantial amendment to a protocol previously agreed in September 2018 for study A-LUT-T-E02-402 (SALUS study) (listed as a category 3 study in the RMP):: an international, non-interventional, post-authorisation long-term safety study of Lutathera (lutetium ($^{177}$Lu) oxodotreotide) in patients with unresectable or metastatic, well-differentiated, somatostatin receptor positive, gastro-enteropancreatic neuroendocrine tumours, together with the third quarterly progress report for study A-LUT-T-E02-402

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

## 7.2.13. Ofatumumab - KESIMPTA (CAP) - EMEA/H/C/005410/MEA 002

Applicant: Novartis Ireland Limited

PRAC Rapporteur: Amelia Cupelli

Scope: 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)

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

## 7.2.14. Ponesimod - PONVORY (CAP) - EMEA/H/C/005163/MEA 004

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: Protocol for study PCSNSP003693 (listed as a category 3 study in the RMP): a survey among healthcare professionals (neurologists treating patients with multiple sclerosis (MS) along with MS specialist nurses) in selected European countries to evaluate knowledge and behaviours required for the safe use of ponesimod

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

## 7.2.15. Satralizumab - ENSPRYNG (CAP) - EMEA/H/C/004788/MEA 002

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Protocol for study WN42856: a global observational 10-year single arm prospective study to assess the frequency of maternal, foetal, and infant adverse outcomes among women with neuromyelitis optica spectrum disorder (NMOSD) exposed to satralizumab during the 6 months prior to the last menstrual period or at any time during pregnancy (from initial opinion/marketing authorisation(s) (MA))

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

## 7.2.16. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/MEA 003.4

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nathalie Gault

Scope: MAH's response to MEA 003.3 [amendment to a protocol previously agreed in May 2017 for study AC-065A403: a PASS to evaluate risk minimisation measures for mEDication errors with Uptravi (selexipag) during the titration phase in patients with pulmonary arterial hypertension (PAH) in Clinical prAcTicE (EDUCATE)] as per the request for supplementary information (RSI) adopted in June 2021

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

## 7.2.17. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 008.4

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 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

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

## 7.2.18. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 009.4

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 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

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

## 7.2.19. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 010.4

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 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

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

## 7.2.20. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 011.4

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 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

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

## 7.2.21. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 013.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 013.2 [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 February 2021 and based 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

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

## 7.2.22. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 014.4

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 014.3 [protocol for study A3921321: a drug utilisation study (DUS) on the utilisation and prescribing patterns of Xeljanz (tofacitinib) in two European countries using administrative claims databases and national registries for assessment, as requested in the conclusions of the referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMEA/H/A-20/1485) finalised in November 2019] as per the request for supplementary information (RSI) adopted in July 2021

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

## 7.2.23. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 047.3

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 047.2 [protocol for study SWIBREG-UST UC: an observational PASS to describe the safety of ustekinumab and other ulcerative colitis treatments in a cohort of patients with ulcerative colitis using the Swedish Inflammatory

Bowel Disease Register (SWIBREG) as requested in the conclusions of variation II/071 finalised in July 2019 [final clinical study report (CSR) expected in May 2027]] as per the request for supplementary information (RSI) adopted in July 2021

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

### 7.2.24. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 048.3

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 048.2 [protocol for study SNDS-UST UC: an observational PASS to describe the safety of ustekinumab and other ulcerative colitis treatments in a cohort of patients with ulcerative colitis using the French administrative healthcare database (SNDS) as requested in the conclusions of variation II/071 finalised in July 2019 [final clinical study report (CSR) expected in May 2027]] as per the request for supplementary information (RSI) adopted in July 2021

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

### 7.2.25. Vosoritide - VOXZOGO (CAP) - EMEA/H/C/005475/MEA 005

Applicant: BioMarin International Limited

PRAC Rapporteur: Zane Neikena

Scope: Protocol for study 111-603: a multicentre, non-interventional study to evaluate long-term safety in patients with achondroplasia treated with Voxzogo (vosoritide) (from initial opinion/marketing authorisation(s) (MA))

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

## 7.3. Results of PASS imposed in the marketing authorisation(s)[52]

None

## 7.4. Results of PASS non-imposed in the marketing authorisation(s)[53]

### 7.4.1. Daunorubicin, cytarabine - VYXEOS LIPOSOMAL (CAP) - EMEA/H/C/004282/II/0017, Orphan

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Submission of the final clinical study report (CSR) for a post-marketing observational study to assess the nature, incidence and severity of infusion-related reactions in adult patients treated with Vyxeos liposomal (daunorubicin/cytarabine)

[52] In accordance with Article 107p-q of Directive 2001/83/EC
[53] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

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

### 7.4.2. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0092

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report for study 20190038 (listed as a category 3 study in the RMP): an observational retrospective cohort study assessing the incidence of cardiovascular and cerebrovascular events among postmenopausal women and men with osteoporosis who initiated treatment with denosumab or zoledronic acid

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

### 7.4.3. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/II/0028

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of the final study report for BO40853 (listed as a category 3 study in the RMP): a survey to prescribers and patients/carers to evaluate awareness, knowledge, and compliance to additional risk minimisation measures. The RMP (version 4.0) is updated accordingly

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

### 7.4.4. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/II/0030

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study B2311060 (listed as a category 3 study in the RMP): a non-interventional PASS of conjugated oestrogens/bazedoxifene (CE/BZA) in the US, with the aim to monitor the safety profile of Duavive (CE/BZA) in comparison to oestrogen and progestin combination hormone therapy (E+P HT)

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

### 7.4.5. Glycerol phenylbutyrate - RAVICTI (CAP) - EMEA/H/C/003822/II/0038/G, Orphan

Applicant: Immedica Pharma AB

PRAC Rapporteur: Ilaria Baldelli

Scope: Grouped variations consisting of: 1) submission of the final report for study HPN-100-014: a non-interventional registry study - a long-term registry of patients with urea cycle disorders (UCDs) conducted in the US; 2) submission of an updated RMP (version 7) to remove the important potential risks of carcinogenicity and phenylacetic acid (PAA) toxicity. The update to the RMP is based on the review of new and available data including the study report for HPN-100-014 and a new toxicological expert examination of pre-clinical carcinogenicity findings as well as a cumulative review of literature and post marketing data. In accordance with the proposed changes to the RMP, an update of Annex II is

requested to waive the imposed condition related to the non-interventional PASS on 'European post-authorisation registry for Ravicti (glycerol phenylbutyrate) oral liquid in partnership with the European registry and network for intoxication type metabolic diseases (E-IMD)'. The SmPC and package leaflet have been updated to delete the information on additional monitoring (including the black triangle)

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

### 7.4.6. Influenza vaccine surface antigen inactivated prepared in cell cultures - FLUCELVAX TETRA (CAP) - EMEA/H/C/004814/II/0023

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.6 of the SmPC in order to update information on pregnancy registry 130_110B (listed as a category 3 study in the RMP) on use in pregnant and breastfeeding women to evaluate pregnancy outcomes. The package leaflet and the RMP (version 3.1) are updated accordingly

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

### 7.4.7. 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

### 7.4.8. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/II/0116

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study 20170701 (listed as a category 3 study in the RMP): an observational study to assess the effectiveness of the Neulasta (pegfilgrastim) patient alert card and to measure medication errors related to the use of the on-body injector. The RMP (version 8.0) is updated accordingly

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

### 7.4.9. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/II/0038

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Submission of the final study report for study OBS12753 (listed as a category 3 study in the RMP): a prospective cohort study of long-term safety of teriflunomide in multiple sclerosis patients in Europe. The RMP (version 7.1) is updated accordingly

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

### 7.4.10. 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. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/MEA 002.8

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 002.7 [five-year interim report for study PTC124-GD-0250-DMD (listed as a category 3 study in the RMP): a post-approval registry observational study exploring the long-term of ataluren safety and effectiveness in usual care setting [final clinical study report (CSR) expected in April 2023]] as per the request for supplementary information (RSI) adopted in July 2021

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

### 7.5.2. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/ANX 002.2

Applicant: Kite Pharma EU B.V., ATMP[54]

PRAC Rapporteur: Anette Kirstine Stark

Scope: First annual interim report for study KT-EU-471-0117: a long-term, non-interventional study of recipients of Yescarta (axicabtagene ciloleucel) to evaluate the incidence rate and severity of adverse drug reactions (ADRs) and further evaluate and characterise the identified risks, potential risks and missing information (EU PAS EUPAS32539)

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

[54] Advanced therapy medicinal product

### 7.5.3. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/MEA 004.4

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: First interim report for study D3250R00042: a descriptive study of the incidence of malignancy in patients with severe asthma overall and among those receiving benralizumab and other therapies in real-world settings

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

### 7.5.4. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/MEA 008.9

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Fifth annual interim report for study CA209234 (listed as a category 3 study in the RMP): a PASS exploring the pattern of use, safety, and effectiveness of nivolumab in routine oncology practice [final clinical study report (CSR) expected in December 2024]

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

### 7.5.5. Semaglutide - OZEMPIC (CAP) - EMEA/H/C/004174/MEA 002.4

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Second study progress report for study NN9535-4447: an epidemiological database study to estimate the risk of pancreatic cancer in patients with type 2 diabetes mellitus (T2DM) taking semaglutide - a cohort study based on Nordic registry data [final clinical study report (CSR) expected in Q3 2025]

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

### 7.5.6. Semaglutide - RYBELSUS (CAP) - EMEA/H/C/004953/MEA 002.2

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: First study progress report for study NN9535-4447: an epidemiological database study to estimate the risk of pancreatic cancer in patients with type 2 diabetes mellitus (T2DM) taking semaglutide - a cohort study based on Nordic registry data [final clinical study report (CSR) expected in Q3 2025]

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

## 7.6. Others

### 7.6.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/ANX 010.1

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: 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

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

### 7.6.2. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/MEA 071

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Feasibility assessment for study OXON 214-04 (listed as a category 3 study in the RMP) : an observational study utilising data from EU national multiple sclerosis (MS) registries to estimate the incidence of anti-natalizumab antibody among patients who receive subcutaneous administration (SC) of natalizumab for treatment of relapsing remitting MS in order to investigate immunogenic potential of SC administration (from X/0116)

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

## 7.7. New 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. Asfotase alfa - STRENSIQ (CAP) - EMEA/H/C/003794/S/0056 (without RMP)

Applicant: Alexion Europe SAS

PRAC Rapporteur: Rhea Fitzgerald

Scope: Annual reassessment of the marketing authorisation

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

### 8.1.2. Cerliponase alfa - BRINEURA (CAP) - EMEA/H/C/004065/S/0035 (without RMP)

Applicant: BioMarin International Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual reassessment of the marketing authorisation

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

### 8.1.3. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/S/0048 (without RMP)

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Annual reassessment of the marketing authorisation

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

### 8.1.4. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/S/0070 (without RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

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. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) - EMEA/H/C/005737/R/0023 (without RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

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

### 8.2.2. Bosutinib - BOSULIF (CAP) - EMEA/H/C/002373/R/0051 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Conditional renewal of the marketing authorisation

### 8.2.3. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/R/0052 (without RMP)

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Laurence de Fays

Scope: Conditional renewal of the marketing authorisation

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

### 8.2.4. Dostarlimab - JEMPERLI (CAP) - EMEA/H/C/005204/R/0004 (without RMP)

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Conditional renewal of the marketing authorisation

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

### 8.2.5. Parathyroid hormone - NATPAR (CAP) - EMEA/H/C/003861/R/0034 (without RMP)

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Rhea Fitzgerald

Scope: Conditional renewal of the marketing authorisation

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

### 8.2.6. Pemigatinib - PEMAZYRE (CAP) - EMEA/H/C/005266/R/0003 (without RMP)

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

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

### 8.2.7. Volanesorsen - WAYLIVRA (CAP) - EMEA/H/C/004538/R/0016 (without RMP)

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Conditional renewal of the marketing authorisation

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

## 8.3. Renewals of the marketing authorisation

### 8.3.1. Beclometasone, formoterol, glycopyrronium bromide - TRIMBOW (CAP) - EMEA/H/C/004257/R/0025 (without RMP)

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.2. Ceritinib - ZYKADIA (CAP) - EMEA/H/C/003819/R/0042 (with RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.3. Dimethyl fumarate - SKILARENCE (CAP) - EMEA/H/C/002157/R/0030 (with RMP)

Applicant: Almirall S.A

PRAC Rapporteur: Annika Folin

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.4. Febuxostat - FEBUXOSTAT MYLAN (CAP) - EMEA/H/C/004374/R/0011 (without RMP)

Applicant: Mylan Pharmaceuticals Limited

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.5. Fluciclovine ($^{18}$F) - AXUMIN (CAP) - EMEA/H/C/004197/R/0027 (without RMP)

Applicant: Blue Earth Diagnostics Ireland Limited

PRAC Rapporteur: Rugile Pilviniene

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.6. Inotuzumab ozogamicin - BESPONSA (CAP) - EMEA/H/C/004119/R/0023 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.7. Ivabradine - IVABRADINE ACCORD (CAP) - EMEA/H/C/004241/R/0010 (with RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.8. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/R/0106 (without RMP)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.9. Nonacog beta pegol - REFIXIA (CAP) - EMEA/H/C/004178/R/0025 (with RMP)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.10. Patiromer - VELTASSA (CAP) - EMEA/H/C/004180/R/0028 (without RMP)

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.11. Rituximab - RIXATHON (CAP) - EMEA/H/C/003903/R/0053 (without RMP)

Applicant: Sandoz GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.12. Rituximab - RIXIMYO (CAP) - EMEA/H/C/004729/R/0054 (without RMP)

Applicant: Sandoz GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.13. Sarilumab - KEVZARA (CAP) - EMEA/H/C/004254/R/0029 (with RMP)

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.14. Spheroids of human autologous matrix-associated chondrocytes - SPHEROX (CAP) - EMEA/H/C/002736/R/0024 (with RMP)

Applicant: CO.DON AG, ATMP[55]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.15. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/R/0040 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

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

[55] Advanced therapy medicinal product

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

## 10.1. Safety related variations of the marketing authorisation

### 10.1.1. Coronavirus (COVID-19) mRNA[56] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0041

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: PRAC consultation on an extension of indication to include use in children of 6-11 years of age based on data from study mRNA-1273-P204: an ongoing phase 2/3, 2-part, open-label, dose-escalation, age de-escalation and subsequent randomised, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of mRNA-1273 in healthy children. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance

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

### 10.1.2. Idecabtagene vicleucel - ABECMA (CAP) - EMEA/H/C/004662/II/0009, Orphan

Applicant: Celgene Europe B.V., ATMP[57]

PRAC Rapporteur: Annika Folin

Scope: PRAC consultation on an update of sections 4.2 and 4.4 of the SmPC and on Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' and package leaflet in order to add statements for the use of Abecma (idecabtagene vicleucel) exceptionally during shortage of tocilizumab following the 'CAT recommendation for the use of chimeric antigen receptor (CAR)-T cell-based therapies in EU during shortages of tocilizumab'. The package leaflet is updated accordingly

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

### 10.1.3. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/II/0047, Orphan

Applicant: Novartis Europharm Limited, ATMP[58]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: PRAC consultation on an update of sections 4.2 and 4.4 of the SmPC and Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' in order to add statements for the use of Kymriah (tisagenlecleucel) exceptionally during shortage of tocilizumab following the 'CAT recommendation for the use of chimeric antigen receptor (CAR)-T cell-based therapies in EU during shortages of tocilizumab'. The package leaflet is updated accordingly

[56] Messenger ribonucleic acid
[57] Advanced therapy medicinal product
[58] Advanced therapy medicinal product

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

None

# 12. Organisational, regulatory and methodological matters

## 12.1. Mandate and organisation of the PRAC

### 12.1.1. PRAC membership

**Action:** For information

### 12.1.2. PRAC Training for Assessors 2021 – course overview

**Action:** For discussion

### 12.1.3. Vote by proxy

None

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

None

## 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

**Action:** For discussion

## 12.5. Cooperation with International Regulators

None

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

None

## 12.7. PRAC work plan

None

## 12.8. Planning and reporting

None

## 12.9. Pharmacovigilance audits and inspections

### 12.9.1. Pharmacovigilance systems and their quality systems

None

### 12.9.2. Pharmacovigilance inspections

None

### 12.9.3. Pharmacovigilance audits

None

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

### 12.10.1. Periodic safety update reports

None

### 12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

**Action:** For discussion

### 12.10.3. PSURs repository

None

### 12.10.4. Union reference date list – consultation on the draft list

**Action:** For adoption

### 12.10.5. Periodic safety update reports single assessment (PSUSA) – update to assessment report (AR) template

PRAC lead: Ulla Wändel Liminga, Menno van der Elst, Jana Lukacisinova

**Action:** For adoption

## 12.11. Signal management

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

PRAC lead: Sabine Straus

**Action:** For discussion

## 12.12. Adverse drug reactions reporting and additional reporting

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

None

### 12.12.2. Additional monitoring

None

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

**Action:** For adoption

## 12.13. EudraVigilance database

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

None

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

### 12.14.1. Risk management systems

None

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

None

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

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

None

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

None

## 12.16. Community procedures

### 12.16.1. Referral procedures for safety reasons

None

## 12.17. Renewals, conditional renewals, annual reassessments

None

## 12.18. Risk communication and transparency

### 12.18.1. Public participation in pharmacovigilance

None

### 12.18.2. Safety communication

None

## 12.19. Continuous pharmacovigilance

### 12.19.1. Incident management

None

## 12.20. Impact of pharmacovigilance activities

### 12.20.1. Strategy on measuring the impact of pharmacovigilance – PRAC interest group (IG) Impact - Impact research on implementation of EU risk minimisation measures for medicinal products in clinical guidelines

**Action:** For discussion

### 12.20.2. Strategy on measuring the impact of pharmacovigilance – PRAC interest group (IG) Impact - review of effectiveness PASS assessed by PRAC between 2016-2019 – final report

**Action:** For discussion

## 12.21. Others

### 12.21.1. Committee members - roles and responsibilities

**Action:** For discussion

### 12.21.2. Lifecycle regulatory submissions metadata project (LRSM)

**Action:** For discussion

### 12.21.3. Rapid data analytics – project update and initiatives on real world evidence (RWE) analyses to support regulatory assessments

**Action:** For discussion

## 13. Any other business

# 14. Explanatory notes

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

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

(Items 2 and 3 of the PRAC agenda)

A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the European Union (EU). For further detailed information on safety related referrals please see:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000150.jsp&mid=WC0b01ac05800240d0

### 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/