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## Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 23-26 November 2020

Chair: Sabine Straus – Vice-Chair: Martin Huber

23 November 2020, 10:30 – 19:30, via teleconference

24 November 2020, 08:30 – 19:30, via teleconference

25 November 2020, 08:30 – 19:30, via teleconference

26 November 2020, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

10 December 2020, 09:00 – 12:00, via teleconference

### Health and safety information

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

### Disclaimers

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

### Note on access to documents

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



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## **1. Introduction**

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 23-26 November 2020. See December 2020 PRAC minutes (to be published post January 2021 PRAC meeting).

### **1.2. Agenda of the meeting on 23-26 November 2020**

**Action:** For adoption

### **1.3. Minutes of the previous meeting on 26-29 October 2020**

**Action:** For adoption

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

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

None

### **2.2. Ongoing procedures**

None

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

None

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

### **3.1. Newly triggered procedures**

None

### **3.2. Ongoing procedures**

None

### 3.3. Procedures for finalisation

None

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

None

### 3.5. Others

None

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

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

#### 4.1.1. Azathioprine (NAP)

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Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of erythema nodosum

**Action:** For adoption of PRAC recommendation

EPITT 19623 – New signal

Lead Member State(s): DK

### 4.2. New signals detected from other sources

#### 4.2.1. Methotrexate – JYLAMVO (CAP), NORDIMET (CAP); NAP

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Applicant(s): Nordic Group B.V. (Nordimet), Therakind (Europe) Limited (Jylamvo); various

PRAC Rapporteur: To be appointed

Scope: Signal of progressive multifocal leukoencephalopathy

**Action:** For adoption of PRAC recommendation

EPITT 18473 – New signal

Lead Member State(s): AT, DE

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

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

### 4.3. Signals follow-up and prioritisation

#### 4.3.1. Capecitabine – CAPECITABINE ACCORD (CAP), CAPECITABINE MEDAC (CAP), CAPECITABINE TEVA (CAP), ECANSYA (CAP), XELODA (CAP) - EMEA/H/C/000316/SDA/036; NAP

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Applicant(s): Accord Healthcare S.L.U. (Capecitabine Accord), Krka, d.d., Novo mesto (Ecansya), Medac Gesellschaft für klinische Spezialpräparate mbH (Capecitabine Medac), Roche Registration GmbH (Xeloda), Teva B.V. (Capecitabine Teva); various

PRAC Rapporteur: Martin Huber

Scope: Signal of anaphylactic reaction

**Action:** For adoption of PRAC recommendation

EPITT 19561 – Follow-up to June 2020

#### 4.3.2. Chloroquine (NAP); hydroxychloroquine (NAP)

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Applicant(s): various

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of psychiatric disorders

**Action:** For adoption of PRAC recommendation

EPITT 19572 – Follow-up to September 2020<sup>3</sup>

#### 4.3.3. Pembrolizumab – KEYTRUDA (CAP) - EMEA/H/C/00328/SDA/028

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

PRAC Rapporteur: Menno van der Elst

Scope: Signal of vasculitis

**Action:** For adoption of PRAC recommendation

EPITT 19578 – Follow-up to September 2020<sup>4</sup>

#### 4.3.4. Teriparatide - FORSTEO (CAP) - EMEA/H/C/000425/SDA/052.1, QUTAVINA (CAP), LIVOGIVA (CAP), MOVYMYA (CAP) - EMEA/H/C/004368/SDA/002.1; TERROSA (CAP) - EMEA/H/C/003916/SDA/002.1; NAP

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Applicant(s): Eli Lilly Nederland B.V. (Forsteo), EuroGenerics Holdings B.V. (Qutavina), Gedeon Richter Plc. (Terrosa), Stada Arzneimittel AG (Movymia), Theramex Ireland Limited (Livogiva); various

PRAC Rapporteur: Adrien Inoubli

Scope: Signal of myeloma

**Action:** For adoption of PRAC recommendation

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<sup>3</sup> Held 31 August – 03 September 2020

<sup>4</sup> Held 31 August – 03 September 2020

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

None

## 5. Risk management plans (RMPs)

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

#### 5.1.1. Berotralstat - EMEA/H/C/005138, Orphan

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Applicant: BioCryst Ireland Limited

Scope: Prevention of hereditary angioedema (HAE)

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

#### 5.1.2. Bevacizumab - EMEA/H/C/005327

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

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

#### 5.1.3. Bevacizumab - EMEA/H/C/005611

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

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

#### 5.1.4. Cenobamate - EMEA/H/C/005377

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Scope: Adjunctive treatment of focal onset seizures with or without secondary generalisation in adult patients with epilepsy who have not been adequately controlled despite a history of treatment with at least 2 anti-epileptic products

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

#### 5.1.5. Dostarlimab - EMEA/H/C/005204

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Scope: Treatment of mismatch repair deficient (dMMR), microsatellite instability-high (MSI-H) endometrial cancer (EC)

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

#### 5.1.6. Evinacumab - EMEA/H/C/005449

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Scope (accelerated assessment): Treatment of homozygous familial hypercholesterolemia (HoFH)

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

#### 5.1.7. Pitolisant - EMEA/H/C/005117

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Scope: Treatment of excessive daytime sleepiness (EDS) in patients with obstructive sleep apnoea (OSA)

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

#### 5.1.8. Sildenafil - EMEA/H/C/005439

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Scope: Treatment of erectile dysfunction

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

#### 5.1.9. Thiotepa - EMEA/H/C/005434

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Scope: Conditioning treatment prior to haematopoietic progenitor cell transplantation (HPCT), treatment of solid tumours

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

#### 5.1.10. Trastuzumab - EMEA/H/C/005066

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

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

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

#### 5.2.1. Alpelisib - PIQRAY (CAP) - EMEA/H/C/004804/II/0001

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 2.0) in order to replace the following studies (listed as category 3 studies in the RMP): 1) study CBYL719C2402: a retrospective cohort study to evaluate the risk of hyperglycaemia in patients with advanced breast cancer treated with Piqray (alpelisib) in the real world setting;;2) study CBYL719A0IC02: an open-label,

multicentre, phase 3b study to evaluate the safety and tolerability of alpelisib in combination with fulvestrant for the treatment of men and postmenopausal women with hormone receptor-positive (HR+), epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer with a PIK3CA<sup>5</sup> mutation, after disease progression following an endocrine based regimen, with: 3) study CBYL719C2404: A non-interventional PASS of Piqray (alpelisib) in combination with fulvestrant in postmenopausal women, and men, with HR+, HER2 negative, locally advanced or metastatic breast cancer with a PIK3CA mutation in the real-world setting in European countries. Additionally, a separated healthcare professional (HCP) survey (CBYL719A0IC02) is proposed as part of the pharmacovigilance plan

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

#### 5.2.2. [Cerliponase alfa - BRINEURA \(CAP\) - EMEA/H/C/004065/II/0027, Orphan](#)

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Applicant: BioMarin International Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 3.2) in order to change the final date for completion from July 2020 to May 2024 of the post-authorisation efficacy study (PAES), study 190-203: a phase 2, open-label, multicentre study to evaluate safety, tolerability, and efficacy of intra-cerebroventricular cerliponase alfa in paediatric patients < 18 years of age with neuronal ceroid lipofuscinosis type 2 (CLN2) disease

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

#### 5.2.3. [Dapagliflozin - EDISTRIDE \(CAP\) - EMEA/H/C/004161/WS1844/0039; FORXIGA \(CAP\) - EMEA/H/C/002322/WS1844/0057](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Re-categorisation of study D169C00011: a retrospective cohort study on the risk of diabetic ketoacidosis (DKA) to determine the effectiveness of additional risk minimisation measures (aRMMs) in place for DKA by assessing the impact of the risk minimisation measures (RMMs) on the risk of DKA in type 1 diabetes mellitus (T1DM) patients who are treated with dapagliflozin in Europe, from a category 1 to a category 3 study in the RMP (version 20). Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated accordingly

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

#### 5.2.4. [Dasabuvir - EXVIERA \(CAP\) - EMEA/H/C/003837/WS1972/0049; Ombitasvir, paritaprevir, ritonavir - VIEKIRAX \(CAP\) - EMEA/H/C/003839/WS1972/0060](#)

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Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope Submission of an updated RMP (version 6) for Viekirax (ombitasvir/paritaprevir/ritonavir) and Exviera (dasabuvir) in line with the outcome of

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<sup>5</sup> Phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alfa



procedure PSA/J/0055 on direct-acting antiviral (DAAV) concluded in June 2020 relating to a substantial amendment for a joint protocol for a non-interventional imposed PASS on early recurrence of hepatocellular carcinoma (HCC) in hepatitis C virus (HCV)-infected patients after DAAV therapy, in order to change the due date for submission of the final study report from Q2 2023 to Q3 2021

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

#### 5.2.5. Ioflupane (<sup>123</sup>I) - DATSCAN (CAP) - EMEA/H/C/000266/II/0060

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Applicant: GE Healthcare B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of the first RMP (version 0.1) following the introduction of a signification change to the marketing authorisation(s)

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

#### 5.2.6. Pioglitazone - PIOGLITAZONE ACCORD (CAP) - EMEA/H/C/002277/II/0020

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Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of an updated RMP (version 5.0) for the removal of safety concerns and additional risk minimisation measures (aRMM) in line with the RMP of Glidipion (pioglitazone) and in line with revision 2 of GVP module V on 'Risk management systems'

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

#### 5.2.7. Trastuzumab - ONTRUZANT (CAP) - EMEA/H/C/004323/II/0026

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Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 4.0) in order to propose the early termination of study SB3-G31-BC-E: a long-term follow-up study for cardiac safety in patients with epidermal growth factor receptor 2 (HER2) positive early or locally advanced breast cancer who have completed study SB3-G31-BC (a phase 3 randomised, double-blind, parallel group, multicentre study to compare the efficacy, safety, pharmacokinetics and immunogenicity between Ontruzant (biosimilar trastuzumab) and Herceptin (trastuzumab) in women with newly diagnosed HER2 positive early or locally advanced breast cancer in neoadjuvant setting)

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

#### 5.2.8. Travoprost - IZBA (CAP) - EMEA/H/C/002738/WS1944/0014; TRAVATAN (CAP) - EMEA/H/C/000390/WS1944/0064

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Submission of an updated RMP (version 10.0) for Travatan and Izba (travoprost) in

order to remove some important identified risks, important potential risks in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00003011/201902) adopted in November 2019 and 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. Andexanet alfa - ONDEXXYA (CAP) - EMEA/H/C/004108/II/0009/G

Applicant: Portola Netherlands B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations consisting of an update of section 5.2 of the SmPC in order to update pharmacokinetic (PK) information based on the clinical study results (CSR) from: 1) study 19-514 evaluating the PK comparability of generation 1 process 3 andexanet and generation 2 andexanet (PK comparability); 2) study 16-508: a phase 2 randomised, double-blind, placebo-controlled study to evaluate the efficacy, safety, tolerability and PK/pharmacodynamics (PD) of andexanet alfa administered to healthy Japanese and Caucasian subjects (Japanese ethnicity study). Annex II-D on 'Specific obligation to complete post-authorisation measures for the conditional marketing authorisation' is updated accordingly. The RMP (version 2.1) is updated in accordance

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

#### 5.3.2. Atazanavir, cobicistat - EVOTAZ (CAP) - EMEA/H/C/003904/II/0038

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Adrien Inoubli

Scope: Extension of indication to include the use of Evotaz (atazanavir/cobicistat) in combination with other antiretroviral agents in the treatment of human immunodeficiency virus 1 (HIV-1) infection in adolescent patients aged  $\geq 12$  to  $< 18$  years, weighing  $\geq 35$  kg without known mutations associated with resistance to atazanavir. 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 8.0) are updated in accordance. In addition, the MAH took the opportunity to make minor editorial corrections

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

#### 5.3.3. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0042

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include in combination with platinum-based chemotherapy first-line treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC). As a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 14.0) are updated accordingly

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

#### 5.3.4. [Avelumab - BAVENCIO \(CAP\) - EMEA/H/C/004338/II/0018](#)

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Applicant: Merck Europe B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Extension of indication to include treatment as monotherapy for the first-line maintenance treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC) whose disease has not progressed with first-line platinum-based induction chemotherapy. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 2.3) are updated in accordance. The MAH took the opportunity to include some editorial changes throughout the product information

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

#### 5.3.5. [Beclometasone dipropionate, formoterol fumarate dihydrate, glycopyrronium - TRIMBOW \(CAP\) - EMEA/H/C/004257/X/0012](#)

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Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Extension application to add a new pharmaceutical form associated with a new strength. The RMP (version 6.2) is updated in accordance

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

#### 5.3.6. [Cabozantinib - CABOMETYX \(CAP\) - EMEA/H/C/004163/II/0017](#)

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Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include in combination with nivolumab first line treatment of advanced renal cell carcinoma. 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 5.0) are updated in accordance

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

#### 5.3.7. [Cemiplimab - LIBTAYO \(CAP\) - EMEA/H/C/004844/II/0011](#)

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Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication as monotherapy to include the first-line treatment of adult patients with non-small cell lung cancer (NSCLC) expressing programmed death-ligand 1 (PD-L1) (in  $\geq 50\%$  tumour cells), with no epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK) or proto-oncogene tyrosine-protein kinase ROS1 aberrations, who have locally advanced NSCLC and who are not candidates for surgical resection or definitive chemoradiation, or have progressed after treatment with definitive chemoradiation, or metastatic NSCLC. The package leaflet and the RMP (version 2.0) are updated accordingly

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

#### 5.3.8. Cemiplimab - LIBTAYO (CAP) - EMEA/H/C/004844/II/0012

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Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication as monotherapy to include the treatment of adult patients with locally advanced basal cell carcinoma (BCC) previously treated with a Hedgehog pathway inhibitor. 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 2.0) are updated accordingly

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

#### 5.3.9. Ceritinib - ZYKADIA (CAP) - EMEA/H/C/003819/II/0034

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to reflect the results of study CLDK378A2112: a multicentre, randomized open label study to assess the systemic exposure, efficacy and safety of 450 mg ceritinib taken with a low-fat meal and 600 mg ceritinib taken with a low-fat meal as compared with that of 750 mg ceritinib taken in the fasted state in adult patients with anaplastic lymphoma kinase (ALK) rearranged (ALK-positive) metastatic non-small cell lung cancer (NSCLC). The package leaflet and the RMP (version 16.0) 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 10.1). The MAH also introduced other editorial changes including information on sodium content in line with the Annex to the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use' and the removal of the black triangle

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

#### 5.3.10. Clopidogrel - ISCOVER (CAP) - EMEA/H/C/000175/WS1769/0140; PLAVIX (CAP) - EMEA/H/C/000174/WS1769/0138

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Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include adult patients with high risk transient ischemic attack (TIA) (ABCD<sup>2</sup> score  $\geq 4$ ) or minor ischemic stroke (IS) (National Institutes of Health Stroke Scale (NIHSS)  $\leq 3$ ) within 24 hours of either the TIA or IS event. The new indication is based on the results of: 1) study POINT: a double-blind, randomised, placebo-controlled phase 3 study on platelet-oriented inhibition in new TIA and minor IS; 2) study CHANCE: a double-blind, randomised, placebo-controlled phase 3 study comparing the effects of a 3-month clopidogrel regimen, combined with acetylsalicylic acid (ASA) during the first 21 days, versus ASA alone for the acute treatment of TIA or minor stroke. As a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 1.0) are updated accordingly

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

### 5.3.11. Dacomitinib - VIZIMPRO (CAP) - EMEA/H/C/004779/II/0003/G

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations to update sections 4.2 and 5.2 of the SmPC in order to revise the dosing recommendation for patients with hepatic impairment and to include relevant pharmacokinetics data based on results of study A7471058: a phase 1, open-label, single-dose, parallel-group study to evaluate the plasma pharmacokinetics and safety of dacomitinib in participants with severely impaired hepatic function relative to participants with normal hepatic function. As a consequence, the MAH proposed to remove 'safety in patient with severe hepatic impairment' as missing information from the list of safety concerns in the RMP. In addition, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1). The MAH took also the opportunity to update the RMP to include study A7471064: a single arm study to evaluate the safety of dacomitinib for the first-line treatment of participants in India with metastatic non-small-cell lung carcinoma (NSCLC) with epidermal growth factor receptor (EGFR)-activating mutations as a category 3 study. The RMP (version 1.1) is updated accordingly

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

### 5.3.12. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/X/0046/G, Orphan

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Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Laurence de Fays

Scope: Grouped applications consisting of: 1) extension application to introduce a new pharmaceutical form associated with a new strength; 2) extension of indication to include the treatment of children of at least 10 kg of body weight for Deltyba (delamanid) 50 mg film-coated tablets. As a consequence, sections 3, 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet, labelling and the RMP (version 3.3) are updated accordingly

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

### 5.3.13. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/II/0049

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Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.7, 4.8, 5.1, 5.2 and 6.6 of the SmPC in order to update efficacy and safety information based on final results from study MDV3100-14 (PROSPER) (listed as a post-authorisation efficacy study (PAES) in Annex II): a phase 3, randomized, double-blind, placebo-controlled, efficacy and safety study of enzalutamide in patients with non-metastatic castration-resistant prostate cancer. The package leaflet, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' and the RMP (version 14.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet, to introduce a few editorial updates and to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

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

#### 5.3.14. Eravacycline - XERAVA (CAP) - EMEA/H/C/004237/X/0009

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Applicant: Tetrphase Pharmaceuticals Ireland Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to add a new strength for eravacycline powder for concentrate for solution for infusion. The RMP (version 3.0) is updated in accordance. Additionally, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

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

#### 5.3.15. Esketamine - SPRAVATO (CAP) - EMEA/H/C/004535/II/0001/G

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Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped variations consisting of: 1) extension of indication to include a new indication for the rapid reduction of depressive symptoms in adult patients with a moderate to severe depressive episode of major depressive disorder (MDD) who have current suicidal ideation with intent. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 the SmPC are updated. The package leaflet and the RMP (version 2.1) are updated accordingly; 2) addition of a new pack size (multipack) of 24 nasal spray devices (multipack of 8 packs of 3 nasal spray devices) corresponding to 4 weeks of treatment in the new indication. The package leaflet and labelling are updated in accordance. In addition, the MAH took the opportunity to clarify the wording in Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product'

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

#### 5.3.16. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - EMEA/H/C/004336/II/0037

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Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Update sections 4.4 and 5.1 of the SmPC following the final results from study ZOSTER-064 (listed as a category 3 study in the RMP): an observational study to assess frailty and other prognostic factors for development of herpes zoster in adult subjects who participated in study ZOSTER-006 (study 110390: a phase 3, randomized, observer-blind, placebo-controlled, multicentre, clinical vaccination trial to assess the prophylactic efficacy, safety, and immunogenicity of Shingrix (herpes zoster vaccine) when administered intramuscularly on a 0, 2-month schedule in adults aged 50 years and older) and ZOSTER-022 (study 113077: a phase 3, randomised, observer blind, placebo-controlled, multicentre, clinical vaccination trial to assess the prophylactic efficacy, safety and immunogenicity of Shingrix (herpes zoster vaccine) when administered intramuscularly on a 0, 2-month schedule in adults aged 70 years and older) and the herpes zoster (HZ) efficacy, immunogenicity and safety of Shingrix (herpes zoster vaccine) by frailty status (in fulfilment of MEA 012). The RMP

(version 4.1) is updated accordingly. The MAH took the opportunity to implement some editorial changes in sections 4.4 and 5.1 of the SmPC and to introduce a correction of the abbreviation CHO cells from Chinese hamster ovarian cells to Chinese hamster ovary cells

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

#### 5.3.17. [Infliximab - REMSIMA \(CAP\) - EMEA/H/C/002576/II/0095](#)

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of section 4.2 of the SmPC to add a new posology for the rheumatoid arthritis indication that does not include intravenous (IV) induction doses prior subcutaneous use. The package leaflet and the RMP (version 13.1) are updated accordingly

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

#### 5.3.18. [Insulin aspart - INSULIN ASPART SANOFI \(CAP\) - EMEA/H/C/005033/X/0003](#)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Annika Folin

Scope: Extension application to introduce a new route of administration for the 10 mL vial presentations only. The RMP (version 1.1) is updated accordingly

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

#### 5.3.19. [Ipilimumab - YERVOY \(CAP\) - EMEA/H/C/002213/WS1881/0085; nivolumab - OPDIVO \(CAP\) - EMEA/H/C/003985/WS1881/0091](#)

Applicant(s): Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include first-line treatment of adult patients with unresectable malignant pleural mesothelioma (MPM) for Opdivo (nivolumab) in combination with Yervoy (ipilimumab). 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 20.0 for Opdivo, version 30.0 for Yervoy) are updated in accordance

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

#### 5.3.20. [Isatuximab - SARCLISA \(CAP\) - EMEA/H/C/004977/II/0003, Orphan](#)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to add combination with carfilzomib and dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy. 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 1.0) are updated accordingly. The MAH took the opportunity to introduce minor changes in sections 4.9, 6.3 and 6.6 of the SmPC and to update

details of the local representatives

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

#### 5.3.21. [Ivacaftor - KALYDECO \(CAP\) - EMEA/H/C/002494/II/0089, Orphan](#)

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Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to extend the indication of Kalydeco (ivacaftor) tablets in combination regimen with Kaftrio (ivacaftor/tezacaftor/elexacaftor) tablets for the treatment of adults and adolescents aged 12 years and older with cystic fibrosis (CF) who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. As a consequence, sections 4.1, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 9.2) are updated in accordance

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

#### 5.3.22. [Ivacaftor, tezacaftor, elexacaftor - KAFTRIO \(CAP\) - EMEA/H/C/005269/II/0001, Orphan](#)

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Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to patients with cystic fibrosis (CF) aged 12 years and older who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR gene), regardless of the second allele (F/any). based on efficacy data from study 104:a phase 3, randomized, double-blind, controlled study evaluating the efficacy and safety of elexacaftor (VX-445) combination therapy in subjects with CF who are heterozygous for the F508del mutation and a gating or residual function mutation (F/G and F/RF genotypes). 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 1.1) are updated accordingly

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

#### 5.3.23. [Lixisenatide - LYXUMIA \(CAP\) - EMEA/H/C/002445/II/0030](#)

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Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Annika Folin

Scope: Submission of the final report from study TDR14311 (listed as a category 3 study in the RMP): a randomised, double-blind, placebo-controlled, dose escalation, study on safety, pharmacokinetics and pharmacodynamics of lixisenatide in paediatric patients with type 2 diabetes mellitus (T2DM) not adequately controlled with metformin and/or basal insulin (in fulfilment of Article 46 requirements). 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. [Methotrexate - NORDIMET \(CAP\) - EMEA/H/C/003983/II/0016](#)

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Applicant: Nordic Group B.V.



PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include the treatment of mild to moderate Crohn's disease either alone or in combination with corticosteroids in patients refractory or intolerant to thiopurines. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 5.0) are updated in accordance. Furthermore, the MAH took the opportunity to update the RMP in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template) and the outcome of the referral procedure for methotrexate-containing products under Article 31 of Directive 2001/83/EC (EMA/H/A-31/1463) finalised in July 2019

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

#### 5.3.25. Midostaurin - RYDAPT (CAP) - EMEA/H/C/004095/II/0014, Orphan

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to change posology recommendations and add special warnings and precautions for use in the paediatric population following the occurrence of severe dose limiting toxicities (DLTs) based on findings in study CPKC412A2218 (currently on clinical hold): a phase 2, open-label, single arm study to evaluate the safety, efficacy, and pharmacokinetics of twice daily midostaurin (PKC412) combined with standard chemotherapy and as a single agent post-consolidation therapy in children with untreated FMS-like tyrosine kinase 3 (FLT3)-mutated acute myeloid leukaemia (AML). The package leaflet and the RMP (version 5.0) are updated accordingly. The MAH took the opportunity to introduce minor editorial changes in the product information and to bring it in line with the latest quality review of documents (QRD) template (version 10.1)

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

#### 5.3.26. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0092

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include Opdivo (nivolumab) in combination with cabozantinib for the first line treatment of advanced renal cell carcinoma. 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 19.0) are updated in accordance

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

#### 5.3.27. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/II/0020

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 5.3 of the SmPC in order to update information on embryo-foetal and pre- and postnatal development in cynomolgus monkeys based on the final report for study 17-1133 (listed as a category 3 study in the RMP): a study assessing the effects of ocrelizumab

on embryo-foetal and pre- and post-natal development when administered once weekly for up to 23-weeks intravenously to pregnant cynomolgus monkeys (in fulfilment of MEA 006). The RMP (version 5.0) is updated accordingly

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

### 5.3.28. [Olaparib - LYNPARZA \(CAP\) - EMEA/H/C/003726/II/0042](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to add myelodysplastic syndrome (MDS)/acute myeloid leukaemia (AML) to the list of adverse drug reactions with the frequency uncommon, to modify the existing warning on MDS/AML and to update efficacy information based on final results from study SOLO-2 (listed as a post-authorisation efficacy study (PAES) in Annex II-D on 'conditions or restrictions with regard to the safe and effective use of the medicinal product'): a phase 3 randomised, double blind, placebo controlled, multicentre study of olaparib maintenance monotherapy in platinum sensitive relapsed BRCA<sup>6</sup> mutated ovarian cancer patients who are in complete or partial response following platinum based chemotherapy. The package leaflet, Annex II and the RMP (version 21.1) are updated accordingly

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

### 5.3.29. [Oritavancin - ORBACTIV \(CAP\) - EMEA/H/C/003785/II/0030](#)

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Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of the final report from study 14-TMC-01 (listed as a category 3 study in the RMP): a surveillance study investigation, part of the global SENTRY antimicrobial surveillance programme platform, to monitor the activity of oritavancin against Gram-positive clinical isolates collected from U.S. and European medical centres (in fulfilment of MEA 003.4). The RMP (version 3.0) is updated accordingly

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

### 5.3.30. [Osimertinib - TAGRISSO \(CAP\) - EMEA/H/C/004124/II/0039/G](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations consisting of an extension of indication to include the adjuvant treatment after complete tumour resection in epidermal growth factor receptor (EGFR) mutant non-small cell lung cancer (NSCLC) patients, based on the results from pivotal study D5164C00001: a phase 3, double blind, randomised, placebo-controlled multicentre study to assess the efficacy and safety of Tagrisso (osimertinib) versus placebo, in patients with EGFR mutation positive stage IB-IIIA NSCLC, following complete tumour resection with or without adjuvant chemotherapy (ADAURA). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.3

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<sup>6</sup> BReast CAncer gene

of the SmPC are updated. The package leaflet and the RMP (version 14.1) are updated accordingly

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

#### 5.3.31. Parathyroid hormone - NATPAR (CAP) - EMEA/H/C/003861/II/0026, Orphan

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final results of study PAR-C10-008: a long-term open-label study investigating the safety and tolerability of a Natpar (parathyroid hormone) for the treatment of adults with hypoparathyroidism – a clinical extension study (RACE). As a consequence, section 5.1 of the SmPC is updated to reflect 72-month data from the study. The RMP (version 3.0) is updated accordingly and in line with revision 2 of GVP module V on 'Risk management systems'

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

#### 5.3.32. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0091

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include first-line treatment of unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer in adults based on the results from study KEYNOTE-177: an international, randomised, open-label phase 3 trial of pembrolizumab versus chemotherapy in MSI-H or dMMR stage IV colorectal carcinoma. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 29.1) are updated in accordance. The MAH took the opportunity to introduce minor correction in section 4.4 of the SmPC on immune related endocrinopathies

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

#### 5.3.33. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/X/0012

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Extension application to add a new strength. The RMP (version 2.0) is updated accordingly

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

#### 5.3.34. Romiplostim - NPLATE (CAP) - EMEA/H/C/000942/II/0077

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to add the use of romiplostim in adult patients who have had

immune thrombocytopenia (ITP) for ≤ 12 months and who have had an insufficient response to corticosteroids or immunoglobulins. As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 20.0) are updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

#### 5.3.35. Rucaparib - RUBRACA (CAP) - EMEA/H/C/004272/II/0023

Applicant: Clovis Oncology Ireland Limited

PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.5, 4.6 and 5.2 of the SmPC to add drug-drug interaction (DDI) information with rosuvastatin and oral contraceptives based on the results of study CO-338-095 (listed as a category 3 study in the RMP): a phase 1, open-label, DDI study to determine the effect of rucaparib on the pharmacokinetics of oral rosuvastatin (arm A) and oral contraceptives (ethinylestradiol and levonorgestrel - arm B) in patients with advanced solid tumours. The RMP (version 4.1) is updated accordingly

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

#### 5.3.36. Tedizolid phosphate - SIVEXTRO (CAP) - EMEA/H/C/002846/II/0037

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of section 5.1 of the SmPC in order to update the description of the potential risk of emergence of drug resistance with tedizolid phosphate based on final results from study 'surveillance of tedizolid activity and resistance (STAR)' (listed as a category 3 study in the RMP): a surveillance study established in January 2014 to monitor tedizolid susceptibility activity and emergence of resistance across the US, 11 European Union countries, Russia and Turkey. The RMP (version 6.2) is updated accordingly

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

#### 5.3.37. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0027

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC of Xeljanz (tofacitinib) 11mg prolonged-release tablets in order to include the treatment of active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have been intolerant to a prior disease modifying antirheumatic drug therapy; as an alternative to the immediate release film-coated tablets. Section 4.2 of the SmPC for Xeljanz (tofacitinib) film-coated tablets is also updated to include switching with the prolonged-release tablet in the treatment of PsA. The package leaflet and the RMP (version 13.1) are updated accordingly

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

### 5.3.38. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/II/0004

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Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to include the treatment of active psoriatic arthritis (PsA) in adult patients. 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 2.0) are updated in accordance. The MAH took the opportunity to introduce minor updates to Annex II

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

### 5.3.39. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/II/0005

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Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to include the treatment of active ankylosing spondylitis in adult patient. 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 3.0) are updated in accordance. The MAH took the opportunity to introduce minor editorial changes throughout the SmPC and Annex II

**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. Andexanet alfa - ONDEXXYA (CAP) - PSUSA/00010764/202004

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Applicant: Portola Netherlands B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.2. Axicabtagene ciloleucel - YESCARTA (CAP) - PSUSA/00010703/202004

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Applicant: Kite Pharma EU B.V., ATMP<sup>7</sup>

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

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

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

### 6.1.3. Benralizumab - FASENRA (CAP) - PSUSA/00010661/202005

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Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

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

### 6.1.4. Bezlotoxumab - ZINPLAVA (CAP) - PSUSA/00010576/202004

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Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

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

### 6.1.5. Brigatinib - ALUNBRIG (CAP) - PSUSA/00010728/202004

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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

### 6.1.6. Cerliponase alfa - BRINEURA (CAP) - PSUSA/00010596/202004

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Applicant: BioMarin International Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

### 6.1.7. Durvalumab - IMFINZI (CAP) - PSUSA/00010723/202004

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Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

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

### 6.1.8. Ebola Zaire vaccine (live, attenuated) - ERVEBO (CAP) - PSUSA/00010834/202005

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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

#### 6.1.9. Febuxostat - ADENURIC (CAP) - PSUSA/00001353/202004

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.10. Fexinidazole - FEXINIDAZOLE WINTHROP (Art 58<sup>8</sup>) - EMEA/H/W/002320/PSUV/0004

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUR procedure

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

#### 6.1.11. Glycopyrronium bromide, formoterol - BEVESPI AEROSPHERE (CAP) - PSUSA/00010739/202004

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.12. Golimumab - SIMPONI (CAP) - PSUSA/00001560/202004

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.13. Insulin glargine - ABASAGLAR (CAP), LANTUS (CAP), SEMGLEE (CAP), TOUJEO (CAP) - PSUSA/00001751/202004

Applicant(s): Eli Lilly Nederland B.V. (Abasaglar), Mylan S.A.S (Semglee), Sanofi-Aventis Deutschland GmbH (Lantus, Toujeo)

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

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

6.1.14. [Insulin lispro - HUMALOG \(CAP\), INSULIN LISPRO SANOFI \(CAP\), LIPROLOG \(CAP\), LYUMJEV \(CAP\) - PSUSA/00001755/202004](#)

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Applicant: 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

6.1.15. [Irinotecan<sup>9</sup> - ONIVYDE PEGYLATED LIPOSOMAL \(CAP\) - PSUSA/00010534/202004](#)

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Applicant: Les Laboratoires Servier

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

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

6.1.16. [Meningococcal group A, C, W-135, Y conjugate vaccine \(conjugated to tetanus toxoid carrier protein\) - NIMENRIX \(CAP\) - PSUSA/00010044/202004](#)

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

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

6.1.17. [Meningococcal group B vaccine \(recombinant, adsorbed\) - TRUMENBA \(CAP\) - PSUSA/00010607/202004](#)

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

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

6.1.18. [Padeliporfin - TOOKAD \(CAP\) - PSUSA/00010654/202005](#)

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Applicant: Steba Biotech S.A

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

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

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<sup>9</sup> Liposomal formulation(s) only



#### 6.1.19. Parathyroid hormone - NATPAR (CAP) - PSUSA/00010591/202004

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Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.20. Parecoxib - DYNASTAT (CAP) - PSUSA/00002314/202003

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.21. Radium (<sup>223</sup>Ra) dichloride - XOFIGO (CAP) - PSUSA/00010132/202005

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Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.22. Rurioctocog alfa pegol - ADYNOVI (CAP) - PSUSA/00010663/202005

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Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.23. Sotagliflozin - ZYNQUISTA (CAP) - PSUSA/00010766/202004

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Applicant: Guidehouse Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

#### 6.1.24. Sunitinib - SUTENT (CAP) - PSUSA/00002833/202004

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

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

#### **6.1.25. Susoctocog alfa - OBIZUR (CAP) - PSUSA/00010458/202005**

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Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

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

#### **6.1.26. Ulipristal<sup>10</sup> - ELLAONE (CAP) - PSUSA/00003074/202005**

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Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

#### **6.1.27. Vestronidase alfa - MEPSEVII (CAP) - PSUSA/00010709/202005**

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Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

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

#### **6.1.28. Volanesorsen - WAYLIVRA (CAP) - PSUSA/00010762/202005**

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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. Amlodipine, telmisartan - TWYNSTA (CAP); NAP - PSUSA/00000180/202004**

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Applicant(s): Boehringer Ingelheim International GmbH (Twynsta), various

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

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<sup>10</sup> Indicated for female emergency contraception only

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

6.2.2. [Bortezomib - BORTEZOMIB ACCORD \(CAP\), BORTEZOMIB FRESENIUS KABI \(CAP\), BORTEZOMIB HOSPIRA \(CAP\); BORTEZOMIB SUN \(CAP\), VELCADE \(CAP\); NAP - PSUSA/00000424/202004](#)

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Applicant(s): Accord Healthcare S.L.U. (Bortezomib Accord), Fresenius Kabi Deutschland GmbH (Bortezomib Fresenius Kabi), Janssen-Cilag International NV (Velcade), Pfizer Europe MA EEIG (Bortezomib Hospira), Sun Pharmaceutical Industries Europe B.V. (Bortezomib Sun), various

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

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

6.2.3. [Ertapenem - INVANZ \(CAP\); NAP - PSUSA/00001256/202003](#)

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

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

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

6.2.4. [Fesoterodine - TOVIAZ \(CAP\); desfesoterodine \(NAP\) - PSUSA/00001387/202004](#)

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Applicant: Pfizer Europe MA EEIG (Toviaz), various

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

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

6.2.5. [Mycophenolate mofetil - CELLCEPT \(CAP\), MYCLAUSEN \(CAP\), MYCOPHENOLATE MOFETIL TEVA \(CAP\), MYFENAX \(CAP\); NAP; mycophenolic acid \(NAP\) - PSUSA/00010550/202005](#)

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

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

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

6.2.6. [Naloxone<sup>11</sup> - NYXOID \(CAP\); NAP - PSUSA/00010657/202005](#)

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Applicant(s): Mundipharma Corporation (Ireland) Limited (Nyxoid), various

PRAC Rapporteur: Liana Gross-Martirosyan

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<sup>11</sup> For use in non-medical setting(s) only

Scope: Evaluation of a PSUSA procedure

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

#### 6.2.7. Somatropin - NUTROPINAQ (CAP), OMNITROPE (CAP); NAP - PSUSA/00002772/202003

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Applicant(s): Ipsen Pharma (NutropinAq), Sandoz GmbH (Omnitrope), various

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

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

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

#### 6.3.1. Aceclofenac (NAP) - PSUSA/00000022/202003

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Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.2. Captopril (NAP) - PSUSA/00000535/202004

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Applicant(s): various

PRAC Lead: Marek Juračka

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.3. Carvedilol, ivabradine (NAP) - PSUSA/00010586/202004

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Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.4. Clarithromycin (NAP) - PSUSA/00000788/202004

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Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

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

### 6.3.5. Deoxycholic acid (NAP) - PSUSA/00010525/202004

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Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

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

### 6.3.6. Doxylamine (NAP) - PSUSA/00001174/202004

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Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

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

### 6.3.7. Estradiol<sup>12</sup> (NAP); estradiol, prednisolone (NAP) - PSUSA/00010441/202004

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Applicant(s): various

PRAC Lead: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

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

### 6.3.8. Gentamicin<sup>13</sup> (NAP) - PSUSA/00009159/202003

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Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

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

### 6.3.9. Hydroxyethyl starch (HES) (NAP) - PSUSA/00001694/202003

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Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

### 6.3.10. Isotretinoin<sup>14</sup> (NAP) - PSUSA/00010488/202005

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Applicant(s): various

PRAC Lead: Maia Uusküla

<sup>12</sup> Cream/balm/emulsion for application in female genital area only

<sup>13</sup> Systemic use only

<sup>14</sup> Oral formulation(s) only

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.11. Ivermectin<sup>15</sup> (NAP) - PSUSA/00010376/202004

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.12. Lamivudine, tenofovir disoproxil (NAP) - PSUSA/00010751/202003

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.13. Phenol (NAP) - PSUSA/00009256/202004

Applicant(s): various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.14. Pimecrolimus (NAP) - PSUSA/00002411/202003

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.15. Piribedil (NAP) - PSUSA/00002436/202003

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

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

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<sup>15</sup> Topical use only

#### 6.3.16. Piroxicam (NAP) - PSUSA/00002438/202004

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Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.17. Porfimer (NAP) - PSUSA/00010332/202004

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Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.18. Pravastatin (NAP) - PSUSA/00002500/202003

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Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.19. Racecadotril (NAP) - PSUSA/00002602/202003

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Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.20. Reboxetine (NAP) - PSUSA/00002615/202004

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Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.21. Simvastatin (NAP) - PSUSA/00002709/202004

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Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

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

#### 6.3.22. Sodium iodide (<sup>123</sup>I) (NAP) - PSUSA/00002752/202003

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Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

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

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

#### 6.4.1. Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - CERVARIX (CAP) - EMEA/H/C/000721/LEG 097

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Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Review on autoimmunity and autoantibodies based on data from the study by *Hineno et al.*<sup>16</sup> and the study *Blitshetyn et al.*<sup>17</sup> as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00009175/201911) adopted in June 2020

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

#### 6.4.2. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/LEG 159

---

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Review on administration of live vaccines, including a literature review on postnatal clearance of tumour necrosis factor alfa (TNF $\alpha$ ) inhibitors in the newborn, particularly of infliximab and of cases of disseminated BCG<sup>18</sup> vaccinations associated with administration of BCG after birth as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010759/201908) adopted in April 2020

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

#### 6.4.3. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/LEG 160

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Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Cumulative review of cases of hidradenitis including data from clinical trials, post-marketing experience and literature, and taking into account the intended use (indication

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<sup>16</sup> Hineno A, Shu-ichi Ikeda, Scheibenbogen C, Heidecke H, Schulze-Forster K, Junker, et al. Autoantibodies against Autonomic Nerve Receptors in Adolescent Japanese Girls after Immunization with Human Papillomavirus Vaccine. *Ann Arthritis Clin Rheumatol.* 2019;2(2):1014

<sup>17</sup> Blitshetyn S, Brinth L, Hendrickson JE, Martinez-Lavin M. Autonomic dysfunction and HPV immunization: an overview. *Immunol Res.* 2018;66(6):744-54

<sup>18</sup> Bacillus Calmette-Guerin



or off-label use) as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010759/201908) adopted in April 2020

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

#### 6.4.4. [Infliximab - REMICADE \(CAP\) - EMEA/H/C/000240/LEG 161](#)

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Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Cumulative review of cases of abnormal lipid values in clinical studies and literature data on lipid derangements following tumour necrosis factor alfa (TNF $\alpha$ ) inhibitor treatment in general and infliximab treatment in particular as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010759/201908) adopted in April 2020

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

#### 6.4.5. [Linacotide - CONSTELLA \(CAP\) - EMEA/H/C/002490/LEG 015.1](#)

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Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 015 [details on study Truven MarketScan<sup>19</sup> and cumulative review of cases of intestinal perforation as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010025/201908) adopted in March 2020] as per the request for supplementary information (RSI) adopted in July 2020

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

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

#### 6.5.1. [Ceftaroline fosamil - ZINFORO \(CAP\) - EMEA/H/C/002252/II/0055](#)

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Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Maia Uusküla

Scope: Update of sections 4.4 and 5.2 of the SmPC in order to include information on the use of ceftaroline in patients with cystic fibrosis, based on a pooled population pharmacokinetic (pop PK) analysis that included data from cystic fibrosis patients treated with ceftaroline fosamil as requested in the conclusions of LEG 016 adopted in June 2020, initially requested in the conclusions of periodic safety update single assessment (PSUSA) procedure (PSUSA/00010013/201810) adopted in May 2019. The MAH took the opportunity to make minor editorial changes in the product information

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

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<sup>19</sup> Truven MarketScan claims database used to assess the potential association between linacotide and gastrointestinal (GI) perforation

## 6.6. Expedited summary safety reviews<sup>20</sup>

### 6.6.1. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/MEA 017.4

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Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Seventh expedited monthly summary safety report for remdesivir for November 2020 including spontaneously reported data and data from compassionate use and expanded access programmes for the duration of the coronavirus disease (COVID-19) pandemic

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

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

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

#### 7.1.1. Hydroxyethyl starch (HES) (NAP) - EMEA/H/N/PSA/J/0056.1

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Applicant(s): Fresenius Kabi (Volulyte, Voluven), B. Braun Melsungen AG (Tetraspan, Venofundin)

PRAC Rapporteur: Adrien Inoubli

Scope: MAHs' response to PSA/J/0056 [amendment to a joint protocol previously agreed in June 2019 for a retrospective, multinational, drug utilisation study (DUS) to assess the non-adherence of physicians in hydroxyethyl starch (HES) accredited hospitals to the approved European product information regarding indication for use, contraindications and posology (dosage) for HES 130-containing medicinal products in clinical routine after implementation of a set of risk minimisation measures, as required in the outcome of the referral procedure under Article 107i of Directive 2001/83/EC for HES completed in 2018 (EMEA/H/A-107i/1457)] as per the request for supplementary information (RSI) adopted in September 2020

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

#### 7.1.2. Pitolisant – WAKIX (CAP) - EMEA/H/C/PSA/S/0060

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Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Substantial amendment to a protocol previously agreed in September 2016 for a 5-year multicentre, observational PASS to document the utilisation of Wakix (pitolisant) in the treatment of narcolepsy with or without cataplexy and to collect information on its long-term safety when used in routine medical practice

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<sup>20</sup> Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC

<sup>21</sup> In accordance with Article 107n of Directive 2001/83/EC

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

### 7.1.3. [Sotagliflozin – ZYNQUISTA \(CAP\) - EMEA/H/C/PSP/S/0084.3](#)

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Applicant: Guidehouse Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSP/S/0084.2 [protocol for an observational retrospective cohort study using existing data sources on the incidence of diabetic ketoacidosis (DKA) in adult patients with type 1 diabetes mellitus (T1DM) treated with sotagliflozin as an adjunct to insulin versus insulin alone, as required in the outcome of the initial opinion/marketing authorisation (EMA/H/C/004889) finalised in February 2019] as per the request for supplementary information (RSI) adopted in July 2020

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

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

### 7.2.1. [Benralizumab - FASENRA \(CAP\) - EMEA/H/C/004433/MEA 004.3](#)

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Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Substantial amendment to a protocol previously agreed in July 2019 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

### 7.2.2. [Emicizumab - HEMLIBRA \(CAP\) - EMEA/H/C/004406/MEA 002.2](#)

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Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Substantial amendment to a protocol previously agreed in June 2019 for study BO40853 (listed as a category 3 study in the RMP): a PASS based on healthcare professional (HCP) and patient/carer survey to evaluate awareness, knowledge and compliance of HCPs and patients/carers to additional risk minimisation measures (guide for HCPs, patient/carer guide, patient alert card), in relation to the safety concerns of thromboembolic events, thrombotic microangiopathy and life-threatening bleeding due to misinterpretation of the standard coagulation tests

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

### 7.2.3. [Fostamatinib - TAVLESSE \(CAP\) - EMEA/H/C/005012/MEA 002.1](#)

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Applicant: Instituto Grifols, S.A.

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<sup>22</sup> In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 002 [protocol for study BIG-CL-PRT-000015: a post-authorisation long term safety surveillance study of fostamatinib in adult patients with chronic immune thrombocytopenia (cITP) who are refractory to previous treatment [final clinical study report (CSR) expected in March 2025]] as per the request for supplementary information (RSI) adopted in July 2020

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

#### 7.2.4. Fremanezumab - AJOVY (CAP) - EMEA/H/C/004833/MEA 002.2

Applicant: Teva GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Substantial amendment to a protocol previously agreed in March 2020 for observational cohort study TV48125-MH-50037: a pregnancy registry assessing pregnancy outcomes in patients treated with Ajoovy (fremanezumab)

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

#### 7.2.5. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/MEA 006.1

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 006 [protocol for study ALN-AS1-006: a global observational longitudinal prospective registry of patients with acute hepatic porphyria (AHP) [ELEVATE]] as per the request for supplementary information (RSI) adopted in July 2020

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

#### 7.2.6. Hydrocortisone - PLENADREN (CAP) - EMEA/H/C/002185/MEA 009.4

Applicant: Shire Services BVBA

PRAC Rapporteur: Annika Folin

Scope: MAH's response to MEA 009.3 [substantial amendment to a protocol previously agreed in April 2020 for study SHP617-400 (EU AIR): an European multicentre, multi-country, post-authorisation observational study (registry) of patients with chronic adrenal insufficiency] as per the request for supplementary information (RSI) adopted in September 2020

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

#### 7.2.7. Luspatercept - REBLOZYL (CAP) - EMEA/H/C/004444/MEA 003

Applicant: Celgene Europe BV

PRAC Rapporteur: Laurence de Fays

Scope: Protocol for a study to evaluate the effectiveness of the additional risk minimisation measures in Europe in order to assess healthcare professionals (HCP) awareness of key messages included in the HCP checklist for luspatercept including recommendations for

counselling of women of child bearing potential (WCBP) and instructions for providing WCBP with the patient card (from initial opinion/marketing authorisation(s) (MA))

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

#### 7.2.8. Siponimod - MAYZENT (CAP) - EMEA/H/C/004712/MEA 002.1

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA 002 [protocol for a study (listed as a category 3 study in the RMP) on pregnancy outcomes intensive monitoring (PRIM) in order to prospectively collect and evaluate safety data on pregnancy outcomes and congenital malformations related to siponimod exposure immediately before and during pregnancy [final clinical study report (CSR) expected in 2030]] as per the request for supplementary information (RSI) adopted in June 2020

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

#### 7.2.9. Siponimod - MAYZENT (CAP) - EMEA/H/C/004712/MEA 004.1

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's response to MEA 004 [protocol for a survey study (listed as a category 3 study in the RMP) among healthcare professionals (HCPs) and patients/caregivers in selected European countries in order to evaluate whether HCPs and patients/caregivers receive the educational materials and to capture their knowledge and behaviour around specific siponimod safety measures] as per the request for supplementary information (RSI) adopted in June 2020

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

#### 7.2.10. Solriamfetol - SUNOSI (CAP) - EMEA/H/C/004893/MEA 002.1

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Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Julia Pallos

Scope: MAH's response to MEA 002 [protocol for study JZP865-401: a PASS to evaluate the long-term safety of solriamfetol in adult patients with obstructive sleep apnoea (OSA) treated with solriamfetol] as per the request for supplementary information (RSI) adopted in July 2020

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

#### 7.2.11. Tacrolimus - ADVAGRAF (CAP) - EMEA/H/C/000712/MEA 030

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Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ronan Grimes

Scope: Protocol for study F506-PV-0001: a non-interventional PASS on outcomes associated with the use of tacrolimus around conception, or during pregnancy or lactation using data from

Transplant Pregnancy Registry International (TPRI) registry

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

#### 7.2.12. Tacrolimus - MODIGRAF (CAP) - EMEA/H/C/000954/MEA 022

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Protocol for study F506-PV-0001: a non-interventional PASS on outcomes associated with the use of tacrolimus around conception, or during pregnancy or lactation using data from Transplant Pregnancy Registry International (TPRI) registry

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

#### 7.2.13. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 014.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 014 [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 2020

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

#### 7.2.14. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 003.1

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 003 [protocol for study P19-150: a long-term post-authorisation safety study (PASS) of upadacitinib use in rheumatoid arthritis (RA) patients in Europe to evaluate the safety of upadacitinib among patients with RA receiving routine clinical care [final study report expected in March 2030]] as per the request for supplementary information (RSI) adopted in June 2020

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

#### 7.2.15. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 004.1

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 004 [protocol for study P19-141: a long-term post-authorisation safety study (PASS) of upadacitinib use in rheumatoid arthritis (RA) patients in the US in order to: 1) compare the incidence of malignancy, non-melanoma skin cancer (NMSC), major adverse cardiovascular events (MACE), venous thromboembolism (VTE)

and serious infection events in adults with RA who receive upadacitinib in the course of routine clinical care relative to those who receive biologic therapy for the treatment of RA; 2) describe the incidence rates of herpes zoster, opportunistic infections and evidence of drug-induced liver injury (DILI); 3) describe the incidence of the above outcomes in very elderly patients (aged  $\geq 75$  years); 4) characterise VTE clinical risk factors and baseline biomarkers in a sub-study of new initiators of upadacitinib and comparator biologic therapies [final study report expected in March 2033]] as per the request for supplementary information (RSI) adopted in June 2020

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

#### 7.2.16. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 005.1

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Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 005 [protocol for study P20-199: a drug utilisation study (DUS) to evaluate the effectiveness of the additional risk minimisation measures (aRMM) in place to describe the baseline characteristics of new users of upadacitinib, and in a similar manner, to describe new users of a biological disease-modifying antirheumatic drugs (bDMARD) for comparison [final study report expected in September 2024]] as per the request for supplementary information (RSI) adopted in June 2020

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

#### 7.2.17. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 044.9

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Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 044.8 [substantial amendment to a protocol previously agreed in October 2019 for study CNTO1275PSO4056: an observational PASS of ustekinumab in the treatment of paediatric patients aged 12 years and older with moderate to severe plaque psoriasis (adolescent registry)] as per the request for supplementary information (RSI) adopted in July 2020

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

### 7.3. Results of PASS imposed in the marketing authorisation(s)<sup>23</sup>

#### 7.3.1. Teicoplanin (NAP) - EMEA/H/N/PSR/S/0025

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Applicant: Sanofi (Targocid)

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSR/S/0025 [results for a PASS study: a prospective, observational cohort, evaluating the incidence of nephrotoxicity and other adverse events of interest in patients treated with the higher recommended teicoplanin loading dose (12mg/kg twice a day), and comparison with external historical comparator data] as per the request for

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<sup>23</sup> In accordance with Article 107p-q of Directive 2001/83/EC

supplementary information (RSI) adopted in October 2020

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

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

### 7.4.1. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/II/0079

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Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of the final report from study ALGMYC07390: prevalence of immunology testing in patients treated with alglucosidase alfa with significant hypersensitivity/anaphylactic reactions to test the effectiveness of the approved safety information packet (SIP)

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

### 7.4.2. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/II/0068

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of the final report related to the physician survey (NO6987) conducted for Exjade (deferasirox) to assess the impact of educational materials on the prescribers' awareness of doses and biological monitoring recommendations and to assess the awareness and appropriate use of both formulations (dispersible tablets and film-coated tablets). The RMP (version 17.1) is updated accordingly

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

### 7.4.3. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/II/0051

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Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: Submission of the final study report for study B009 (listed as a category 3 study in the RMP): a multi-database collaborative research programme of observational studies to monitor the drug utilisation and safety of dulaglutide in the EU (in fulfilment of MEA 002). The RMP (version 6.1) is updated accordingly

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

### 7.4.4. Edoxaban - LIXIANA (CAP) - EMEA/H/C/002629/WS1760/0024; ROTEAS (CAP) - EMEA/H/C/004339/WS1760/0011

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Applicant(s): Daiichi Sankyo Europe GmbH (Lixiana), Berlin Chemie AG (Roteas)

PRAC Rapporteur: Adrien Inoubli

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<sup>24</sup> In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013



Scope: Submission of the final study report from study ETNA-DUS (listed as a category 3 study in the RMP): edoxaban treatment in routine clinical practice drug utilisation study - a retrospective drug utilisation chart review study to gain insight on how edoxaban is used in real practice, to identify prescription patterns and to measure the effectiveness of the educational programmes

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

#### 7.4.5. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/WS1653/0230; LIFMIOR<sup>25</sup> - EMEA/H/C/004167/WS1653/0024

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Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Eva Segovia

Scope: Submission of the second 5-year report from the British Society for Rheumatology Biologics Register (BSRBR) also referred as study B1801309 (listed as a category 3 study in the RMP). This is a prospective observational cohort study which investigates the long-term outcomes of patients with rheumatoid arthritis treated with etanercept with particular reference to safety

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

#### 7.4.6. Florbetaben (<sup>18</sup>F) - NEURACEQ (CAP) - EMEA/H/C/002553/II/0033

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Applicant: Life Radiopharma Berlin GmbH

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study FBB-01\_03\_13 (PASS-2) (listed as a category 3 study in the RMP): a non-interventional, cross-sectional, retrospective, multicentre, multi-country registry to observe usage pattern, safety and tolerability of the diagnostic agent NeuraCeq (florbetaben (<sup>18</sup>F)) in European clinical practice. The RMP (version 5.9) is updated accordingly

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

#### 7.4.7. Nitisinone - ORFADIN (CAP) - EMEA/H/C/000555/II/0074

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Applicant: Swedish Orphan Biovitrum International AB

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of the final report from study Sobi.NTBC-005 (listed as a category 3 study in the RMP): a non-interventional PASS to evaluate the long-term safety of Orfadin (nitisinone) treatment in hereditary tyrosinaemia type 1 (HT-1) patients in standard clinical care. The RMP (version 5.3) is updated accordingly

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

#### 7.4.8. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/II/0113

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Applicant: Amgen Europe B.V.

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<sup>25</sup> Marketing authorisation(s) ceased to be valid in the European Union (EU) on 16 February 2020

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study 20160176 (listed as a category 3 study in the RMP): a retrospective cohort study with the time from index date to diagnosis of myelodysplastic syndrome (MDS) or acute myeloid leukaemia (AML) as a primary outcome

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

#### **7.4.9. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/II/0082**

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Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final safety registry report of study CNTO1275PSO4005 (listed as a category 3 study in the RMP): a Nordic database initiative for exposure to ustekinumab - a review and analysis of adverse events from the Swedish and Danish national registry systems. The RMP (version 18.2) is updated accordingly

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

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

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Applicant: Shire Pharmaceuticals Ireland Limited

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. Filgrastim - FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/MEA 007.8**

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Applicant: Hexal AG

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 007.7 [5-year interim results for study EP06-501 (SMART): a non-interventional, prospective, long-term safety data collection of Zarzio/Filgrastim Hexal (filgrastim) in healthy unrelated stem cell donors undergoing peripheral blood progenitor cell (PBPC) mobilisation, in light of available data [final clinical study report (CSR) expected in December 2024]] as per the request for supplementary information (RSI) adopted in June 2020

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

## 7.5.2. Filgrastim - ZARZIO (CAP) - EMEA/H/C/000917/MEA 007.8

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Applicant: Sandoz GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 007.7 [5-year interim results for study EP06-501 (SMART): a non-interventional, prospective, long-term safety data collection of Zarzio/Filgrastim Hexal (filgrastim) in healthy unrelated stem cell donors undergoing peripheral blood progenitor cell (PBPC) mobilisation, in light of available data [final clinical study report (CSR) expected in December 2024]] as per the request for supplementary information (RSI) adopted in June 2020

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

## 7.5.3. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/ANX 041.9

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Applicant: Celgene Europe BV

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to ANX 041.8 [second interim descriptive report for study CC-5013-MDS-012 (listed as a category 1 study in Annex II): a post-authorisation, non-interventional, retrospective, drug-utilisation study (DUS) to describe the pattern of use of lenalidomide in patients with myelodysplastic syndromes (MDS)] as per the request for supplementary information (RSI) adopted in June 2020

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

## 7.5.4. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/MEA 008.8

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Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Fourth 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

## 7.6. Others

### 7.6.1. Guanfacine - INTUNIV (CAP) - EMEA/H/C/003759/ANX 004.3

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Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Substantial amendment to a protocol previously agreed by CHMP in September 2017 for study SHP503-401: a phase 4, interventional, multicentre, 2-part study composed of a 1-year randomised, double-blind, parallel-group, placebo-controlled, active-comparator, dose-optimisation evaluation followed by a 1-year open-label evaluation to assess the long-term safety of Intuniv (guanfacine) on selected domains of cognition in children and

adolescents aged 6-17 years with attention deficit hyperactivity disorder (ADHD) for whom stimulants are not suitable, not tolerable, or shown to be ineffective

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

#### 7.6.2. Radium (<sup>223</sup>Ra) dichloride - XOFIGO (CAP) - EMEA/H/C/002653/MEA 015

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Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Interim report for study PEACE-3 - European Organisation for Research and Treatment of Cancer (EORTC)-sponsored phase 3 study: a randomised multicentre phase 3 trial comparing enzalutamide vs a combination of radium-223 dichloride and enzalutamide in asymptomatic or mildly symptomatic castration resistant prostate cancer (CRPC) patients metastatic to bone in order to address the important identified risk of bone fractures [final clinical study report (CSR) expected in April 2021] as required in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in 2018 (EMEA/H/A-20/1459)

**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/0048 (without RMP)

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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/0028 (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/0043 (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/0064 (with RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Annual reassessment of the marketing authorisation

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

### 8.1.5. Vestronidase alfa - MEPSEVII (CAP) - EMEA/H/C/004438/S/0017 (without RMP)

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Eva Segovia

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. Andexanet alfa - ONDEXXYA (CAP) - EMEA/H/C/004108/R/0015 (with RMP)

Applicant: Portola Netherlands B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

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

### 8.2.2. Bosutinib - BOSULIF (CAP) - EMEA/H/C/002373/R/0045 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Conditional renewal of the marketing authorisation

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

#### **8.2.3. Cabozantinib - COMETRIQ (CAP) - EMEA/H/C/002640/R/0042 (with RMP)**

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Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

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

#### **8.2.4. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/R/0047 (without RMP)**

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Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Laurence de Fays

Scope: Conditional renewal of the marketing authorisation

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

#### **8.2.5. Parathyroid hormone - NATPAR (CAP) - EMEA/H/C/003861/R/0027 (without RMP)**

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Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Conditional renewal of the marketing authorisation

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

#### **8.2.6. Volanesorsen - WAYLIVRA (CAP) - EMEA/H/C/004538/R/0009 (without RMP)**

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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. Autologous CD34<sup>+</sup> enriched cell fraction that contains CD34<sup>+</sup> cells transduced with retroviral vector that encodes for the human adenosine deaminase (ADA) complementary deoxyribonucleic acid (cDNA) sequence - STRIMVELIS (CAP) - EMEA/H/C/003854/R/0029 (without RMP)**

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Applicant: Orchard Therapeutics (Netherlands) BV; ATMP<sup>26</sup>

PRAC Rapporteur: Menno van der Elst

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

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.2. [Ceftazidime, avibactam - ZAVICEFTA \(CAP\) - EMEA/H/C/004027/R/0024 \(without RMP\)](#)

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Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Rugile Pilviniene

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.3. [Eftrenonacog alfa - ALPROLIX \(CAP\) - EMEA/H/C/004142/R/0032 \(without RMP\)](#)

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Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.4. [Infliximab - FLIXABI \(CAP\) - EMEA/H/C/004020/R/0064 \(without RMP\)](#)

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Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.5. [Lutetium \(<sup>177</sup>Lu\) chloride - ENDOLUCINBETA \(CAP\) - EMEA/H/C/003999/R/0019 \(without RMP\)](#)

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Applicant: ITM Medical Isotopes GmbH

PRAC Rapporteur: Rugile Pilviniene

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.6. [Migalastat - GALAFOLD \(CAP\) - EMEA/H/C/004059/R/0027 \(with RMP\)](#)

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Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.7. Opicapone - ONGENTYS (CAP) - EMEA/H/C/002790/R/0031 (with RMP)

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Applicant: Bial - Portela & C<sup>a</sup>, S.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.8. Palonosetron - PALONOSETRON ACCORD (CAP) - EMEA/H/C/004129/R/0009 (without RMP)

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Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Rhea Fitzgerald

Scope: 5-year renewal of the marketing authorisation

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

### 8.3.9. Sacubitril, valsartan - NEPARVIS (CAP) - EMEA/H/C/004343/R/0032 (without RMP)

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Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

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

#### 9.1.1. Risk-based programme for routine pharmacovigilance inspections of marketing authorisation holders connected with human centrally authorised products

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Scope: Pharmacovigilance inspection programme 2020-2023 (first revision for 2020)

**Action:** For adoption

### 9.2. Ongoing or concluded pharmacovigilance inspections

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

### 9.3. Others

None



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

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

None

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

None

### 10.3. Other requests

None

### 10.4. Scientific Advice

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

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

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

#### 11.1.1. Dinoprostone (NAP) - SE/H/PSUFU/00001104/201909

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Applicant(s): Ferring (Propess), Pfizer (Minprostin, Prepidil, Prostaglandin E2 Pfizer, Prostin E2)

PRAC Lead: Annika Folin

Scope: PRAC consultation on a PSUR follow-up (PSU FU) procedure on risk minimisation measures to further minimise the risk of uterine hyperstimulation, including serious complications as uterine rupture, foetal and neonatal death and uterine haemorrhage, as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure (PSUSA/00001104/201909) concluded in May 2020, on request of Sweden

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

## 11.2. Other requests

### 11.2.1. Levonorgestrel<sup>27</sup> (NAP) - DE/H/PSUFU/00001856/201905

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Applicant(s): Bayer (Mirena, Jaydess/Fleree/Luadei/Skyla, Kyleena); Gedeon Richter (Levosert)

PRAC Lead: Martin Huber

Scope: Second PRAC consultation on a PSUR follow-up (PSU FU) procedure on a review of cases reporting meningioma together with a causality assessment, biological plausibility and literature analysis, as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure (PSUSA/00001856/201905) concluded in January 2020, following a previous advice adopted in September 2020, on request of Germany

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

## 12. Organisational, regulatory and methodological matters

### 12.1. Mandate and organisation of the PRAC

None

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

None

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

#### 12.3.1. Infectious disease working party (IDWP): product information update across all medicinal products with indication in human immunodeficiency virus (HIV) - proposal

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**Action:** For discussion

### 12.4. Cooperation within the EU regulatory network

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

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**Action:** For discussion

#### 12.4.2. Heads of Medicines Agencies (HMA)-EMA joint big data – Big data training signpost

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**Action:** For discussion

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<sup>27</sup> Levonorgestrel intrauterine device (LNG-IUD)

## 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

### 12.6.1. Coronavirus (COVID-19)-vaccines monitoring: ACCESS<sup>28</sup> consortium project - safety and effectiveness - protocols

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PRAC lead: John Joseph Borg, Jean Michel Dogné, Adrien Inoubli, Brigitte Keller-Stanislawski

**Action:** For discussion

### 12.6.2. Coronavirus (COVID-19)-medicines monitoring: CONSIGN<sup>29</sup> consortium project – COVID-19 infection and medicines in pregnancy – protocol

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PRAC lead: Sabine Straus, Ulla Wändel Liminga

**Action:** For discussion

## 12.7. PRAC work plan

### 12.7.1. PRAC work plan 2021 – preparation

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PRAC lead: Sabine Straus, Martin Huber

**Action:** For discussion

## 12.8. Planning and reporting

None

## 12.9. Pharmacovigilance audits and inspections

### 12.9.1. Pharmacovigilance systems and their quality systems

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None

### 12.9.2. Pharmacovigilance inspections

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None

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<sup>28</sup> vACcine Covid-19 monitoring readinESS

<sup>29</sup> Covid-19 infectiOn aNd medicineS In pregnancy

### 12.9.3. Pharmacovigilance audits

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None

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

### 12.10.1. Periodic safety update reports

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None

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

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PRAC lead: Menno van der Elst, Maia Uusküla

**Action:** For discussion

### 12.10.3. PSURs repository

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None

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

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**Action:** For adoption

## 12.11. Signal management

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

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PRAC lead: Menno van der Elst

**Action:** For discussion

## 12.12. Adverse drug reactions reporting and additional reporting

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

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None

### 12.12.2. Additional monitoring

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None

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

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**Action:** For adoption

**12.13. EudraVigilance database**

12.13.1. Activities related to the confirmation of full functionality

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None

12.13.2. EudraVigilance – Expert Working Group (EV-EWG) – nomination of PRAC representative

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**Action:** For discussion

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

12.14.1. Risk management systems

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None

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

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None

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

12.15.1. Post-authorisation Safety Studies – imposed PASS

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None

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

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None

**12.16. Community procedures**

12.16.1. Referral procedures for safety reasons

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None

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

None

## 12.18. Risk communication and transparency

### 12.18.1. Coronavirus (COVID-19)-vaccines – EMA safety updates to the public

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**Action:** For discussion

### 12.18.2. PRAC meeting highlights – proposal for revision

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**Action:** For discussion

### 12.18.3. Public participation in pharmacovigilance

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None

### 12.18.4. Safety communication

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None

## 12.19. Continuous pharmacovigilance

### 12.19.1. Incident management

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None

## 12.20. Others

### 12.20.1. Commission implementing Regulation (EU) No 520/2012 – scoping paper

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**Action:** For discussion

### 12.20.2. Strategy on measuring the impact of pharmacovigilance – PRAC interest group (IG) Impact – update on engagement workstream

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PRAC lead: Antoine Pariente

**Action:** For discussion

## 13. Any other business

## 14. Explanatory notes

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

### **EU Referral procedures for safety reasons: Urgent EU procedures and Other EU referral procedures** (Items 2 and 3 of the PRAC agenda)

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

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

### **Signals assessment and prioritisation**

(Item 4 of the PRAC agenda)

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

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

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

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

(Item 5 of the PRAC agenda)

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

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

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

(Item 6 of the PRAC agenda)

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

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

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

(Item 7 of the PRAC agenda)

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

### **Product related pharmacovigilance inspections**

(Item 9 of the PRAC agenda)

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

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