



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

23 January 2023  
EMA/CHMP/953395/2023  
Human Medicines Division

## Committee for medicinal products for human use (CHMP)

### Draft agenda for the meeting on 23-26 January 2023

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

23 January 2023, 13:00 – 19:30, virtual meeting/room 1C

24 January 2023, 08:30 – 19:30, virtual meeting/room 1C

25 January 2023, 08:30 – 19:30, virtual meeting/room 1C

26 January 2023, 08:30 – 15:00, virtual meeting/room 1C

#### Health and safety information

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

#### Disclaimers

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

Of note, this agenda is a working document primarily designed for CHMP 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 ongoing 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).



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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 CHMP plenary session to be held 23-26 January 2023. See January 2023 CHMP minutes (to be published post February 2023 CHMP meeting).

The CHMP is reminded that the majority will be reduced to 16, as long as the 5<sup>th</sup> co-opted member position is vacant (see 14.1.2).

### 1.2. Adoption of agenda

CHMP agenda for 23-26 January 2023.

### 1.3. Adoption of the minutes

CHMP minutes for 12-15 December 2022.

Minutes from PReparatory and Organisational Matters (PROM) meeting held on 16 January 2023.

## 2. Oral Explanations

### 2.1. Pre-authorisation procedure oral explanations

#### 2.1.1. pegunigalsidase alfa - Orphan - EMEA/H/C/005618

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Chiesi Farmaceutici S.p.A.; treatment of Fabry disease

Scope: Oral explanation

**Action:** Oral explanation to be held on Tuesday 24 January 2023 at 09:00

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 23.06.2022.

#### 2.1.2. vadadustat - EMEA/H/C/005131

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treatment of anaemia

Scope: Oral explanation

**Action:** Oral explanation to be held on Tuesday 24 January 2023 at 16:00

List of Outstanding Issues adopted on 15.12.2022, 15.09.2022. List of Questions adopted

on 24.03.2022.

## 2.2. Re-examination procedure oral explanations

No items

## 2.3. Post-authorisation procedure oral explanations

No items

## 2.4. Referral procedure oral explanations

No items

# 3. Initial applications

## 3.1. Initial applications; Opinions

### 3.1.1. dabigatran etexilate - EMEA/H/C/005639

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prevention of venous thromboembolic events

Scope: Opinion

**Action:** For adoption

List of Outstanding Issues adopted on 15.09.2022, 23.06.2022, 24.02.2022. List of Questions adopted on 12.11.2020.

### 3.1.2. dapagliflozin - EMEA/H/C/006006

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treatment of type 2 diabetes mellitus, heart failure and chronic kidney disease

Scope: Opinion

**Action:** For adoption

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 23.06.2022.

### 3.1.3. sitagliptin / metformin hydrochloride - EMEA/H/C/005778

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treatment of type 2 diabetes mellitus

Scope: Opinion

**Action:** For adoption

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 23.06.2022.



### 3.1.4. palovarotene - Orphan - EMEA/H/C/004867

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Ipsen Pharma; treatment of fibrodysplasia ossificans progressiva

Scope: Opinion

**Action:** For adoption

List of Outstanding Issues adopted on 15.09.2022. List of Questions adopted on 16.09.2021.

### 3.1.5. deucravacitinib - EMEA/H/C/005755

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treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy

Scope: Opinion

**Action:** For adoption

List of Outstanding Issues adopted on 15.12.2022, 21.07.2022. List of Questions adopted on 24.02.2022.

### 3.1.6. tolvaptan - EMEA/H/C/005961

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treatment of hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Scope: Opinion

**Action:** For adoption

List of Outstanding Issues adopted on 13.10.2022. List of Questions adopted on 22.04.2022.

## 3.2. Initial applications; List of outstanding issues (Day 180; Day 120 for procedures with accelerated assessment timetable)

### 3.2.1. aripiprazole - EMEA/H/C/005929

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Maintenance treatment of schizophrenia

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 13.10.2022.

### 3.2.2. ublituximab - EMEA/H/C/005914

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treatment of relapsing forms of multiple sclerosis (RMS)

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 22.04.2022.

### 3.2.3. mirikizumab - EMEA/H/C/005122

treatment of moderately to severely active ulcerative colitis

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 15.09.2022.

### 3.2.4. ganaxolone - Orphan - EMEA/H/C/005825

Marinus Pharmaceuticals Emerald Limited; treatment of epileptic seizures associated with cyclindependent kinase-like 5 deficiency disorder (CDD)

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 25.01.2022.

## **3.3. Initial applications; List of questions (Day 120; Day 90 for procedures with accelerated assessment timetable)**

### 3.3.1. recombinant respiratory syncytial virus pre-fusion F protein, adjuvanted with AS01E - EMEA/H/C/006054

#### **Accelerated assessment**

active immunisation or the prevention of lower respiratory tract disease (LRTD)

Scope: List of questions

**Action:** For adoption

### 3.3.2. latanoprost - EMEA/H/C/005933

Reduction of elevated intraocular pressure (IOP)

Scope: List of questions

**Action:** For adoption

### 3.3.3. dabrafenib - Orphan - EMEA/H/C/005885

Novartis Europharm Limited; Treatment of glioma

Scope: List of questions

**Action:** For adoption

### 3.3.4. leniolisib - Orphan - EMEA/H/C/005927

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#### **Accelerated assessment**

Pharming Technologies B.V.; Treatment of activated phosphoinositide 3-kinase delta syndrome (APDS)

Scope: List of questions

**Action:** For adoption

### 3.3.5. trametinib - Orphan - EMEA/H/C/005886

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Novartis Europharm Limited; Treatment of paediatric patients aged 1 year and older with glioma

Scope: List of questions

**Action:** For adoption

### 3.3.6. tocilizumab - EMEA/H/C/005984

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treatment of rheumatoid arthritis, active systemic juvenile idiopathic arthritis (sJIA), juvenile idiopathic polyarthritis (pJIA), chimeric antigen receptor (CAR) T cell-induced cytokine release syndrome (CRS) and COVID-19

Scope: List of questions

**Action:** For adoption

### 3.3.7. fezolinetant - EMEA/H/C/005851

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treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause

Scope: List of questions

**Action:** For adoption

### 3.3.8. zilucoplan - Orphan - EMEA/H/C/005450

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UCB Pharma S.A.; treatment of generalised myasthenia gravis in adults

Scope: List of questions

**Action:** For adoption

## 3.4. Update on on-going initial applications for Centralised procedure

### 3.4.1. crisantaspase - EMEA/H/C/005917

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Indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukaemia (ALL) and lymphoblastic lymphoma (LBL).

Scope: Letter by the applicant dated 10.01.2023 requesting an extension to the clock stop

to respond to the list of questions adopted in October 2022.

**Action:** For adoption

List of Question adopted on 13.10.2022

### 3.4.2. [bevacizumab - EMEA/H/C/005574](#)

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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.

Scope: Letter by the applicant dated 21.12.2022 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in February 2022.

**Action:** For adoption

List of Outstanding Issues adopted on 24.02.2022. List of Questions adopted on 22.04.2021.

### 3.4.3. [daprodustat - EMEA/H/C/005746](#)

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treatment of anaemia associated with chronic kidney disease (CKD) in adults

Scope: Letter by the applicant dated 04.01.2023 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in November 2022.

**Action:** For adoption

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 23.06.2022.

## 3.5. **Re-examination of initial application procedures under Article 9(2) of Regulation no 726/2004**

No items

## 3.6. **Initial applications in the decision-making phase**

No items

## 3.7. **Withdrawals of initial marketing authorisation application**

No items

## 4. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008

### 4.1. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Opinion

#### 4.1.1. Byfavo - remimazolam - EMEA/H/C/005246/X/0002

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Paion Deutschland GmbH

Rapporteur: Bruno Sepodes, Co-Rapporteur: Selma Arapovic Dzakula, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Extension application to introduce a new pharmaceutical form associated with new strength (50 mg powder for concentrate for solution for injection/infusion). The new presentation is indicated to include the intravenous induction and maintenance of general anaesthesia (GA) in adults for Byfavo 50 mg, based on final results from two pivotal trials: Study ONO-2745-05, a phase IIb/III, single-blind, randomised, parallel-group study assessing safety and efficacy in induction and maintenance of anaesthesia in ASA I/II patients (general surgery), and study CNS-7056-022, a phase III, randomized, propofol controlled, parallel group, confirmatory single-blind efficacy and safety trial during induction and maintenance of anaesthesia in ASA III/IV patients.

A new combined version of the SmPC, labelling and Package Leaflet solely for the 50 mg strength and the GA indication is provided accordingly.

Version 1.3 of the RMP has also been submitted."

**Action:** For adoption

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 19.05.2022.

#### 4.1.2. Hefiya - adalimumab - EMEA/H/C/004865/X/0036/G

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Sandoz GmbH

Rapporteur: Christian Gartner, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add a new strength (80 mg/0.8 ml) of the solution for injection grouped with quality variations. The Package Leaflet and Labelling are updated in accordance.

The RMP (version 9.0) has also been submitted.

Additionally, the applicant takes the opportunity to include editorial changes in the pack sizes (approved (001-003) and new presentations) in the List of All Authorised Presentations (Annex A) to differentiate packs of pre-filled syringes with or without needle safety device."

**Action:** For adoption

List of Questions adopted on 13.10.2022.

#### 4.1.3. Hyrimoz - adalimumab - EMEA/H/C/004320/X/0036/G

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Sandoz GmbH

Rapporteur: Christian Gartner, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add a new strength (80 mg/0.8 ml) of the solution for injection grouped with quality variations. The Package Leaflet and Labelling are updated in accordance.

The RMP (version 9.0) has also been submitted.

Additionally, the applicant takes the opportunity to include editorial changes in the pack sizes (approved (001-003) and new presentations) in the List of All Authorised Presentations (Annex A) to differentiate packs of pre-filled syringes with or without needle safety device."

**Action:** For adoption

List of Questions adopted on 13.10.2022.

#### 4.2. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 180 list of outstanding issues

##### 4.2.1. Ultomiris - ravulizumab - EMEA/H/C/004954/X/0027/G

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Alexion Europe SAS

Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension application to introduce a new pharmaceutical form (solution for injection) associated with new strength (245 mg) and route of administration (subcutaneous use), grouped with a type II variation (C.I.4) to align the Summary of product characteristics and Labelling of Ultomiris intravenous formulation (IV) with the proposed Ultomiris subcutaneous formulation (SC). The RMP (version 5.0) is updated in accordance."

**Action:** For adoption

List of Outstanding Issues adopted on 13.10.2022. List of Questions adopted on 21.07.2022.

#### 4.3. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 120 List of question

##### 4.3.1. Esperoct - turoctocog alfa pegol - EMEA/H/C/004883/X/0016

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Novo Nordisk A/S

Rapporteur: Daniela Philadelphy

Scope: "Extension application to add two new strengths of 4000 IU and 5000 IU powder and solvent for solution for injection."

**Action:** For adoption

#### 4.3.2. Ofev - nintedanib - EMEA/H/C/003821/X/0052/G

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Boehringer Ingelheim International GmbH

Rapporteur: Finbarr Leacy, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension application to add a new strength of 25 mg soft capsule grouped with a type II variation C.I.6.a to add a new indication of treatment of fibrosing Interstitial Lung Diseases (ILDs) in children and adolescents from 6 to 17 years of age, based on results from study 1199 0337 (InPedILD); a randomised, placebo-controlled, double-blind, multicentre, multinational, phase III clinical trial undertaken to evaluate dose-exposure and safety of nintedanib on top of standard of care in children and adolescents (6 to 17 years old) with clinically significant fibrosing ILD. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes to the list of local representatives in the Package Leaflet. The updated RMP version 12.0 is also submitted."

**Action:** For adoption

#### 4.3.3. Olumiant - baricitinib - EMEA/H/C/004085/X/0035/G

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Eli Lilly Nederland B.V.

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension application to introduce a new strength (1 mg film-coated tablet), grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment, as monotherapy or in combination with conventional synthetic disease modifying antirheumatic drugs (DMARDs), of active juvenile idiopathic arthritis (JIA) in patients 2 years of age and older who have had an inadequate response or intolerance to one or more prior conventional synthetic or biologic DMARDs, based on final results from the pivotal study JAHV (I4V-MC-JAHV); this is a multicentre, double-blind, randomised, placebo-controlled, medication-withdrawal Phase 3 study in children from 2 years to less than 18 years of age with JIA who have had an inadequate response or intolerance to treatment with at least 1 cDMARD or bDMARD. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 15.1 of the RMP has also been submitted."

**Action:** For adoption

#### 4.3.4. Viagra - sildenafil - EMEA/H/C/000202/X/0115

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Upjohn EESV

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Maria Concepcion Prieto Yerro

Scope: "Extension application to introduce a new pharmaceutical form (orodispersible film)."

**Action:** For adoption

#### 4.4. Update on on-going extension application according to Annex I of Commission Regulation (EC) No 1234/2008

No items

#### 4.5. Re-examination procedure of extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008

No items

### 5. Type II variations - variation of therapeutic indication procedure according to Annex I of Commission Regulation (EC) No 1234/2008

#### 5.1. Type II variations - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008; Opinions or Requests for supplementary information

##### 5.1.1. Dupixent - dupilumab - EMEA/H/C/004390/II/0060

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sanofi-aventis groupe

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Finbarr Leacy, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension of indication to include treatment of atopic dermatitis in paediatric patients from 6 months to <6 years of age based on final results from study R668-AD-1539; this is a phase 2/3 study investigating the pharmacokinetics, safety and efficacy of dupilumab in patients aged  $\geq$ 6 months to <6 years with moderate-to-severe atopic dermatitis.

As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 7.0 of the RMP has also been submitted."

**Action:** For adoption

Request for Supplementary Information adopted on 13.10.2022, 23.06.2022.

##### 5.1.2. Nubeqa - darolutamide - EMEA/H/C/004790/II/0009

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Bayer AG

Rapporteur: Alexandre Moreau, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Jan Neuhauser

Scope: "Extension of indication to include treatment of adult men with metastatic hormone-sensitive prostate cancer (mHSPC) in combination with docetaxel, based on final results from study 17777 (ARASENS); this is a randomized, double-blind, placebo-controlled Phase 3 study designed to demonstrate the superiority of darolutamide in combination with docetaxel over placebo in combination with docetaxel in OS in patients with mHSPC. As a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package



Leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted. As part of the application, the MAH is also requesting one additional year of market protection.”, Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

**Action:** For adoption

Request for Supplementary Information adopted on 15.12.2022, 15.09.2022, 23.06.2022.

### 5.1.3. [Reblozyl - luspaterecept - Orphan - EMEA/H/C/004444/II/0009](#)

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Bristol-Myers Squibb Pharma EEIG

Rapporteur: Daniela Philadelphly, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Jo Robays

Scope: “C.I.6 (Extension of indication)

Extension of indication in  $\beta$ -thalassaemia to include adult patients with non-transfusion dependent  $\beta$ -thalassaemia (NTDT) for Reblozyl; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.”, Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

**Action:** For adoption

Request for Supplementary Information adopted on 15.12.2022, 10.11.2022, 23.06.2022, 27.01.2022.

### 5.1.4. [Rinvoq - upadacitinib - EMEA/H/C/004760/II/0027](#)

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AbbVie Deutschland GmbH & Co. KG

Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: “Extension of indication to include treatment of moderately to severely active Crohn's disease in adult patients for Rinvoq, based on final results from three Phase III studies, two confirmatory placebo-controlled induction studies (study M14 431/U-EXCEED/CD-1 and study M14 433/U-EXCEL/CD-2) and a placebo-controlled maintenance/long-term extension study (study M14-430/U-ENDURE/CD-3). M14-431 study is a Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled Induction Study of the Efficacy and Safety of Upadacitinib (ABT-494) in Subjects with Moderately to Severely Active Crohn's Disease Who Have Inadequately Responded to or are Intolerant to Biologic Therapy.

M14-433 study is a Phase III, Multicenter, Randomized, Double-Blind, Placebo Controlled Induction Study of the Efficacy and Safety of Upadacitinib (ABT-494) in Subjects with Moderately to Severely Active Crohn's Disease Who Have Inadequately Responded to or are Intolerant to Conventional and/or Biologic Therapies.

M14-430 study is an ongoing Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled Maintenance and Long-Term Extension Study of the Efficacy and Safety of Upadacitinib (ABT-494) in Subjects with Crohn's Disease Who Completed the Studies M14-431 or M14-433.

As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are

updated. The Package Leaflet is updated in accordance. Version 11 of the RMP has also been submitted.”

**Action:** For adoption

Request for Supplementary Information adopted on 10.11.2022.

#### 5.1.5. TachoSil - human thrombin / human fibrinogen - EMEA/H/C/000505/II/0117

Corza Medical GmbH

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: “Extension of indication to include treatment of children aged 1 month to 18 years, based on available bibliographical data, results from study TC-2402-040-SP which compared TachoSil with Surgicel Original as adjunct to primary surgical treatment in both adult and paediatric subjects, and results from study TC-019-IN; a prospective, uncontrolled study in paediatric subjects. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes in the product information. Version 0.1 of the RMP has also been submitted.”

**Action:** For adoption

Request for Supplementary Information adopted on 15.09.2022.

#### 5.1.6. Trecondi - treosulfan - Orphan - EMEA/H/C/004751/II/0014

medac Gesellschaft für klinische Spezialpräparate mbH

Rapporteur: Fátima Ventura, PRAC Rapporteur: Julia Pallos

Scope: “Extension of indication to include additional non-malignant transplant indications (non-malignant diseases in the paediatric population) for Trecondi 1 g/5 g powder for solution for infusion based on final 12-months follow-up results of study MC-FludT.16/NM; a randomised phase II interventional study aimed to compare Treosulfan-based conditioning therapy with Busulfan-based conditioning prior to allogeneic haematopoietic stem cell transplantation in paediatric patients with non-malignant diseases.

Further, the MAH proposes to amend an existing warning on skin toxicity based on new literature data. Moreover, the MAH proposes to introduce a slightly modified dosing regimen according to the patient’s body surface based on long-term follow-up data of paediatric study MC-FludT.17/M, a Phase II trial to describe the safety and efficacy of Treosulfan based conditioning therapy prior to allogeneic haematopoietic stem cell transplantation in paediatric patients with haematological malignancies, as well as a final analysis of the population pharmacokinetics of treosulfan in paediatric patients. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.0 of the RMP has also been submitted.”

**Action:** For adoption

Request for Supplementary Information adopted on 10.11.2022, 21.07.2022.

### 5.1.7. Trulicity - dulaglutide - EMEA/H/C/002825/II/0065

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Eli Lilly Nederland B.V.

Rapporteur: Martina Weise, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to include treatment of type 2 diabetes mellitus (T2DM) in children and adolescents aged 10 to less than 18 years based on final results from study H9X-MC-GBGC; this is a phase 3, double-blind, randomised, multi-centre, placebo-controlled superiority trial to evaluate PK, PD, safety and efficacy of dulaglutide in children from 10 to less than 18 years of age, with an open label extension to evaluate safety. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 7.1 of the RMP has also been submitted."

**Action:** For adoption

Request for Supplementary Information adopted on 13.10.2022.

### 5.1.8. Valdoxan - agomelatine - EMEA/H/C/000915/II/0051

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Les Laboratoires Servier

Rapporteur: Eva Skovlund, PRAC Rapporteur: Pernille Harg

Scope: "Extension of indication to include new therapeutic indication in adolescents aged 12 to 17 years for the treatment of moderate to severe major depressive episodes, if depression is unresponsive to psychological therapy alone, for Valdoxan, further to the results of the phase 2 (CL2-20098-075) and phase 3 (CL3-20098-076) paediatric clinical studies included in the Paediatric Investigation Plan number EMEA-001181-PIP-11; As a consequence, the sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated accordingly. The updated RMP version 25.1 has also been submitted."

**Action:** For adoption

### 5.1.9. Vemlidy - tenofovir alafenamide - EMEA/H/C/004169/II/0040

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Gilead Sciences Ireland UC

Rapporteur: Janet Koenig, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Valentina Di Giovanni

Scope: "Extension of indication to include treatment of chronic hepatitis B-infected children from 6 years and older and weighing at least 25 kilograms for Vemlidy, based on the interim results from Week 24 clinical study report (CSR) for Cohort 1 and Cohort 2 Group 1 and supporting modular summaries for the category 3 study GS-US-320-1092, 'A Randomized, Double-Blind Evaluation of the Pharmacokinetics, Safety, and Antiviral Efficacy of Tenofovir Alafenamide (TAF) in Children and Adolescent Subjects with Chronic Hepatitis B Virus Infection'. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.

In addition, the MAH took the opportunity to update the wording in section 4.6 of the SmPC related to breastfeeding and pregnancies exposed to TAF, and to update the contact details of the local representative in Romania in the Package Leaflet.

An updated RMP version 8.2 has been provided.”

**Action:** For adoption

Request for Supplementary Information adopted on 15.09.2022.

#### 5.1.10. **Wakix - pitolisant - Orphan - EMEA/H/C/002616/II/0030**

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Bioprojet Pharma

Rapporteur: Jean-Michel Race, PRAC Rapporteur: Kirsti Villikka

Scope: “Extension of indication to include treatment of narcolepsy with or without cataplexy in adolescents and children from the age of 6 years, based on results from study P11-06; an ongoing phase III, double-blind, multicentre, randomized, placebo-controlled trial undertaken to evaluate safety and efficacy of pitolisant in children from 6 to less than 18 years with narcolepsy with/without cataplexy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 7.0 of the RMP has also been submitted.”

**Action:** For adoption

Request for Supplementary Information adopted on 15.09.2022.

#### **5.2. Update on on-going Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008**

No items

#### **5.3. Re-examination of Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008**

No items

## **6. Medical devices**

### **6.1. Ancillary medicinal substances - initial consultation**

No items

### **6.2. Ancillary medicinal substances – post-consultation update**

No items

## 6.3. Companion diagnostics - initial consultation

### 6.3.1. in vitro diagnostic medical device - EMEA/H/D/006201

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to detect internal tandem duplication (ITD) and tyrosine kinase domain (TKD) mutations D835 and I836

Scope: Opinion

**Action:** For adoption

## 6.4. Companion diagnostics – follow-up consultation

No items

## 7. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)

### 7.1. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use)

No items

## 8. Pre-submission issues

### 8.1. Pre-submission issue

#### 8.1.1. danicopan - H0005517

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Paroxysmal nocturnal hemoglobinuria (PNH)

Scope: Briefing note and the Rapporteurs' recommendation on the request for accelerated assessment.

**Action:** For adoption

### 8.2. Priority Medicines (PRIME)

Information related to priority medicines cannot be released at present time as these contain commercially confidential information

#### 8.2.1. List of applications received

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**Action:** For information

## 8.2.2. Recommendation for PRIME eligibility

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**Action:** For adoption

# 9. Post-authorisation issues

## 9.1. Post-authorisation issues

### 9.1.1. Lynparza - olaparib - EMEA/H/C/003726/II/0058

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AstraZeneca AB

Rapporteur: Alexandre Moreau

Scope: "Update of section 5.1 of the SmPC in order to provide the Final Overall Survival (OS) Analysis from Study D0816C00020 (OPINION). This is a Phase IIIb single-arm, open-label, multicentre study of maintenance therapy in PSR non-germline BRCA mutated ovarian cancer patients who are in complete or partial response following platinum-based chemotherapy."

**Action:** For adoption

### 9.1.2. Kogenate Bayer – octocog alfa – EMEA/H/C/000275

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Bayer AG

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Filip Josephson

Scope: Expiry of marketing authorisation due to Sunset Clause

**Action:** For information

### 9.1.3. Pazenir – paclitaxel – EMEA/H/C/004441

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Ratiopharm GmbH

Rapporteur: Daniela Philadelphy

Scope: DHPC and communication plan

The DHPC and communication plan have been adopted via written procedure on 12 January 2023.

**Action:** For information

### 9.1.4. Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0056

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Orexigen Therapeutics Ireland Limited

Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber

Scope: "Submission of updated study design and protocol synopsis for the CVOT-2 study, a category 1 study listed in Annex II.D (ANX/001.7) undertaken to assess the effect of naltrexone extended release (ER) / bupropion ER on the occurrence of major adverse cardiovascular events (MACE), as requested in the CHMP AR for ANX/001.6. The Annex II and the RMP version 13 are updated accordingly."

**Action:** For adoption

Request for Supplementary Information adopted on 15.09.2022, 24.03.2022.

#### 9.1.5. Translarna - ataluren - EMEA/H/C/002720/II/0069, Orphan

PTC Therapeutics International Limited

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information following results from study PTC124-GD-041-DMD, listed as a specific obligation in the Annex II; This is a Phase 3 multicentre, randomised, double-blind, 18-month, placebo-controlled study, followed by a 18-month open label extension to confirm the efficacy and safety of ataluren in the treatment of ambulant patients with mnDMD aged 5 years or older.

Annex II, and Annex IIB are updated to delete the SOB and to reflect the switch from conditional to full marketing authorisation. The Package Leaflet is updated accordingly. The RMP version 11.0 has also been submitted. Minor corrections were done to align the PI with the latest QRD templates."

Request to switch to standard MA.

**Action:** For adoption

#### 9.1.6. Rubraca - rucaparib - EMEA/H/C/004272/II/0037

Clovis Oncology Ireland Limited

Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information and the list of adverse drug reactions (ADRs) based on the final results from study CO-338-014 (ARIEL 3) listed as a category 1 PAES in the Annex II; this is a phase 3, multicenter, randomized, double-blind, placebo-controlled study of rucaparib as switch maintenance following platinum-based chemotherapy in patients with platinum-sensitive, high grade serous or endometrioid epithelial ovarian, primary peritoneal or fallopian tube cancer. The Package Leaflet is updated accordingly. The RMP version 6.4 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Update on procedure.

**Action:** For information

#### 9.1.7. Paxlovid - nirmatrelvir / ritonavir - EMEA/H/C/005973/II/0019/G

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Pfizer Europe MA EEIG

Rapporteur: Jean-Michel Race

Scope: quality variation

**Action:** For adoption

Request for Supplementary Information adopted on 13.10.2022.

#### 9.1.8. Sirturo - bedaquiline - EMEA/H/C/002614/II/0051, Orphan

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Janssen-Cilag International N.V.

Rapporteur: Filip Josephson

Scope: "Update of section 4.6 of the SmPC in order to update information on breast-feeding based on new literature."

**Action:** For adoption

Request for Supplementary Information adopted on 15.12.2022.

#### 9.1.9. Vaxneuvance - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/005477/II/0011

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Merck Sharp & Dohme B.V.

Rapporteur: Johann Lodewijk Hillege

Scope: "To update sections 4.2 and 5.1 of the SmPC in order to update the information for immune response after subcutaneous administration based on final results from study V114-P033 (EudraCT: 2019-003644-68), in accordance with Article 46 of the paediatric regulation. V114-P033 is a phase 3 Active-Comparator controlled study to evaluate the Safety, Tolerability and Immunogenicity of V114 in Healthy Japanese Infants. The Package Leaflet is updated accordingly."

**Action:** For adoption



## 10. Referral procedures

### 10.1. Procedure for Centrally Authorised products under Article 20 of Regulation (EC) No 726/2004

#### 10.1.1. Janus kinase (JAK) inhibitors<sup>1</sup>: abrocitinib - CIBINQO (CAP); baricitinib - OLUMIANT (CAP); filgotinib - JYSELECA (CAP); tofacitinib - XELJANZ (CAP); upadacitinib - RINVOQ (CAP) – EMEA/H/A-20/1517

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AbbVie Deutschland GmbH & Co. KG (Rinvoq), Eli Lilly Nederland B.V. (Olumiant), Galapagos N.V. (Jyseleca), Pfizer Europe MA EEIG (Cibinqo, Xeljanz)

Referral PRAC Rapporteur: Ulla Wändel Liminga; Referral PRAC Co-rapporteur(s): Liana Gross-Martirosyan (Olumiant, Xeljanz), Nikica Mirošević Skvrce (Cibinqo, Jyseleca, Rinvoq)

Scope: Review of the benefit-risk balance following notification by the European Commission (EC) of a referral under Article 20 of Regulation (EC) No 726/2004, based on pharmacovigilance data

Revised opinion; the PRAC adopted a revised recommendation to CHMP at their January 2023 meeting.

**Action:** For adoption

CHMP opinion adopted on 10 November 2022.

### 10.2. Requests for CHMP Opinion under Article 5(3) of Regulation (EC) No 726/2004

#### 10.2.1. Colistimethate sodium (CMS) – EMEA/H/A-5(3)/1524

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Various MAHs

Referral Rapporteur: TBC, Referral Co-Rapporteur: TBC

Scope: Start of procedure, appointment of rapporteurs

Review of ratios of polymyxin E1 and E2 in colistin starting material and of the (sulfomethylation) composition profile of CMS finished product.

**Action:** For adoption

### 10.3. Procedure under Articles 5(2) and 10 of Regulation (EC) No 726/2004

No items

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<sup>1</sup> Indicated for the treatment of inflammatory disorders

**10.4. Disagreement between Member States on application for medicinal product (potential serious risk to public health) –under Article 29(4) of Directive 2001/83/EC**

No items

**10.5. Harmonisation - Referral procedure under Article 30 of Directive 2001/83/EC**

No items

**10.6. Community Interests - Referral under Article 31 of Directive 2001/83/EC**

**10.6.1. Topiramate (NAP); topiramate, phentermine (NAP) - EMEA/H/A-31/1520**

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Applicant(s): various

PRAC Rapporteur: Ulla Wändel Liminga; PRAC Co-rapporteur: Martin Huber

Scope: List of questions (LoQ) for the SAG Neurology adopted by the PRAC on 12.01.2023

**Action:** For endorsement

**10.7. Re-examination Procedure under Article 32(4) of Directive 2001/83/EC**

No items

**10.8. Procedure under Article 107(2) of Directive 2001/83/EC**

No items

**10.9. Disagreement between Member States on Type II variation– Arbitration procedure initiated by MAH under Article 6(13) of Commission Regulation (EC) No 1084/2003**

No items

**10.10. Procedure under Article 29 of Regulation (EC) 1901/2006**

No items

**10.11. Referral under Article 13 Disagreement between Member States on Type II variation– Arbitration procedure initiated by Member State under Article 13 (EC) of Commission Regulation No 1234/2008**

No items

## 11. Pharmacovigilance issue

### 11.1. Early Notification System

January 2023 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

**Action:** For information

## 12. Inspections

### 12.1. GMP inspections

Information related to GMP inspections will not be published as it undermines the purpose of such inspections.

### 12.2. GCP inspections

Information related to GCP inspections will not be published as it undermines the purpose of such inspections.

### 12.3. Pharmacovigilance inspections

Information related to Pharmacovigilance inspections will not be published as it undermines the purpose of such inspections.

### 12.4. GLP inspections

Information related to GLP inspections will not be published as it undermines the purpose of such inspections.

## 13. Innovation Task Force

### 13.1. Minutes of Innovation Task Force

No items

### 13.2. Innovation Task Force briefing meetings

No items

### 13.3. Requests for CHMP Opinion under Article 57(1)J and (1)P of Regulation (EC) No 726/2004

No items

## 13.4. Nanomedicines activities

No items

# 14. Organisational, regulatory and methodological matters

## 14.1. Mandate and organisation of the CHMP

### 14.1.1. Vote by proxy

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No topics

### 14.1.2. CHMP membership

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CHMP co-opted membership

With his nomination as CHMP alternate for Austria, the co-opted member mandate for Christian Gartner came to an end on 31.12.2022.

CHMP decided at the January 2023 PROM that the co-opted member position should be filled again. Members are asked to send proposals for the area(s) of expertise.

A discussion and agreement on the area(s) of expertise for the co-opted member position is expected at this meeting.

**Action:** For discussion

## 14.2. Coordination with EMA Scientific Committees

### 14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

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List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for January 2023

**Action:** For adoption

### 14.2.2. Paediatric Committee (PDCO)

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PIPs reaching D30 at January 2023 PDCO

**Action:** For information

Report from the PDCO meeting held on 17-20 January 2023

**Action:** For information

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

### 14.3.1. Biologics Working Party (BWP)

---

Chair: Sol Ruiz/ Sean Barry

Reports from BWP January 2023 meeting to CHMP for adoption:

- 10 reports on products in scientific advice and protocol assistance
- 6 reports on products in pre-authorisation procedures
- 5 reports on products in plasma master file

**Action:** For adoption

### 14.3.2. Scientific Advice Working Party (SAWP)

---

Chair: Paolo Foggi

Report from the SAWP meeting held on 09-12 January 2023. Table of conclusions

**Action:** For information

Scientific advice letters:

Information related to scientific advice letters cannot be released at present time as these contain commercially confidential information.

### 14.3.3. Quality Working Party (QWP)

---

Election of Quality Working Party chair. QWP Chair Blanka Hirschlerova's first term will expire in February 2023. A call for nomination of a QWP chair was launched during the December 2022 PROM meeting.

Nomination(s) received

**Action:** For election

### 14.3.4. Rheumatology and Immunology Working Party (RIWP)

---

Election of Rheumatology and Immunology Working Party chair. A call for nomination of a RIWP chair was launched during the December 2022 PROM meeting.

Nomination(s) received

**Action:** For election

## 14.4. Cooperation within the EU regulatory network

No items

## 14.5. Cooperation with International Regulators

No items

## 14.6. Contacts of the CHMP with external parties and interaction with the Interested Parties to the Committee

No items

## 14.7. CHMP work plan

No items

## 14.8. Planning and reporting

No items

## 14.9. Others

No items

# 15. Any other business

## 15.1. AOB topic

### 15.1.1. Update on COVID-19

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**Action:** For information

### 15.1.2. COVID-19 vaccine - EMEA/H/C/006058

---

immunisation to prevent COVID-19 caused by SARS-CoV-2

Scope: rolling review, list of questions

**Action:** For adoption

## Explanatory notes

The notes below give a brief explanation of the main sections and headings in the CHMP agenda and should be read in conjunction with the agenda or the minutes.

### Oral explanations (section 2)

The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures (section 10) but can relate to any other issue for which the CHMP would like to discuss with company representatives in person.

### Initial applications (section 3)

This section lists applications for marketing authorisations of new medicines that are to be discussed by the Committee.

Section 3.1 is for medicinal products nearing the end of the evaluation and for which the CHMP is expected to adopt an **opinion** at this meeting on whether marketing authorisation should be granted. Once adopted, the CHMP opinion will be forwarded to the European Commission for a final legally binding decision valid throughout the EU.

The other items in the section are listed depending on the stage of the evaluation, which is shown graphically below:



The assessment of an application for a new medicine takes up to 210 'active' days. This active evaluation time is interrupted by at least one 'clock-stop' during which time the applicant prepares the answers to questions from the CHMP. The clock stop happens after day 120 and may also happen after day 180, when the CHMP has adopted a list of questions or outstanding issues to be addressed by the company. Related discussions are listed in the agenda under sections 3.2 (**Day 180 List of outstanding issues**) and 3.3 (**Day 120 list of questions**).

CHMP discussions may also occur at any other stage of the evaluation, and these are listed under section 3.4, **update on ongoing new applications for centralised procedures**.

The assessment leads to an opinion from the CHMP by day 210. Following a CHMP opinion the European Commission takes usually 67 days to issue a legally binding decision (i.e. by day 277 of the procedure). CHMP discussions on products that have received a CHMP opinion and are awaiting a decision are listed under section 3.6, **products in the decision making phase**.

### **Extension of marketing authorisations according to Annex I of Reg. 1234/2008** (section 4)

Extensions of marketing authorisations are applications for the change or addition of new strengths, formulations or routes of administration to existing marketing authorisations. Extension applications follow a 210-day evaluation process, similarly to applications for new medicines (see figure above).

### **Type II variations - Extension of indication procedures** (section 5)

Type II variations are applications for a change to the marketing authorisation which requires an update of the product information and which is not covered in section 4. Type II variations include applications for a new use of the medicine (extension of indication), for which the assessment takes up to 90 days. For the applications listed in this section, the CHMP may adopt an opinion or request supplementary information from the applicant.

### **Ancillary medicinal substances in medical devices** (section 6)

Although the EMA does not regulate medical devices it can be asked by the relevant authorities (the so-called Notified Bodies) that are responsible for regulating these devices to give a scientific opinion on a medicinal substance contained in a medical device.

### **Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004** (section 3.5)

This section lists applications for new marketing authorisation for which the applicant has requested a re-examination of the opinion previously issued by the CHMP.

### **Re-examination procedures** (section 5.3)

This section lists applications for type II variations (including extension of indication applications) for which the applicant has requested re-examination of the opinion previously issued by the CHMP.

### **Withdrawal of application** (section 3.7)

Applicants may decide to withdraw applications at any stage during the assessment and a CHMP opinion will therefore not be issued. Withdrawals are included in the agenda for information or discussion, as necessary.

### **Procedure under article 83(1) of regulation (EC) 726/2004 (compassionate use)** (section 7)

Compassionate use is a way of making available to patients with an unmet medical need a promising medicine which has not yet been authorised (licensed) for their condition. Upon request, the CHMP provides recommendations to all EU Member States on how to administer, distribute and use certain medicines for compassionate use.

### **Pre-submission issues** (section 8)

In some cases the CHMP may discuss a medicine before a formal application for marketing authorisation is submitted. These cases generally refer to requests for an accelerated assessment for medicines that are of major interest for public health or can be considered a therapeutic innovation. In case of an accelerated assessment the assessment timetable is reduced from 210 to 150 days.

### **Post-authorisation issues** (section 9)

This section lists other issues concerning authorised medicines that are not covered elsewhere in the agenda. Issues include supply shortages, quality defects, some annual reassessments or renewals or type II variations to marketing authorisations that would require specific discussion at the plenary.



### **Referral procedures** (section 10)

This section lists referrals that are ongoing or due to be started at the plenary meeting. 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 EU. Further information on such procedures can be found [here](#).

### **Pharmacovigilance issues** (section 11)

This section lists issues that have been discussed at the previous meeting of the PRAC, the EMA's committee responsible for evaluating and monitoring safety issues for medicines. Feedback is provided by the PRAC. This section also refers to the early notification system, a system used to notify the European regulatory network on proposed EMA communication on safety of medicines.

### **Inspections Issues** (section 12)

This section lists inspections that are undertaken for some medicinal products. Inspections are carried out by regulatory agencies to ensure that marketing authorisation holders comply with their obligations. Inspection can relate to good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP) or good pharmacovigilance practice (GVP).

### **Innovation task force** (section 13)

The Innovation Task Force (ITF) is a body set up to encourage early dialogue with applicants developing innovative medicines. Minutes from the last ITF meeting as well as any related issue that requires discussion with the CHMP are listed in this section of the agenda. Further information on the ITF can be found [here](#).

### **Scientific advice working party (SAWP)** (section 14.3.1)

This section refers to the monthly report from the CHMP's Scientific Advice Working Party (SAWP) on scientific advice given to companies during the development of medicines. Further general information on SAWP can be found [here](#).

### **Satellite groups / other committees** (section 14.2)

This section refers to the reports from groups and committees making decisions relating to human medicines: the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), the Committee for Orphan Medicinal Products (COMP), the Committee for Herbal Medicinal Products (HMPC), Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT) and the Pharmacovigilance Risk Assessment Committee (PRAC).

### **Invented name issues** (section 14.3)

This section list issues related to invented names proposed by applicants for new medicines. The CHMP has established the Name Review Group (NRG) to perform reviews of the invented names. The group's main role is to consider whether the proposed names could create a public-health concern or potential safety risk. Further information can be found [here](#).

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



23 January 2023  
EMA/CHMP/954789/2022

## Annex to 23-26 January 2023 CHMP Agenda

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### **A. PRE-SUBMISSION ISSUES**

#### **A.1. ELIGIBILITY REQUESTS**

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Report on Eligibility to Centralised Procedure for  
January 2023: **For adoption**

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#### **A.2. Appointment of Rapporteur / Co-Rapporteur Full Applications**

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Final Outcome of Rapporteurship allocation for  
January 2023: **For adoption**

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#### **A.3. PRE-SUBMISSION ISSUES FOR INFORMATION**

Information related to pre-submission of initial applications cannot be released at the present time as these contain commercially confidential information.

### **B. POST-AUTHORISATION PROCEDURES OUTCOMES**

#### **B.1. Annual re-assessment outcomes**

##### **B.1.1. Annual reassessment for products authorised under exceptional circumstances**

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**Myalepta - metreleptin -  
EMA/H/C/004218/S/0030, Orphan**  
Amryt Pharmaceuticals DAC, Rapporteur: Karin  
Janssen van Doorn, Co-Rapporteur: Robert  
Porszasz, PRAC Rapporteur: Adam  
Przybylkowski

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#### **B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES**

##### **B.2.1. Renewals of Marketing Authorisations requiring 2nd Renewal**

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**Myalepta - metreleptin -  
EMA/H/C/004218/R/0031, Orphan**  
Amryt Pharmaceuticals DAC, Rapporteur: Karin  
Janssen van Doorn, Co-Rapporteur: Robert  
Porszasz, PRAC Rapporteur: Adam  
Przybylkowski

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**Verkazia - ciclosporin -**

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**EMEA/H/C/004411/R/0021, Orphan**

Santen Oy, Duplicate, Duplicate of IKERVIS,  
Rapporteur: Jayne Crowe, Co-Rapporteur:  
Alexandre Moreau, PRAC Rapporteur: Jan  
Neuhauser

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**B.2.2. Renewals of Marketing Authorisations for unlimited validity**

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**BLINCYTO - blinatumomab -****EMEA/H/C/003731/R/0048, Orphan**

Amgen Europe B.V., Rapporteur: Alexandre  
Moreau, Co-Rapporteur: Armando Genazzani,  
PRAC Rapporteur: Eva Jirsová

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**Carmustine Obvius - carmustine -****EMEA/H/C/004326/R/0009**

Obvius Investment B.V, Generic, Rapporteur:  
Elita Poplavska, PRAC Rapporteur: Jan  
Neuhauser  
Request for Supplementary Information adopted  
on 15.12.2022.

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**Dzuveo - sufentanil -****EMEA/H/C/004335/R/0009**

Laboratoire Aguetant, Rapporteur: Hrefna  
Gudmundsdottir, PRAC Rapporteur: Adam  
Przybylkowski

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**Lojuxta - lomitapide -****EMEA/H/C/002578/R/0054**

Amryt Pharmaceuticals DAC, Rapporteur:  
Johann Lodewijk Hillege, Co-Rapporteur:  
Armando Genazzani, PRAC Rapporteur: Menno  
van der Elst

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**Lonquex - lipegfilgrastim -****EMEA/H/C/002556/R/0077**

Teva B.V., Rapporteur: Outi Mäki-Ikola, Co-  
Rapporteur: Johann Lodewijk Hillege, PRAC  
Rapporteur: Kirsti Villikka

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**Nerlynx - neratinib -****EMEA/H/C/004030/R/0031**

Pierre Fabre Medicament, Rapporteur: Bruno  
Sepodes, Co-Rapporteur: Alexandre Moreau,  
PRAC Rapporteur: Menno van der Elst

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**Nityr - nitisinone -****EMEA/H/C/004582/R/0015**

Cycle Pharmaceuticals (Europe) Limited,  
Generic, Generic of Orfadin, Rapporteur: Jayne  
Crowe, PRAC Rapporteur: Amelia Cupelli

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**Prasugrel Mylan - prasugrel -  
EMA/H/C/004644/R/0014**

Mylan Pharmaceuticals Limited, Generic,  
Generic of Efient, Rapporteur: Alar Irs, PRAC  
Rapporteur: Anette Kirstine Stark  
Request for Supplementary Information adopted  
on 10.11.2022.

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**RXULTI - brexipiprazole -  
EMA/H/C/003841/R/0014**

Otsuka Pharmaceutical Netherlands B.V.,  
Rapporteur: Armando Genazzani, Co-  
Rapporteur: Martina Weise, PRAC Rapporteur:  
Lucia Kuráková

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**Tegsedi - inotersen -  
EMA/H/C/004782/R/0035, Orphan**

Akcea Therapeutics Ireland Limited, Rapporteur:  
Martina Weise, Co-Rapporteur: Outi Mäki-Ikola,  
PRAC Rapporteur: Rhea Fitzgerald

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**Trazimera - trastuzumab -  
EMA/H/C/004463/R/0020**

Pfizer Europe MA EEIG, Rapporteur: Jan  
Mueller-Berghaus, Co-Rapporteur: Sol Ruiz,  
PRAC Rapporteur: Brigitte Keller-Stanislawski

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### **B.2.3. Renewals of Conditional Marketing Authorisations**

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**CARVYKTI - ciltacabtagene autoleucel -  
EMA/H/C/005095/R/0008, Orphan,  
ATMP**

Janssen-Cilag International NV, Rapporteur: Jan  
Mueller-Berghaus, Co-Rapporteur: Marcos  
Timón, CHMP Coordinators: Jan Mueller-  
Berghaus and Blanca Garcia-Ochoa, PRAC  
Rapporteur: Jo Robays

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**Deltyba - delamanid -  
EMA/H/C/002552/R/0062, Orphan**

Otsuka Novel Products GmbH, Rapporteur:  
Christophe Focke, PRAC Rapporteur: Jo Robays  
Request for Supplementary Information adopted  
on 15.12.2022.

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**Lorviqua - lorlatinib -  
EMA/H/C/004646/R/0025**

Pfizer Europe MA EEIG, Rapporteur: Aaron Sosa  
Mejia, Co-Rapporteur: Armando Genazzani,  
PRAC Rapporteur: Nikica Mirošević Skvrce

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**Ondexxya - andexanet alfa -  
EMA/H/C/004108/R/0034**

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AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst

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**Pandemic influenza vaccine H5N1**  
**AstraZeneca - pandemic influenza vaccine (h5n1) (live attenuated, nasal) - EMEA/H/C/003963/R/0057**

AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sonja Hrabcik

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**WAYLIVRA - volanesorsen - EMEA/H/C/004538/R/0022, Orphan**

Akcea Therapeutics Ireland Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Martin Huber

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**B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES**

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**Signal detection**

PRAC recommendations on signals adopted at the PRAC meeting held on 09-12 January 2023  
PRAC:

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**Signal of myasthenia gravis**

Pravafenix / Cholib - 3-hydroxy 3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins): atorvastatin; fluvastatin; lovastatin; pitavastatin; pravastatin; rosuvastatin; simvastatin and other relevant fixed dose combinations; pravastatin, fenofibrate; simvastatin, fenofibrate

Rapporteurs: multiple, Co-Rapporteurs: multiple, PRAC Rapporteur: Nathalie Gault

PRAC recommendation on a variation

**Action:** For adoption

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**Signal of haemophagocytic lymphohistiocytosis (HLH)**

Tafinlar / Mekinist - Dabrafenib; trametinib

Rapporteurs: multiple, Co-Rapporteurs: multiple, PRAC Rapporteur: Ulla Wändel Liminga

PRAC recommendation on a variation

**Action:** For adoption

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**Signal of thrombotic microangiopathy**

Stivarga - Regorafenib

Rapporteur: Johann Lodewijk Hillege, Co-

Rapporteur: Armando Genazzani, PRAC

Rapporteur: Menno van der Elst

PRAC recommendation on a variation

**Action:** For adoption

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PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its January 2023 meeting:

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**EMA/H/C/PSUSA/0000209/202205**

(anakinra)

CAPS:

**Kineret** (EMA/H/C/000363) (anakinra),  
Swedish Orphan Biovitrum AB (publ),  
Rapporteur: Thalia Marie Estrup Blicher, PRAC  
Rapporteur: Anette Kirstine Stark,  
"01/05/2019 To: 01/05/2022"

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**EMA/H/C/PSUSA/00010389/202206**

(human papillomavirus 9-valent vaccine  
(recombinant, adsorbed))

CAPS:

**Gardasil 9** (EMA/H/C/003852) (human  
papillomavirus vaccine [types 6, 11, 16, 18,  
31, 33, 45, 52, 58] (recombinant, adsorbed)),  
Merck Sharp & Dohme B.V., Rapporteur:  
Kristina Dunder, PRAC Rapporteur: Jean-  
Michel Dogné, "09/06/2021 To: 09/06/2022"

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**EMA/H/C/PSUSA/00010671/202205**

(semaglutide)

CAPS:

**Ozempic** (EMA/H/C/004174) (semaglutide),  
Novo Nordisk A/S, Rapporteur: Johann  
Lodewijk Hillege  
**Rybelsus** (EMA/H/C/004953) (semaglutide),  
Novo Nordisk A/S, Rapporteur: Johann  
Lodewijk Hillege  
**Wegovy** (EMA/H/C/005422) (semaglutide),  
Novo Nordisk A/S, Rapporteur: Johann  
Lodewijk Hillege, PRAC Rapporteur: Mari  
Thorn, "01/06/2021 To: 31/05/2022"

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**EMA/H/C/PSUSA/00010761/202205**

(pegvaliase)

CAPS:

**Palynziq** (EMA/H/C/004744) (pegvaliase),  
BioMarin International Limited, Rapporteur:  
Johann Lodewijk Hillege, PRAC Rapporteur:  
Rhea Fitzgerald, "24/05/2021 To:  
23/05/2022"

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**EMA/H/C/PSUSA/00010912/202206**

(COVID-19 Vaccine (ChAdOx1-S  
[recombinant])) (Vaxzevria))

CAPS:

**Vaxzevria** (EMA/H/C/005675) (COVID 19  
vaccine (ChAdOx1 S [recombinant])),  
AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC  
Rapporteur: Jean-Michel Dogné, "29/12/2021  
To: 28/06/2022"

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**EMA/H/C/PSUSA/00010942/202205**

(relugolix / estradiol / norethisterone acetate)

CAPS:

**Ryeqo** (EMA/H/C/005267) (relugolix /  
estradiol / norethisterone acetate), Gedeon  
Richter Plc., Rapporteur: Paula Boudewina van  
Hennik, PRAC Rapporteur: Martin Huber,  
"25/11/2021 To: 25/05/2022"

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**B.4. EPARs / WPARs**

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**Dimethyl fumarate Accord - dimethyl fumarate - EMA/H/C/005950**

Accord Healthcare S.L.U., treatment of multiple sclerosis, Generic, Generic of TECFIDERA, Generic application (Article 10(1) of Directive No 2001/83/EC)

For information only. Comments can be sent to the PL in case necessary.

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**Hemgenix - etranacogene dezaparvovec - EMA/H/C/004827, Orphan, ATMP**

CSL Behring GmbH, treatment of adults with Haemophilia B, New active substance (Article 8(3) of Directive No 2001/83/EC)

For information only. Comments can be sent to the PL in case necessary.

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**IMJUDO - tremelimumab - EMA/H/C/006016**

AstraZeneca AB, For use in combination with durvalumab for the treatment of adults with unresectable hepatocellular carcinoma., New active substance (Article 8(3) of Directive No 2001/83/EC)

For information only. Comments can be sent to the PL in case necessary.

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**OMBLASTYS - iodine (131I) omburtamab - EMA/H/C/005499, Orphan**

For information only. Comments can be sent to

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Y-Mabs Therapeutics A/S, treatment of neuroblastoma, New active substance (Article 8(3) of Directive No 2001/83/EC)	the PL in case necessary.
<b>Pombiliti - cipaglucosidase alfa - EMEA/H/C/005703, Orphan</b> Amicus Therapeutics Europe Limited, treatment of adults aged 18 years and older with a confirmed diagnosis of Pompe disease, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
<b>Tremelimumab AstraZeneca - tremelimumab - EMEA/H/C/004650</b> AstraZeneca AB, treatment of adults with metastatic NSCLC with no sensitising epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) genomic tumour aberrations, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
<b>B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES</b>	
Scopes related to Chemistry, Manufacturing, and Controls cannot be released at the present time as these contain commercially confidential information.	
<b>B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects</b>	
<b>Adjupanrix - pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - EMEA/H/C/001206/II/0081/G</b> GlaxoSmithkline Biologicals SA, Informed Consent of Pandemrix (EXP), Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 19.01.2023.	Request for supplementary information adopted with a specific timetable.
<b>Afstyla - lonococog alfa - EMEA/H/C/004075/II/0046/G</b> CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 19.01.2023.	Request for supplementary information adopted with a specific timetable.
<b>Aybintio - bevacizumab - EMEA/H/C/005106/II/0016</b> Samsung Bioepis NL B.V., Rapporteur: Christian Gartner Request for Supplementary Information adopted on 12.01.2023.	Request for supplementary information adopted with a specific timetable.
<b>Benepali - etanercept -</b>	Positive Opinion adopted by consensus on

<p><b>EMA/H/C/004007/II/0069</b>  Samsung Bioepis NL B.V., Rapporteur: Christian Gartner  Opinion adopted on 12.01.2023.</p>	<p>12.01.2023.</p>
<p><b>Besremi - ropeginterferon alfa-2b - EMA/H/C/004128/II/0026</b>  AOP Orphan Pharmaceuticals GmbH, Rapporteur: Janet Koenig  Opinion adopted on 19.01.2023.  Request for Supplementary Information adopted on 08.12.2022.</p>	<p>Positive Opinion adopted by consensus on 19.01.2023.</p>
<p><b>CEVENFACTA - eptacog beta (activated) - EMA/H/C/005655/II/0002</b>  Laboratoire Francais du Fractionnement et des Biotechnologies, Rapporteur: Daniela Philadelphly  Request for Supplementary Information adopted on 12.01.2023.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p><b>COMIRNATY - tozinameran - EMA/H/C/005735/II/0159/G</b>  BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson  Opinion adopted on 12.01.2023.</p>	<p>Positive Opinion adopted by consensus on 12.01.2023.</p>
<p><b>Cosentyx - secukinumab - EMA/H/C/003729/II/0095/G</b>  Novartis Europharm Limited, Rapporteur: Outi Mäki-Ikola  Opinion adopted on 19.01.2023.</p>	<p>Positive Opinion adopted by consensus on 19.01.2023.</p>
<p><b>Cosentyx - secukinumab - EMA/H/C/003729/II/0096</b>  Novartis Europharm Limited, Rapporteur: Outi Mäki-Ikola  Request for Supplementary Information adopted on 19.01.2023.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p><b>Defitelio - defibrotide - EMA/H/C/002393/II/0059, Orphan</b>  Gentium S.r.l., Rapporteur: Kristina Dunder  Opinion adopted on 12.01.2023.  Request for Supplementary Information adopted on 17.11.2022.</p>	<p>Positive Opinion adopted by consensus on 12.01.2023.</p>
<p><b>Flixabi - infliximab - EMA/H/C/004020/II/0077/G</b>  Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus  Opinion adopted on 12.01.2023.</p>	<p>Positive Opinion adopted by consensus on 12.01.2023.</p>
<p><b>Grepid - clopidogrel -</b></p>	

<p><b>EMA/H/C/001059/II/0054</b> Pharmathen S.A., Generic, Generic of Plavix, Rapporteur: Nevenka Trsinar Brodt Request for Supplementary Information adopted on 15.09.2022.</p>	
<p><b>Hemlibra - emicizumab - EMA/H/C/004406/II/0033</b> Roche Registration GmbH, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 12.01.2023.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p><b>Humira - adalimumab - EMA/H/C/000481/II/0215</b> AbbVie Deutschland GmbH &amp; Co. KG, Rapporteur: Kristina Dunder Opinion adopted on 12.01.2023.</p>	<p>Positive Opinion adopted by consensus on 12.01.2023.</p>
<p><b>Idefirix - imlifidase - EMA/H/C/004849/II/0010, Orphan</b> Hansa Biopharma AB, Rapporteur: Martina Weise Request for Supplementary Information adopted on 19.01.2023.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p><b>IMVANEX - smallpox vaccine (live modified vaccinia virus ankara) - EMA/H/C/002596/II/0079</b> Bavarian Nordic A/S, Rapporteur: Jan Mueller- Berghaus Request for Supplementary Information adopted on 27.10.2022.</p>	
<p><b>Ivabradine Zentiva - ivabradine - EMA/H/C/004117/II/0014</b> Zentiva k.s., Generic, Generic of Procoralan, Rapporteur: Tomas Radimersky Request for Supplementary Information adopted on 12.01.2023.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p><b>Kovaltry - octocog alfa - EMA/H/C/003825/II/0040/G</b> Bayer AG, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 12.01.2023.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>
<p><b>LifeGlobal Media - human albumin solution - EMA/H/D/004287/II/0005/G</b> LifeGlobal Group LLC, Rapporteur: Maria Grazia Evandri Request for Supplementary Information adopted on 12.01.2023.</p>	<p>Request for supplementary information adopted with a specific timetable.</p>

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**Lonsurf - trifluridine / tipiracil -  
EMA/H/C/003897/II/0025**

Les Laboratoires Servier, Rapporteur: Paula  
Boudewina van Hennik

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**LUTATHERA - lutetium (177Lu)  
oxodotreotide -**

**EMA/H/C/004123/II/0039, Orphan**

Advanced Accelerator Applications, Rapporteur:  
Janet Koenig

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**Menveo - meningococcal group a, c, w135  
and y conjugate vaccine -**

**EMA/H/C/001095/II/0115/G**

GSK Vaccines S.r.l, Rapporteur: Johann  
Lodewijk Hillege

Request for Supplementary Information adopted  
on 12.01.2023.

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Request for supplementary information adopted  
with a specific timetable.

**Natpar - parathyroid hormone -**

**EMA/H/C/003861/II/0047/G, Orphan**

Takeda Pharmaceuticals International AG,  
Rapporteur: Karin Janssen van Doorn

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**NUVAXOVID - NVX-CoV2373 -**

**EMA/H/C/005808/II/0035/G**

Novavax CZ, a.s., Rapporteur: Johann Lodewijk  
Hillege

Request for Supplementary Information adopted  
on 12.01.2023.

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Request for supplementary information adopted  
with a specific timetable.

**NUVAXOVID - NVX-CoV2373 -**

**EMA/H/C/005808/II/0039/G**

Novavax CZ, a.s., Rapporteur: Johann Lodewijk  
Hillege

Request for Supplementary Information adopted  
on 19.01.2023.

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Request for supplementary information adopted  
with a specific timetable.

**Ocrevus - ocrelizumab -**

**EMA/H/C/004043/II/0035/G**

Roche Registration GmbH, Rapporteur: Thalia  
Marie Estrup Blicher

Request for Supplementary Information adopted  
on 12.01.2023.

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Request for supplementary information adopted  
with a specific timetable.

**Padcev - enfortumab vedotin -**

**EMA/H/C/005392/II/0006/G**

Astellas Pharma Europe B.V., Rapporteur: Aaron  
Sosa Mejia

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**Paxlovid - nirmatrelvir / ritonavir -**

**EMA/H/C/005973/II/0019/G**

Pfizer Europe MA EEIG, Rapporteur: Jean-Michel  
Race

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See 9.1

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Request for Supplementary Information adopted on 13.10.2022.

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**Replagal - agalsidase alfa -  
EMA/H/C/000369/II/0122**

Takeda Pharmaceuticals International AG  
Ireland Branch, Rapporteur: Johann Lodewijk  
Hillege

Request for Supplementary Information adopted on 12.01.2023.

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Request for supplementary information adopted with a specific timetable.

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**Rotarix - rotavirus vaccine (live, oral) -  
EMA/H/C/000639/II/0128**

GlaxoSmithKline Biologicals S.A., Rapporteur:  
Christophe Focke

Opinion adopted on 12.01.2023.

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Positive Opinion adopted by consensus on 12.01.2023.

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**Rybelsus - semaglutide -  
EMA/H/C/004953/II/0030**

Novo Nordisk A/S, Rapporteur: Johann Lodewijk  
Hillege

Opinion adopted on 12.01.2023.

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Positive Opinion adopted by consensus on 12.01.2023.

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**Somavert - pegvisomant -  
EMA/H/C/000409/II/0104**

Pfizer Europe MA EEIG, Rapporteur: Jean-Michel  
Race

Request for Supplementary Information adopted on 15.12.2022, 10.11.2022.

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**Surgiflo Haemostatic Matrix Kit - human  
thrombin - EMA/H/D/002301/II/0032/G**

Ferrosan Medical Devices A/S, Rapporteur: Jan  
Mueller-Berghaus

Opinion adopted on 12.01.2023.

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Positive Opinion adopted by consensus on 12.01.2023.

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**TEZSPIRE - tezepelumab -  
EMA/H/C/005588/II/0001**

AstraZeneca AB, Rapporteur: Finbarr Leacy,  
PRAC Rapporteur: Eva Jirsová

Opinion adopted on 12.01.2023.

Request for Supplementary Information adopted on 01.12.2022.

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Positive Opinion adopted by consensus on 12.01.2023.

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**Vimizim - elosulfase alfa -  
EMA/H/C/002779/II/0039, Orphan**

BioMarin International Limited, Rapporteur:  
Johann Lodewijk Hillege

Opinion adopted on 12.01.2023.

Request for Supplementary Information adopted on 27.10.2022.

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Positive Opinion adopted by consensus on 12.01.2023.

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**Vydura - rimegepant -  
EMA/H/C/005725/II/0002/G**

Positive Opinion adopted by consensus on 12.01.2023.

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Pfizer Europe MA EEIG, Rapporteur: Janet Koenig  
Opinion adopted on 12.01.2023.  
Request for Supplementary Information adopted on 20.10.2022.

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**Xofigo - radium-223 -**  
**EMA/H/C/002653/II/0047**  
Bayer AG, Rapporteur: Janet Koenig  
Opinion adopted on 19.01.2023.  
Request for Supplementary Information adopted on 10.11.2022.

Positive Opinion adopted by consensus on 19.01.2023.

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**Zercepac - trastuzumab -**  
**EMA/H/C/005209/II/0022**  
Accord Healthcare S.L.U., Rapporteur: Sol Ruiz  
Opinion adopted on 19.01.2023.

Positive Opinion adopted by consensus on 19.01.2023.

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**ZYNRELEF - bupivacaine / meloxicam -**  
**EMA/H/C/005205/II/0009/G**  
Heron Therapeutics, B.V., Rapporteur: Alexandre Moreau  
Opinion adopted on 12.01.2023.  
Request for Supplementary Information adopted on 22.09.2022.

Positive Opinion adopted by consensus on 12.01.2023.

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**WS2344**  
**Ryzodeg-**  
**EMA/H/C/002499/WS2344/0048**  
**Tresiba-EMA/H/C/002498/WS2344/0056**  
**Xultophy-**  
**EMA/H/C/002647/WS2344/0044**  
Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder  
Opinion adopted on 12.01.2023.  
Request for Supplementary Information adopted on 01.12.2022, 27.10.2022.

Positive Opinion adopted by consensus on 12.01.2023.

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**WS2362**  
**Edistride-**  
**EMA/H/C/004161/WS2362/0057**  
**Forxiga-**  
**EMA/H/C/002322/WS2362/0078**  
AstraZeneca AB, Lead Rapporteur: Kristina Dunder

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**WS2388/G**  
**Fluenz Tetra-**  
**EMA/H/C/002617/WS2388/0122/G**  
**Pandemic influenza vaccine H5N1**  
**AstraZeneca-**  
**EMA/H/C/003963/WS2388/0056/G**  
AstraZeneca AB, Lead Rapporteur: Christophe

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Focke

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**WS2394**

**Hexacima-**

**EMA/H/C/002702/WS2394/0141**

**Hexyon-**

**EMA/H/C/002796/WS2394/0145**

Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

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**B.5.2. CHMP assessed procedures scope: Non-Clinical and Clinical aspects**

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**Beyfortus - nirsevimab -**

**EMA/H/C/005304/II/0001**

AstraZeneca AB, Rapporteur: Thalia Marie Estrup Blicher, "Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update efficacy information based on additional results from study D5290C00004 (MELODY); this is a Phase III Randomized, Double-blind, Placebo-controlled Study to Evaluate the Safety and Efficacy of MEDI8897, for the Prevention of Medically Attended Lower Respiratory Tract Infection Due to Respiratory Syncytial Virus in Healthy Late Preterm and Term Infants."

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**Calquence - acalabrutinib -**

**EMA/H/C/005299/II/0013**

AstraZeneca AB, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to update efficacy and safety information based on final results from study ACE-CL-309 (A Phase 3 randomized open-label active-control study investigating Calquence for the Treatment of Subjects With Relapsed or Refractory Chronic Lymphocytic Leukaemia) listed as a category 3 study in the RMP."

Opinion adopted on 12.01.2023.

Request for Supplementary Information adopted on 15.09.2022.

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Positive Opinion adopted by consensus on 12.01.2023.

**Dupilumab - dupilumab -**

**EMA/H/C/004390/II/0068**

Sanofi Winthrop Industrie, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.8 and 5.1 of the SmPC to include long-term safety and efficacy information in children based on final results from study LTS14424 - EXCURSION. This is an interventional one-year study, to evaluate the long-term safety and tolerability of dupilumab in children 6 to 11 years of age with asthma, who participated in a previous

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Request for supplementary information adopted with a specific timetable.



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dupilumab asthma clinical study EFC14153.”  
Request for Supplementary Information adopted  
on 19.01.2023.

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**Eliquis - apixaban -  
EMA/H/C/002148/II/0088**

Bristol-Myers Squibb / Pfizer EEIG, Rapporteur:  
Johann Lodewijk Hillege, “Update of sections 4.2  
and 5.1 of the SmPC in order to update efficacy  
and safety information in the paediatric  
population based on results of the paediatric  
studies performed in compliance with the  
paediatric investigation plan (PIP), including  
studies CV185155 and CV185362. In addition,  
the MAH took the opportunity to introduce  
minor editorial changes to the PI.”

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**Enbrel - etanercept -  
EMA/H/C/000262/II/0249**

Pfizer Europe MA EEIG, Rapporteur: Maria  
Concepcion Prieto Yerro, “Update of section 4.6  
of the SmPC in order to update information on  
breast feeding exposure based on the  
cumulative review of etanercept specific  
pharmacology, safety database and published  
medical literature.

The Package Leaflet is updated accordingly.  
In addition, the MAH is taking this opportunity  
to correct minor administrative and  
typographical changes to the SmPC, Labelling  
and Package Leaflet.

In addition, the MAH took the opportunity to  
update the list of local representatives in the  
Package Leaflet.”

Request for Supplementary Information adopted  
on 12.01.2023.

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Request for supplementary information adopted  
with a specific timetable.

**Evoltra - clofarabine -  
EMA/H/C/000613/II/0077**

Genzyme Europe BV, Rapporteur: Alexandre  
Moreau, “Update of the Package Leaflet in order  
to update information regarding breast-feeding  
based on a comprehensive safety review. In  
addition, the MAH took the opportunity to  
update the list of local representatives in the  
Package Leaflet.”

Request for Supplementary Information adopted  
on 12.01.2023, 08.09.2022.

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Request for supplementary information adopted  
with a specific timetable.

**Evrysdi - risdiplam -  
EMA/H/C/005145/II/0011, Orphan**

Roche Registration GmbH, Rapporteur: Bruno

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Sepodes, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to delete an existing warning on "Use with SMA gene therapy" and to update the safety profile and efficacy data in patients previously treated with other SMA-modifying therapies based on the 24-month primary analysis data from study BP39054 (JEWELFISH); this is a multicenter, open-label study to investigate the safety, tolerability, and pharmacokinetics/pharmacodynamics of risdiplam in adult and paediatric patients with SMA. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

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**Imfinzi - durvalumab -  
EMA/H/C/004771/II/0054**

AstraZeneca AB, Rapporteur: Aaron Sosa Mejia, "Submission of final report from non-clinical study ONC4736-PB-0401 (Profiling of Biomarkers Relevant to Immunotherapies in Paediatric Solid Tumours)."  
Opinion adopted on 12.01.2023.

Positive Opinion adopted by consensus on 12.01.2023.

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**INREBIC - fedratinib -  
EMA/H/C/005026/II/0010/G, Orphan**

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sonja Hrabcik, "Update of section 4.4 of the SmPC in order to add new warnings on major adverse cardiac events (MACE), thrombosis and secondary malignancies. The updates pertain to three signals, assessed by the FDA, which were identified with another JAK inhibitor (tofacitinib) indicated in rheumatoid arthritis; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."  
Request for Supplementary Information adopted on 10.06.2022.

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**Keytruda - pembrolizumab -  
EMA/H/C/003820/II/0128**

Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, "Update of section 5.1 of the SmPC in order to update information based on the final OS data for the overall population as well as for MMR subgroups from study 309/KEYNOTE-775 in order to fulfil the Recommendation: REC/033. This Recommendation was agreed with the approval of study 309/KEYNOTE-775; this is a multicenter, open-label, randomized, phase 3

Request for supplementary information adopted with a specific timetable.

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trial to compare the efficacy and safety of lenvatinib in combination with pembrolizumab versus treatment of physician's choice in participants with advanced endometrial cancer." Request for Supplementary Information adopted on 19.01.2023.

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**Lenvima - lenvatinib -  
EMA/H/C/003727/II/0049**

Eisai GmbH, Rapporteur: Karin Janssen van Doorn, "Update of section 5.1 of the SmPC in order to update the efficacy information of "Endometrial carcinoma" based on the final OS analysis data for the overall population as well as for MMR subgroups from study E7080-G000-309 / KEYNOTE-775. This is a Multicenter, Open-label, Randomized, Phase III study to compare the efficacy and safety of lenvatinib in combination with pembrolizumab versus treatment of physician's choice in participants with advanced endometrial cancer.

In addition, the MAH took the opportunity to implement editorial changes in the SmPC."

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**Lynparza - olaparib -  
EMA/H/C/003726/II/0057**

AstraZeneca AB, Rapporteur: Alexandre Moreau, "Update of sections 4.8 and 5.1 of the SmPC in order to update the long-term safety data and the final OS analysis from PAOLA-1 study (D0817C00003). This is a Randomized, Double-Blind, Phase III Trial of Olaparib vs. Placebo in Patients with Advanced FIGO Stage IIIB – IV High Grade Serous or Endometrioid Ovarian, Fallopian Tube, or Peritoneal Cancer Treated with Standard First Line Treatment, Combining Platinum-Taxane Chemotherapy and Bevacizumab Concurrent with Chemotherapy and in Maintenance. The Package Leaflet is updated accordingly."

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**Lynparza - olaparib -  
EMA/H/C/003726/II/0058**

See 9.1

AstraZeneca AB, Rapporteur: Alexandre Moreau, "Update of section 5.1 of the SmPC in order to provide the Final Overall Survival (OS) Analysis from Study D0816C00020 (OPINION). This is a Phase IIIb single-arm, open-label, multicentre study of maintenance therapy in PSR non-germline BRCA mutated ovarian cancer patients who are in complete or partial response

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following platinum-based chemotherapy.”

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**Nexpovio - selinexor -  
EMA/H/C/005127/II/0011**

Stemline Therapeutics B.V., Rapporteur: Blanca Garcia-Ochoa, “Update of section 4.5 of the SmPC in order to add drug-drug interaction information regarding the strong CYP3A4 inhibitor, clarithromycin, based on results from the drug-drug interaction (DDI) pharmacokinetic (PK) portion of study KCP 330-017 (STOMP) following procedure EMA/H/C/005127/REC/003.1. This is a Phase 1b/2, multi-center, open-label, clinical study with Dose Escalation (Phase 1) and Expansion (Phase 2) to independently assess the MTD, efficacy, and safety of 10 combination therapies in 11 arms in patients with RRMM (Relapsed/Refractory Multiple Myeloma) and NDMM (Newly Diagnosed Multiple Myeloma).”

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**Ondexxa - andexanet alfa -  
EMA/H/C/004108/II/0035**

AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, “Update of section 4.8 of the SmPC in order to remove the information referring to healthy volunteers and to add infusion related adverse reactions in bleeding patients following an internal review of the labels and based on ANNEXA-4 study.

The Package Leaflet is updated accordingly. In addition, the MAH would like to take this opportunity to make some corrections in the SmPC.”

Request for Supplementary Information adopted on 12.01.2023.

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Request for supplementary information adopted with a specific timetable.

**Onpattro - patisiran -  
EMA/H/C/004699/II/0025, Orphan**

Alnylam Netherlands B.V., Rapporteur: Kristina Dunder, “Update of sections 4.2 and 5.1 of the SmPC based on interim results from study ALN-TTR02-006 listed as a category 3 study in the RMP; this is a multicenter, open-label, extension study to evaluate the long-term safety and efficacy of patisiran in patients with familial amyloidotic polyneuropathy who have completed a prior clinical study with patisiran. In addition, the MAH took the opportunity to update section 3 of the SmPC in order to update the pH .”

Opinion adopted on 12.01.2023.

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Positive Opinion adopted by consensus on 12.01.2023.

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Request for Supplementary Information adopted on 06.10.2022, 23.06.2022.

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**Paxlovid - nirmatrelvir / ritonavir -  
EMA/H/C/005973/II/0026/G**

Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, "Grouped application comprising four type II variations as follows:

- Update of sections 4.6, 5.1 and 5.3 in order to update the latest non-clinical virology and toxicology data based on Phase 2/3 studies C4671002, C4671005 and C4671006 and the pre- and postnatal development study report 21GR149
  - Update of section 5.2 in order to update pertinent clinical pharmacology information based on completed clinical pharmacology studies with Paxlovid in both healthy participants (Phase 1 studies C4671008, C4671012, C4671013, C467104, C4671015, C4671019) and also participants with mild-to-moderate COVID-19 (Pivotal Phase 2/3 Study C4671005) and final PopPK report (PMAR-EQDD-C467a-DP4-1323)
  - Update of sections 4.8 and 5.1 in order to include final clinical efficacy and safety data based on the pivotal C4671005 (REC35) study
  - Update of sections 4.8 and 5.1 in order to include final clinical efficacy and safety data based on the supportive C4671006 study and interim clinical efficacy and safety data based on the supportive C4671002 (REC36) study
- The Package Leaflet is updated accordingly.  
In addition, MAH is taking this opportunity to introduce editorial changes."

Request for Supplementary Information adopted on 10.11.2022.

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**Piqray - alpelisib -  
EMA/H/C/004804/II/0017**

Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa, "Update of section 5.3 of the SmPC in order to update non-clinical information based on data from two skin toxicology studies conducted in rats: study 1770766 and study 1870156."  
Opinion adopted on 12.01.2023.

Positive Opinion adopted by consensus on 12.01.2023.

**Reblozyl - luspatercept -  
EMA/H/C/004444/II/0011, Orphan**

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Daniela Philadelphia, "Update of sections 4.2,

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4.4 and 4.8 of the SmPC in order to include new safety information about Extramedullary Hematopoietic Masses in transfusion-dependent beta-thalassemia patients based on the open-label phase of the ACE-536-B-THAL-001 Phase III study, the long-term follow-up study and post marketing data. The Package Leaflet is updated accordingly.”

Request for Supplementary Information adopted on 15.09.2022.

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**Retsevmo - selpercatinib -**

**EMA/H/C/005375/II/0016**

Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, “Update of section 4.8 of the SmPC in order to add chylothorax and chylous ascites to the list of adverse drug reactions (ADRs) based on a review of adverse events. The Package Leaflet is updated accordingly.”

Request for Supplementary Information adopted on 06.10.2022.

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**Ronapreve - casirivimab / imdevimab -**

**EMA/H/C/005814/II/0009**

Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, “Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning and to add convulsive syncope to the list of adverse drug reactions (ADRs) with frequency not known, following a signal assessment conducted by the MAH.

The Package Leaflet is updated accordingly.”

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**SIRTURO - bedaquiline -**

See 9.1

**EMA/H/C/002614/II/0051, Orphan**

Janssen-Cilag International N.V., Rapporteur: Filip Josephson, “Update of section 4.6 of the SmPC in order to update information on breast-feeding based on new literature.”

Request for Supplementary Information adopted on 15.12.2022.

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**Spectrila - asparaginase -**

**EMA/H/C/002661/II/0032/G**

medac Gesellschaft für klinische Spezialpräparate mbH, Rapporteur: Christian Gartner, “Grouped variation (Type II & Type IB):

C.I.4: Update of sections 4.4 and 4.6 of the SmPC in order to include the recommendations from the SWP regarding genotoxic medicinal products and contraception duration period; the

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Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. C.I.6.b: Deletion of the indication lymphoblastic lymphoma (LBL) in section 5.3 of the SmPC, as Spectrila is not approved for LBL.”

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**Spikevax - elasomeran -  
EMA/H/C/005791/II/0088**

Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, “Submission of the final report from study DMID 20-0003 listed as a category 3 study in the RMP. This is a Phase I, Open Label, Dose-ranging Study of the Safety and Immunogenicity of 2019-nCoV Vaccine (mRNA-1273) in Healthy Adults.”  
Request for Supplementary Information adopted on 19.01.2023.

Request for supplementary information adopted with a specific timetable.

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**Taltz - ixekizumab -  
EMA/H/C/003943/II/0046**

Eli Lilly and Co (Ireland) Limited, Rapporteur: Kristina Dunder, “Update of section 4.8 of the SmPC in order to add ‘oesophageal candidiasis’ to the list of adverse drug reactions (ADRs) with frequency rare based on a safety review of all associated data; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and update instructions for use to clarify information on product stability at room temperature.”  
Opinion adopted on 12.01.2023.

Positive Opinion adopted by consensus on 12.01.2023.

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**TEZSPIRE - tezepelumab -  
EMA/H/C/005588/II/0004**

AstraZeneca AB, Rapporteur: Finbarr Leacy, “Submission of the final report detailing the extended follow-up data from study D5180C00018 (DESTINATION) listed as a category 3 study in the RMP; this is a multicentre, randomised, double-blind, placebo-controlled, parallel group, long-term extension study designed to evaluate the safety and efficacy of 210 mg Q4W subcutaneous of tezepelumab in adults and adolescents with severe uncontrolled asthma for up to 2 continuous years of treatment.”

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**TRODELVY - sacituzumab govitecan -  
EMA/H/C/005182/II/0018/G**

Gilead Sciences Ireland UC, Rapporteur: Jan

Positive Opinion adopted by consensus on 12.01.2023.

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Mueller-Berghaus, "Grouped application comprising two type II variations as follows:  
- To update section 4.8 of the SmPC based on an integrated summary of immunogenicity.  
- To update sections 4.5 and 5.2 of the SmPC based on data on the impact of concomitant medications including UGT1A1 inhibitors/inducers on SN-38 pharmacokinetic (PK) based on the PopPK model refinement."  
Opinion adopted on 12.01.2023.  
Request for Supplementary Information adopted on 08.12.2022.

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**Vargatef - nintedanib -  
EMA/H/C/002569/II/0047/G**

Boehringer Ingelheim International GmbH,  
Rapporteur: Aaron Sosa Mejia, "Grouped application containing:

C.I.4: Update of sections 4.2, 5.1 and 5.2 of the SmPC in order to update information regarding the paediatric population based on results from study 1199-0337; this is a double blind, randomised, placebo-controlled trial to evaluate the dose-exposure and safety of nintedanib on top of standard of care for 24 weeks, followed by open label treatment with nintedanib of variable duration, in children and adolescents (6 to 17 year-old) with clinically significant fibrosing interstitial lung disease. The Package Leaflet is updated accordingly.

C.I.4: Update of sections 4.2 and 5.2 of the SmPC in order to improve the recommendation for the administration of nintedanib based on food compatibility data. The Package Leaflet is updated accordingly.

In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to introduce minor editorial changes to the PI."

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**Vaxelis - diphtheria, tetanus, pertussis  
(acellular, component), hepatitis b (rdna),  
poliomyelitis (inact.) and haemophilus type  
b conjugate vaccine (adsorbed) -  
EMA/H/C/003982/II/0110**

MCM Vaccine B.V., Rapporteur: Christophe Focke, "Update of section 4.8 of the SmPC in order to add 'hypersensitivity' and 'anaphylactic reaction' to the list of adverse drug reactions (ADRs) with frequency not known based on the safety assessment of post-marketing reports of

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hypersensitivity including anaphylactic reactions; the Package Leaflet is updated accordingly.”

Request for Supplementary Information adopted on 15.12.2022.

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**Vaxneuvance - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/005477/II/0011**

See 9.1

Merck Sharp & Dohme B.V., Rapporteur: Johann Lodewijk Hillege, “To update sections 4.2 and 5.1 of the SmPC in order to update the information for immune response after subcutaneous administration based on final results from study V114-P033 (EudraCT: 2019-003644-68), in accordance with Article 46 of the paediatric regulation. V114-P033 is a phase 3 Active-Comparator controlled study to evaluate the Safety, Tolerability, and Immunogenicity of V114 in Healthy Japanese Infants. The Package Leaflet is updated accordingly.”

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**Verzenio - abemaciclib - EMEA/H/C/004302/II/0024**

Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, “Update of section 5.1 of the SmPC in order to include overall survival data based on final results from study MONARCH 2; this is a A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study of Fulvestrant with or without Abemaciclib, a CDK4/6 Inhibitor, for Women with Hormone Receptor-Positive, HER2-Negative Locally Advanced or Metastatic Breast Cancer.”

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**VEYVONDI - vonicog alfa - EMEA/H/C/004454/II/0026**

Positive Opinion adopted by consensus on 12.01.2023.

Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus, “Update of sections 4.8 and 5.1 of the SmPC in order to add ‘headache’ to the list of adverse drug reactions (ADRs) with frequency very common and to update information based on final results from study 071301 and other available data; study 071301 is a prospective, phase 3, open-label, international multicenter study on efficacy and safety of prophylaxis with rVWF in severe von Willebrand disease. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to introduce minor editorial changes to the PI and

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bring it in line with the latest QRD template.”  
Opinion adopted on 12.01.2023.  
Request for Supplementary Information adopted  
on 20.10.2022.

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**VPRIV - velaglucerase alfa -  
EMA/H/C/001249/II/0054**

Takeda Pharmaceuticals International AG  
Ireland Branch, Rapporteur: Martina Weise,  
“Submission of the final report from study SHP-  
GCB-402: a multicenter, open-label, single-arm,  
phase 4 study designed to prospectively  
evaluate the effects of VPRIV on bone-related  
pathology in treatment-naïve subjects with type  
1 Gaucher disease.”  
Request for Supplementary Information adopted  
on 12.01.2023, 28.04.2022.

Request for supplementary information adopted  
with a specific timetable.

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**XALKORI - crizotinib -  
EMA/H/C/002489/II/0078**

Pfizer Europe MA EEIG, Rapporteur: Alexandre  
Moreau, “Submission of the final report from  
study A8081001 (A Phase 1 Safety,  
Pharmacokinetic and Pharmacodynamic Study  
Of PF-02341066, A MET/HGFR Selective  
Tyrosine Kinase Inhibitor, Administered Orally to  
Patients with Advanced Cancer), to fulfil  
recommendation 8 of the Xalkori MAA to further  
investigate the role of c-Met status in ALK-  
negative patients.”

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**Xarelto - rivaroxaban -  
EMA/H/C/000944/II/0096**

Bayer AG, Rapporteur: Kristina Dunder,  
“Submission of the final report from study  
15786 (COMPASS LTOLE). This is a phase 3,  
multicenter, randomized, double-blind, double-  
dummy, active comparator, event-driven study,  
in which subjects were randomized 1:1:1 to  
rivaroxaban 2.5 mg bid/ASA 100 mg od, or  
rivaroxaban 5 mg bid, or ASA 100 mg od.”  
Request for Supplementary Information adopted  
on 13.10.2022.

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**Zercepac - trastuzumab -  
EMA/H/C/005209/II/0020**

Accord Healthcare S.L.U., Rapporteur: Sol Ruiz,  
“Submission of the final report from study  
HLX02-BC01 in order to fulfil REC/006. This is a  
double-blind, randomised, parallel-controlled,  
multicentre, international, phase 3 study to  
compare the efficacy, safety, and

Positive Opinion adopted by consensus on  
12.01.2023.

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immunogenicity of HLX02 versus EU-sourced Herceptin in combination with docetaxel.”  
Opinion adopted on 12.01.2023.  
Request for Supplementary Information adopted on 01.09.2022.

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**WS2358**  
**Elebrato Ellipta-**  
**EMA/H/C/004781/WS2358/0028**

**Trelegy Ellipta-**  
**EMA/H/C/004363/WS2358/0025**  
GlaxoSmithKline Trading Services Limited, Lead Rapporteur: Finbarr Leacy, “Update of section 4.8 of the SmPC in order to add ‘urinary retention’ and ‘dysuria’ to the list of adverse drug reactions (ADRs) with frequency rare; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and bring it in line with the latest QRD template.”  
Request for Supplementary Information adopted on 12.01.2023, 10.11.2022.

Request for supplementary information adopted with a specific timetable.

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**WS2377**  
**Jentaduetto-**  
**EMA/H/C/002279/WS2377/0067**  
**Synjardy-**  
**EMA/H/C/003770/WS2377/0067**

Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on Vitamin B12 decrease or deficiency and to update the list of adverse drug reactions (ADRs) in accordance with the recent update of the PI for Glucophage, which is the reference label for the compound metformin, and following the request by MHRA on 20 June 2022 for all products containing metformin; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and to update the list of local representatives in the Package Leaflet.”  
Request for Supplementary Information adopted on 12.01.2023.

Request for supplementary information adopted with a specific timetable.

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### **B.5.3. CHMP-PRAC assessed procedures**

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**Beovu - brolocizumab -**  
**EMA/H/C/004913/II/0021**

Novartis Europharm Limited, Rapporteur:

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Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to change posology recommendation including an additional dose regimen (q16w) for DME patients during the maintenance phase, update the frequency of adverse drug reactions, update pharmacokinetic, pharmacodynamic, efficacy and safety information, following the assessment of procedure II/10, based on final results from studies CRTH258B2301 (KESTREL) and CRTH258B2302 (KITE).  
The Package Leaflet is updated accordingly. The RMP version 10 has also been submitted."

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**Cablivi - caplacizumab - EMEA/H/C/004426/II/0040, Orphan**

Abylnx NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Jan Neuhauser, "Update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC in order to update information on long-term efficacy and safety based on final results from study ALX0681-C302/LTS16371 - Prospective Follow-up Study for Patients who Completed Study ALX0681-C301 (HERCULES) to Evaluate Long-term Safety and Efficacy of Caplacizumab (Post-HERCULES), listed as a category 3 study in the RMP. The Post-HERCULES study was a Phase III, 36-month follow-up study from HERCULES (parent study) to evaluate the long-term outcomes as well as the safety and efficacy of repeat use of caplacizumab in patients who experienced a recurrence of aTTP.  
The RMP version 3.0 has also been submitted."  
Opinion adopted on 12.01.2023.  
Request for Supplementary Information adopted on 01.12.2022.

Positive Opinion adopted by consensus on 12.01.2023.

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**Evicel - human fibrinogen / human thrombin - EMEA/H/C/000898/II/0099**

Omrix Biopharmaceuticals N. V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.8 and 5.1 of the SmPC in order to update the frequency of adverse drug reactions (ADRs), add Pseudomeningocele to the list of ADRs with frequency uncommon and to update efficacy and safety information on the paediatric population, following P46/0030 based on the final results from the paediatric clinical study BIOS-13-006. This is a Prospective Randomized

Request for supplementary information adopted with a specific timetable.

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Controlled Study Evaluating the Safety and Efficacy of EVICEL used for Suture- Line Sealing in Dura-Mater Closure during Paediatric Neurosurgical Cranial Procedures.

The Package Leaflet is updated accordingly.

Editorial changes are proposed to sections of the product information.

In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.3.

The RMP version 15 has also been submitted.”

Request for Supplementary Information adopted on 12.01.2023.

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**Fintepla - fenfluramine -  
EMA/H/C/003933/II/0015, Orphan**

Zogenix ROI Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber,

“To update sections 4.2 and 5.2 of the SmPC to update the safety information based on final results from study ZX008-1903 listed as a category 3 study in the RMP; this is a Phase 1, Open-Label, Single-Dose Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of ZX008 (Fenfluramine Hydrochloride) in Subjects with Varying Degrees of Hepatic Impairment.

The primary objective of this study was to compare the PK of a single dose of ZX008 (fenfluramine HCl) in subjects with varying degrees of hepatic impairment with that of healthy matched control subjects.

The updated RMP version 2.7 has also been submitted.”

Request for Supplementary Information adopted on 12.01.2023, 29.09.2022.

Request for supplementary information adopted with a specific timetable.

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**GIVLAARI - givosiran -  
EMA/H/C/004775/II/0011/G, Orphan**

Alnylam Netherlands B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur:

Martin Huber, “Update of section 5.3 of the SmPC based on final results from study AS1-GLP18-007 listed as a category 3 study in the RMP; This is a 104-week Subcutaneous Injection Carcinogenicity Study in Sprague Dawley Rats.

Update of section 5.3 of the SmPC based on final results from study AS1-GLP18-004; This is a 26-week Subcutaneous Injection Carcinogenicity Study in TgRasH2 Mice.

The RMP version 2.1 has also been submitted.

Request for supplementary information adopted with a specific timetable.

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In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.”

Request for Supplementary Information adopted on 12.01.2023, 29.09.2022.

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**IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0059, Orphan**

CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, “Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update information and amend the frequencies of adverse drug reactions (ADRs) based on the final results from study CSL654\_3003 listed as a category 3 study in the RMP; this is an open-label, multicentre, uncontrolled study to evaluate the safety, pharmacokinetics and clinical response of rIX-FP with regard to the prevention and treatment of bleeding in previously untreated patients (PUPs) with Haemophilia B. The Package Leaflet is updated accordingly. The RMP version 4.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and update the list of local representatives in the Package Leaflet.”

Request for Supplementary Information adopted on 12.01.2023, 27.10.2022, 10.06.2022.

Request for supplementary information adopted with a specific timetable.

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**Ilumetri - tildrakizumab - EMEA/H/C/004514/II/0036**

Almirall S.A, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Adam Przybylkowski

Request for Supplementary Information adopted on 27.10.2022.

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**Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0056**

Orexigen Therapeutics Ireland Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, “Submission of updated study design and protocol synopsis for CVOT-2 study, a category 1 study listed in Annex II.D (ANX/001.7) undertaken to assess the effect of naltrexone extended release (ER) / bupropion ER on the occurrence of major adverse cardiovascular events (MACE), as requested in the CHMP AR for ANX/001.6. The Annex II and the RMP version 13 are updated accordingly.”

Request for Supplementary Information adopted

See 9.1

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on 15.09.2022, 24.03.2022.

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**NINLARO - ixazomib -  
EMA/H/C/003844/II/0041, Orphan**  
Takeda Pharma A/S, Rapporteur: Armando  
Genazzani, PRAC Rapporteur: Ulla Wändel  
Liminga, "Submission of the final report from  
study NSMM-5001 (INSIGHT) listed as a Specific  
Obligation in the Annex II of the Product  
Information. This is a global, prospective, non-  
interventional, observational study of  
presentation, treatment patterns, and outcomes  
in multiple myeloma patients. The Annex II and  
the RMP (submitted version 9.0) are updated  
accordingly.

Positive Opinion adopted by consensus on  
12.01.2023.

In addition, the MAH took the opportunity to  
introduce minor editorial changes to the PI.  
The requested variation proposed amendments  
to the Annex II and to the Risk Management  
Plan (RMP)."

Opinion adopted on 12.01.2023.

Request for Supplementary Information adopted  
on 29.09.2022.

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**NUBEQA - darolutamide -  
EMA/H/C/004790/II/0012**  
Bayer AG, Rapporteur: Alexandre Moreau, PRAC  
Rapporteur: Jan Neuhauser, "Update of section  
5.3 of the SmPC based on the final report of  
carcinogenicity study T104877-7 listed as a  
category 3 study in the RMP. This is a non-  
clinical study to assess the carcinogenic  
potential in mice. The study evaluates the  
effects of daily oral administration of  
darolutamide for a period of 6 months in tg-  
rasH2 transgenic mouse model. The updated  
RMP version 3.2 is approved."

Positive Opinion adopted by consensus on  
12.01.2023.

Opinion adopted on 12.01.2023.

Request for Supplementary Information adopted  
on 01.12.2022, 01.09.2022.

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**Ondexxya - andexanet alfa -  
EMA/H/C/004108/II/0033**  
AstraZeneca AB, Rapporteur: Jan Mueller-  
Berghaus, PRAC Rapporteur: Menno van der  
Elst, "Update of section 5.1 of the SmPC based  
on interim results from study PK/PD study listed  
as a specific obligation in the Annex II in order  
to fulfil SOB 1 and SOB 3; this is a PK and  
PK/PD Analysis of Intravenously Administered  
Andexanet after dosing to steady state with a  
factor Xa inhibitor, rivaroxaban or Apixaban, in

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healthy subjects and patients who have acute major bleeding. In addition, the MAH took the opportunity implement editorial changes in Annex II of the SmPC. The RMP version 3.0 has also been submitted.”

Request for Supplementary Information adopted on 13.10.2022.

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**Polivy - polatuzumab vedotin -  
EMA/H/C/004870/II/0018, Orphan**

Roche Registration GmbH, Rapporteur:  
Alexandre Moreau, PRAC Rapporteur: Ulla Wändel Liminga, “Submission of the final report from study GO29365 listed as a category 3 study in the RMP in order to address MEA/002. This is a phase Ib/II, multicenter, open-label study evaluating the safety, tolerability, and anti-tumour activity of polatuzumab vedotin in combination with rituximab or obinutuzumab plus bendamustine in patients with R/R follicular lymphoma or R/R diffuse large B-cell lymphoma. The RMP version 3.0 has also been submitted.”

Opinion adopted on 12.01.2023.

Request for Supplementary Information adopted on 29.09.2022.

Positive Opinion adopted by consensus on 12.01.2023.

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**QINLOCK - ripretinib -  
EMA/H/C/005614/II/0004, Orphan**

Deciphera Pharmaceuticals (Netherlands) B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Željana Margan Koletić, “Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations in patients with hepatic impairment and update the description of pharmacokinetics based on final results from study DCC-2618-01-004; a Phase 1 study of the Pharmacokinetics, Safety, and Tolerability of Ripretinib in Subjects With Hepatic Impairment Compared to Healthy Control Subjects. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted.”

Request for Supplementary Information adopted on 15.09.2022.

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**Rozlytrek - entrectinib -  
EMA/H/C/004936/II/0014**

Roche Registration GmbH, Rapporteur:  
Armando Genazzani, PRAC Rapporteur: Menno van der Elst, “Update of sections 4.2 and 5.2 the SmPC in order to update pharmacokinetic information based on final results from study GP411174 listed as an additional



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pharmacovigilance activity in the RMP; this is a Phase I, non-randomized, single-dose, open-label study to investigate the effect of impaired hepatic function on the pharmacokinetics of entrectinib in volunteers with different levels of hepatic function. The RMP version 4.0 has also been submitted.

In addition, the MAH took the opportunity to update in Annex II section C and to update the list of local representatives in the Package Leaflet.”

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**Simponi - golimumab -  
EMA/H/C/000992/II/0109**

Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “Update of the Package Leaflet in order to update the Instructions for Use (IFU) for the pre-filled pen.”

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**Stelara - ustekinumab -  
EMA/H/C/000958/II/0096**

Janssen-Cilag International N.V., Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald, “Update of section 5.1 of the SmPC in order to update information with the 4-year clinical data in patients with ulcerative colitis based on the final report from study CNTO1275UCO3001 listed as a category 3 study in the RMP; this is a phase 3, randomized, double blind, placebo-controlled, parallel-group, multicenter study to evaluate the safety and efficacy of ustekinumab induction and maintenance therapy in subjects with moderately to severely active ulcerative colitis. The RMP version 23.1 has also been submitted. In addition, the MAH took the opportunity to introduce a correction to the PI.”

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**Tecentriq - atezolizumab -  
EMA/H/C/004143/II/0075**

Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Inês Ribeiro-Vaz, “Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add ‘pericardial disorders’ to the list of adverse drug reactions (ADRs) with frequency common in monotherapy and uncommon in combination therapy/based on final results from Drug Safety Report (DSR 1115896) including review of available clinical trial data, post-marketing data and literature. In addition, the MAH took the opportunity to

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update Annex II section D of the SmPC and to implement editorial changes in the SmPC. The Package Leaflet was updated accordingly. The RMP version 23.1 has also been submitted.”

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**Translarna - ataluren -**

See 9.1

**EMA/H/C/002720/II/0069, Orphan**

PTC Therapeutics International Limited,  
Rapporteur: Johann Lodewijk Hillege, PRAC  
Rapporteur: Liana Gross-Martirosyan, “Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information following results from study PTC124-GD-041-DMD, listed as a specific obligation in the Annex II; This is a Phase 3 multicentre, randomised, double-blind, 18-month, placebo-controlled study, followed by a 18-month open label extension to confirm the efficacy and safety of ataluren in the treatment of ambulant patients with mnDMD aged 5 years or older.

Annex II and Annex IIB are updated to delete the SOB and to reflect the switch from conditional to full marketing authorisation. The Package Leaflet is updated accordingly. The RMP version 11.0 has also been submitted. Minor corrections were done to align the PI with the latest QRD templates.”

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**Vaxneuvance - pneumococcal polysaccharide conjugate vaccine (adsorbed) -**

**EMA/H/C/005477/II/0013/G**

Merck Sharp & Dohme B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Grouped application comprising two type II variations as follows:  
- To update sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to add safety data on recipients of haematopoietic stem cell transplant (HSCT) based on final results from study V114-022, listed as a category 3 study in the RMP; This is a Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of Vaxneuvance in Recipients of Allogeneic Hematopoietic Stem Cell Transplant.  
- To update sections 4.2 and 5.1 of the SmPC in order to update the information regarding a 3-dose regimen based on final results from study V114-026; a Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of a 3-dose Regimen of Vaxneuvance in Healthy

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Infants.

The Package Leaflet is updated accordingly.

The RMP version 2.1 has also been submitted.”

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**Zeposia - ozanimod -**

**EMA/H/C/004835/II/0016**

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maria del Pilar Rayon, “Update of sections 4.2 and 5.2 of the SmPC in order to add a dose adjustment after completion of the dose escalation regimen in patients with mild or moderate chronic hepatic impairment (Child-Pugh class A or B) based on the final results from study RPC-1063-CP-004; this is a Phase I, multicenter, open-label study to evaluate the effect of mild or moderate hepatic impairment on the multiple-dose pharmacokinetics of ozanimod. The Package Leaflet is updated accordingly. The updated RMP version 5.0 has also been submitted.”

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**WS2307**

**Rixathon-**

**EMA/H/C/003903/WS2307/0062**

**Riximyo-**

**EMA/H/C/004729/WS2307/0063**

Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus, Lead PRAC Rapporteur: Anette Kirstine Stark, “Update of section 4.1 of the SmPC in order to include the rapid infusion regimen (90 minutes) for second and subsequent infusions in the label for patients with non-Hodgkin’s lymphoma (NHL) or chronic lymphocytic leukaemia (CLL) based on non-interventional PASS CGP2013ES01R and scientific literature.

The RMP version 7.0 has also been submitted.”

Request for Supplementary Information adopted on 15.09.2022.

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**B.5.4. PRAC assessed procedures**

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PRAC Led

**Alecensa - alectinib -**

**EMA/H/C/004164/II/0044**

Roche Registration GmbH, PRAC Rapporteur: Jana Lukacisinova, PRAC-CHMP liaison: Ondřej Slanař, “Submission of an updated RMP version 3.3 in order to remove the important identified risks of Interstitial Lung Disease

Positive Opinion adopted by consensus on 12.01.2023.

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(ILD)/Pneumonitis, Hepatotoxicity, Photosensitivity, Bradycardia, Severe myalgia and Creatine Phosphokinase (CPK) elevations as well as the important potential risk of Embryo-fetal toxicity as safety concerns. Furthermore, template updates in line with the GVP Product or Population-Specific Considerations III: Pregnant and breastfeeding women are made.”  
Opinion adopted on 12.01.2023.

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PRAC Led

**COMIRNATY - tozinameran -  
EMA/H/C/005735/II/0152**

BioNTech Manufacturing GmbH, PRAC  
Rapporteur: Menno van der Elst, PRAC-CHMP  
liaison: Johann Lodewijk Hillege, “Update of section 4.8 of the SmPC in order to add “Dizziness” to the list of adverse drug reactions (ADRs) with frequency ‘Uncommon’, based on a cumulative review. The Package Leaflet is updated accordingly.”  
Opinion adopted on 12.01.2023.

Positive Opinion adopted by consensus on 12.01.2023.

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PRAC Led

**Cotellic - cobimetinib -  
EMA/H/C/003960/II/0027**

Roche Registration GmbH, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Update of sections 4.4 and 5.1 of the SmPC in order to update information based on final results from study ML39302 listed as a category 3 study in the RMP in order to fulfil MEA/003.5; this is a non-interventional PASS study to investigate the effectiveness, safety and utilization of cobimetinib and vemurafenib in patients with and without brain metastasis with BRAF V600 mutant melanoma under real world conditions. The RMP version 5.0 has also been submitted.”  
Opinion adopted on 12.01.2023.  
Request for Supplementary Information adopted on 01.09.2022.

Positive Opinion adopted by consensus on 12.01.2023.

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PRAC Led

**Fintepla - fenfluramine -  
EMA/H/C/003933/II/0017, Orphan**

Zogenix ROI Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, “Submission of an updated RMP version 2.10 in order to implement a targeted follow-up questionnaire (FUQ) to further improve the collection of

Request for supplementary information adopted with a specific timetable.

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follow-up information on cases of vascular heart disease (VHD) and pulmonary arterial hypertension (PAH) suggested by PRAC following the assessment of procedure EMEA/H/C/PSUSA/00010907/202112.” Request for Supplementary Information adopted on 12.01.2023.

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PRAC Led  
**IMVANEX - smallpox vaccine (live modified vaccinia virus ankara) - EMEA/H/C/002596/II/0081**

Bavarian Nordic A/S, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, “Submission of an updated RMP version 9.1 in order to update the safety specifications in line with extension of the indication to “active immunisation against smallpox, monkeypox and disease caused by vaccinia virus in adults”, update the missing information from the list of safety concerns, differentiate routine pharmacovigilance activities and additional pharmacovigilance activities, addition of non-BN sponsored clinical study SEMVAc to additional pharmacovigilance activities and deletion of paediatric study POX-MVA-035 upon request by PRAC following the assessment of procedure II/76.” Request for Supplementary Information adopted on 12.01.2023.

Request for supplementary information adopted with a specific timetable.

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PRAC Led  
**NutropinAq - somatropin - EMEA/H/C/000315/II/0077**

Ipsen Pharma, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Thalia Marie Estrup Blicher, “Submission of an updated RMP version 4.0 in order to remove some of the safety concerns in compliance with GVP Module V Revision 2.  
In addition, the MAH took the opportunity to add data from final clinical study report of International Cooperative Growth Study (iNCGS) registry (non-interventional study) and exposure and safety information.” Request for Supplementary Information adopted on 12.01.2023.

Request for supplementary information adopted with a specific timetable.

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PRAC Led  
**Olumiant - baricitinib - EMEA/H/C/004085/II/0031**  
Eli Lilly Nederland B.V., Rapporteur: Johann

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Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski, PRAC-CHMP liaison: Ewa Balkowiec Iskra, "C.I.4 - Update of section 4.4 of the SmPC in order to add new warnings on Major Adverse Cardiac Events (MACE) and amend existing warning on Malignancy and Venous thromboembolism (VTE) following the request made in PSUSA (EMA/H/C/PSUSA/00010578/202102) and based on interim results from study I4V-MC-B023; this is a retrospective observational study to compare baricitinib relative to the standard of care. The Package Leaflet is updated accordingly. The RMP version 13.1 has also been submitted. In addition, the MAH has submitted a proposal for a DHPC and communication plan."

Request for Supplementary Information adopted on 22.04.2022, 13.01.2022.

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PRAC Led  
**Paxlovid - nirmatrelvir / ritonavir - EMEA/H/C/005973/II/0032**  
Pfizer Europe MA EEIG, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Update of section 4.8 of the SmPC in order to add 'hypertension' to the list of adverse drug reactions (ADRs) with frequency 'uncommon', following procedure EMEA/H/C/005973/LEG/006, based on review of aggregate post-marketing data. The Package Leaflet is updated accordingly."  
Request for Supplementary Information adopted on 12.01.2023.

Request for supplementary information adopted with a specific timetable.

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PRAC Led  
**Sialanar - glycopyrronium - EMEA/H/C/003883/II/0026**  
Proveca Pharma Limited, PRAC Rapporteur: Zane Neikena, PRAC-CHMP liaison: Elita Poplavska, "Submission of an updated RMP version 3.1 in order to remove a Drug Utilisation Study (DUS)."  
Request for Supplementary Information adopted on 12.01.2023.

Request for supplementary information adopted with a specific timetable.

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PRAC Led  
**Spikevax - elasmomeran - EMEA/H/C/005791/II/0085/G**  
Moderna Biotech Spain, S.L., PRAC Rapporteur: Marie Louise Schougaard Christiansen, PRAC-CHMP liaison: Thalia Marie Estrup Blicher,

Request for supplementary information adopted with a specific timetable.

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“Grouped application comprising two type II variations as follows:

C.I.11.b - To add Spikevax bivalent Original/Omicron BA.4-5 vaccine (mRNA-1273.222), to update studies mRNA-1273-P904, mRNA-1273-P905 and mRNA-1273-P910 in the Pharmacovigilance Plan to include exposure to Spikevax bivalent vaccines, to update the INN to elasomeran/davesomeran, and to reclassify studies mRNA-1273-P205 from category 2 to category 3 studies in the Pharmacovigilance Plan.

C.I.13 - To submit the final CSR from study mRNA-1273-P201, a Phase 2a, Randomized, Observer-Blind, Placebo-Controlled, Dose-Confirmation Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults  $\geq$  18 Years listed as a category 3 study including addition of clinical trial exposure data for part C of the study mRNA-1273-P201. RMP version 6.0 will be updated accordingly.”

Request for Supplementary Information adopted on 12.01.2023.

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PRAC Led

**Stivarga - regorafenib -  
EMA/H/C/002573/II/0039**

Bayer AG, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Update of section 4.4 of the SmPC in order to remove the disease specific precaution for hepatocellular carcinoma based on final results from study REFINE (study number 19244) listed as a category 3 study in the RMP; this is an international, prospective, open-label, multi-center, observational study to describe the safety and effectiveness of treatment with regorafenib in real-world settings.

The RMP version 6.1 has also been submitted.”  
Opinion adopted on 12.01.2023.

Positive Opinion adopted by consensus on 12.01.2023.

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PRAC Led

**Stocrin - efavirenz -  
EMA/H/C/000250/II/0130**

Merck Sharp & Dohme B.V., Duplicate, Duplicate of Sustiva, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, “Submission of an updated RMP version 9.0 in accordance with the new template and thereby to remove safety concerns.”

Request for supplementary information adopted with a specific timetable.

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Request for Supplementary Information adopted on 12.01.2023.

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PRAC Led  
**SYLVANT - siltuximab - EMEA/H/C/003708/II/0038, Orphan**  
EUSA Pharma (Netherlands) B.V, PRAC  
Rapporteur: Brigitte Keller-Stanislawski,  
"Submission of the report from study ACCELERATE (Advancing Castleman Care with an Electronic Longitudinal Registry, E-Repository, And Treatment/Effectiveness Research): An International Registry for Patients with Castleman Disease - NCT02817997 listed as an obligation in the Annex II of the Product Information. This is a study report to cover the data collected for 100 patients over a 5-year period in the ACCELERATE Registry study to collect information on patients with Castleman's Disease who are candidates to receive Sylvant or are currently receiving treatment with Sylvant. The obligation has now been fulfilled, the Annex II is updated accordingly."  
Opinion adopted on 12.01.2023.  
Request for Supplementary Information adopted on 27.10.2022.

Positive Opinion adopted by consensus on 12.01.2023.

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PRAC Led  
**Tarceva - erlotinib - EMEA/H/C/000618/II/0071**  
Roche Registration GmbH, PRAC Rapporteur: Marie Louise Schougaard Christiansen, PRAC-CHMP liaison: Aaron Sosa Mejia, "Update of section 4.8 of the SmPC in order to provide a single table listing all ADRs following PSUSA/00001255/202111. The Package Leaflet is updated accordingly."  
Request for Supplementary Information adopted on 12.01.2023.

Request for supplementary information adopted with a specific timetable.

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PRAC Led  
**WS2270 Vfend-EMEA/H/C/000387/WS2270/0147**  
Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "To update the Annex II and RMP to version 6.0 to include the results from the final clinical study report (CSR) following the completion of a non-

Request for supplementary information adopted with a specific timetable.



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interventional (NI) post-authorisation safety study (PASS), A1501103 "An Active Safety Surveillance Program to Monitor Selected Events in Patients with Long-term Voriconazole Use" - MEA091.

In addition, the MAH is taking this opportunity to introduce editorial changes."

Request for Supplementary Information adopted on 12.01.2023, 01.09.2022.

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PRAC Led

**WS2320**

**Stribild-EMEA/H/C/002574/WS2320/0120**

**Truvada-**

**EMEA/H/C/000594/WS2320/0177**

Gilead Sciences Ireland UC, Lead PRAC  
Rapporteur: Ana Sofia Diniz Martins, PRAC-  
CHMP liaison: Bruno Sepodes, "To update Annex II and the RMP for Truvada and Stribild to version 18.1 and 14.1 to remove of the paediatric additional Risk Minimisation Measures (aRMMs) for HIV indication.

In addition, the MAH took the opportunity to introduce changes to the PI."

Opinion adopted on 12.01.2023.

Request for Supplementary Information adopted on 29.09.2022.

Positive Opinion adopted by consensus on 12.01.2023.

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PRAC Led

**WS2356**

**Epclusa-**

**EMEA/H/C/004210/WS2356/0068**

**Harvoni-**

**EMEA/H/C/003850/WS2356/0107**

**Sovaldi-EMEA/H/C/002798/WS2356/0081**

**Vosevi-EMEA/H/C/004350/WS2356/0057**

Gilead Sciences Ireland UC, Lead PRAC  
Rapporteur: Ana Sofia Diniz Martins, "To provide an updated RMP, following finalisation of procedure EMEA/H/C/WS2222 providing the final CSR for the non-imposed joint PASS study to evaluate the risk of de novo hepatocellular carcinoma in patients with compensated cirrhosis treated with direct-acting antivirals for chronic hepatitis C (study B20-146). In particular, the list of safety concerns has been updated to remove the important potential risks: "Recurrence of hepatocellular carcinoma (HCC)" and "Emergence of HCC", and to remove "safety in patients with previous HCC" as an area of missing information. In addition, the

Positive Opinion adopted by consensus on 12.01.2023.

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completed PASS studies: DAA PASS and De Novo DAA PASS have been removed from the pharmacovigilance plan.”  
Opinion adopted on 12.01.2023.

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PRAC Led

**WS2369**

**Filgrastim Hexal-**

**EMA/H/C/000918/WS2369/0066**

**Zarzio-EMA/H/C/000917/WS2369/0067**

Sandoz GmbH, Lead PRAC Rapporteur: Menno van der Elst, “C.I.11.z - To amend the RMP to reduce the list of safety concerns and remove risks which are well characterised and already included in the product information, following PRAC Assessment Report of PSUR P14 (EMA/H/C/PSUSA/00001391/202109) dated 05-May-2022. Additionally, the due date of the final study report EP06-501 (MEA007) has been updated from Q3 2025 to Q1 2025.

Furthermore, the MAH took the opportunity to introduce the following editorial changes:

- Removal of pharmaceutical forms and strengths no longer registered in Japan;
- Editorial changes in Part V “Risk minimization measures”.”

Opinion adopted on 12.01.2023.

Request for Supplementary Information adopted on 01.12.2022.

Positive Opinion adopted by consensus on 12.01.2023.

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PRAC Led

**WS2378**

**Exelon-EMA/H/C/000169/WS2378/0140**

**Prometax-**

**EMA/H/C/000255/WS2378/0141**

Novartis Europharm Limited, Lead PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, “C.I.11.z - To amend the RMP to:

- remove the standalone multiple patch use annual report as an additional pharmacovigilance activity from the Exelon/Prometax RMP, which was endorsed by PRAC (EMA/CHMP/PRAC/342229/2021) on 22-Jul-2021.
- include the initial risks reviewed at the time of initial marketing authorisation that were agreed to within RMP Version 1.1 (final: 16-Jul-2007); and the rationale for the removal of some safety concerns from the currently approved RMP Version 10.0, following the PRAC Assessment

Positive Opinion adopted by consensus on 12.01.2023.

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Report from the currently approved RMP (version 10.0) (EMA/H/C/XXX/WS/1773).

Furthermore, the MAH took the opportunity to introduce editorial changes in the following sections of the RMP:

- epidemiology literature, where relevant (Module SI, Epidemiology of the indications and target populations).
- worldwide reporting rate of cases of current safety concerns for rivastigmine, as of the latest data lock point of 31-Jan-2022 (Module SV.1, Post-authorisation exposure).
- editorial update of preventability of current safety concerns for rivastigmine to reflect the existing educational material (Module SVII.3, Details of important identified risks, important potential risks, and missing information).

The requested worksharing procedure proposed amendments to the None and to the Risk Management Plan (RMP)."

Opinion adopted on 12.01.2023.

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#### **B.5.5. CHMP-CAT assessed procedures**

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##### **Upstaza - eladocagene exuparvovec - EMA/H/C/005352/II/0005/G, Orphan, ATMP**

PTC Therapeutics International Limited,  
Rapporteur: Maura O'Donovan, CHMP  
Coordinator: Finbarr Leacy

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##### **Yescarta - axicabtagene ciloleucel - EMA/H/C/004480/II/0057, Orphan, ATMP**

Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus,  
Request for Supplementary Information adopted on 20.01.2023.

Request for supplementary information adopted with a specific timetable.

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#### **B.5.6. CHMP-PRAC-CAT assessed procedures**

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##### **Zolgensma - onasemnogene abeparvovec - EMA/H/C/004750/II/0033/G, Orphan, ATMP**

Novartis Europharm Limited, Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege, PRAC Rapporteur: Ulla Wändel Liminga,  
"Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to introduce additional guidance on liver function laboratory tests and monitoring

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before and after infusion and update information based on new safety information on the topic of acute liver failure (ALF) following two reports of fatal ALF.

Update of sections 4.2 and 4.4 of the SmPC in order to provide additional guidance relevant to patient's overall health status prior to dosing and to strengthen the existing description and guidance on systemic immune response.

Update of section 4.4 of the SmPC in order to indicate prompt attention to thrombotic microangiopathy (TMA) and to reflect the risk of life-threatening or fatal outcomes.

The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to update the Annex II."

Opinion adopted on 20.01.2023.

Request for Supplementary Information adopted on 04.11.2022.

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#### **B.5.7. PRAC assessed ATMP procedures**

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PRAC Led

##### **Imlygic - talimogene laherparepvec - EMA/H/C/002771/II/0059, ATMP**

Amgen Europe B.V., PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 10 in order to update and reclassify identified risk of 'Disseminated herpetic infection' based on the cumulative assessment of literature review and MAH Global Safety Database and to remove studies 20180062 and 20180099 from Planned and Ongoing Studies from the list of Pharmacovigilance Plan studies in the Annex II."

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#### **B.5.8. Unclassified procedures and worksharing procedures of type I variations**

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##### **WS2276**

##### **Herceptin-**

##### **EMA/H/C/000278/WS2276/0186**

##### **Phesgo-EMA/H/C/005386/WS2276/0015**

Roche Registration GmbH, Lead Rapporteur: Jan Mueller-Berghaus

Opinion adopted on 12.01.2023.

Positive Opinion adopted by consensus on 12.01.2023.

##### **WS2361**

##### **HBVAXPRO-**

##### **EMA/H/C/000373/WS2361/0080**

Positive Opinion adopted by consensus on 19.01.2023.

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**Vaxelis-EMEA/H/C/003982/WS2361/0112**

MCM Vaccine B.V., Lead Rapporteur: Christophe

Focke

Opinion adopted on 19.01.2023.

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**WS2363/G****Copalia-****EMEA/H/C/000774/WS2363/0127/G****Dafiro-****EMEA/H/C/000776/WS2363/0131/G****Exforge-****EMEA/H/C/000716/WS2363/0126/G**

Novartis Europharm Limited, Lead Rapporteur:

Thalia Marie Estrup Blicher

Request for Supplementary Information adopted

on 01.12.2022.

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**WS2366****Flebogamma DIF-****EMEA/H/C/000781/WS2366/0074**

Instituto Grifols, S.A., Lead Rapporteur: Jan

Mueller-Berghaus

Opinion adopted on 12.01.2023.

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Positive Opinion adopted by consensus on

12.01.2023.

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**WS2381****Hexacima-****EMEA/H/C/002702/WS2381/0142****Hexyon-****EMEA/H/C/002796/WS2381/0146**

Sanofi Pasteur, Lead Rapporteur: Jan Mueller-

Berghaus

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**WS2382****Ebymect-****EMEA/H/C/004162/WS2382/0060****Xigduo-EMEA/H/C/002672/WS2382/0070**

AstraZeneca AB, Lead Rapporteur: Kristina

Dunder, "To update sections 4.2, 4.4 and 5.1 of

Xigduo and Ebymect SmPCs to harmonise the

applicable dapagliflozin-specific information in

the Xigduo and Ebymect QRDs with the Forxiga

(dapagliflozin) product information, which has

undergone several updates via procedure DAPA-

HF (EMEA/H/C/002322/WS1737) and DAPA-

CKD (EMEA/H/C/002322/WS1941). Wording

approved for Forxiga in these procedures are

proposed for the combination products. In

addition, the revised QRDs also include

proposals for other administrative changes. The

corresponding section 2 and 4 of the PIL have

also been updated."

Opinion adopted on 12.01.2023.

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Positive Opinion adopted by consensus on

12.01.2023.

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**WS2392/G****Efficib-****EMA/H/C/000896/WS2392/0109/G****Janumet-****EMA/H/C/000861/WS2392/0108/G****Ristfor-****EMA/H/C/001235/WS2392/0097/G****Velmetia-****EMA/H/C/000862/WS2392/0114/G**

Merck Sharp &amp; Dohme B.V., Lead Rapporteur:

Johann Lodewijk Hillege

Request for Supplementary Information adopted  
on 12.01.2023.Request for supplementary information adopted  
with a specific timetable.

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**WS2397/G****Incresync-****EMA/H/C/002178/WS2397/0045/G****Vipdomet-****EMA/H/C/002654/WS2397/0042/G****Vipidia-****EMA/H/C/002182/WS2397/0034/G**

Takeda Pharma A/S, Lead Rapporteur: Johann

Lodewijk Hillege

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**WS2399/G****Mirapexin-****EMA/H/C/000134/WS2399/0104/G****Sifrol-****EMA/H/C/000133/WS2399/0095/G**

Boehringer Ingelheim International GmbH, Lead

Rapporteur: Thalia Marie Estrup Blicher

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**WS2400****Lixiana-EMA/H/C/002629/WS2400/0041****Roteas-EMA/H/C/004339/WS2400/0028**

Daiichi Sankyo Europe GmbH, Lead Rapporteur:

Maria Concepcion Prieto Yerro,

Opinion adopted on 19.01.2023.

Positive Opinion adopted by consensus on  
19.01.2023.

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**WS2403****Kaftrio-EMA/H/C/005269/WS2403/0032****Symkevi-****EMA/H/C/004682/WS2403/0036**

Vertex Pharmaceuticals (Ireland) Limited, Lead

Rapporteur: Johann Lodewijk Hillege

### **B.5.9. Information on withdrawn type II variation / WS procedure**

### **B.5.10. Information on type II variation / WS procedure with revised timetable**

## **B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION**

### **B.6.1. Start of procedure for New Applications: timetables for information**

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#### **azacitidine - EMEA/H/C/006154**

Treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukaemia (CMML) and acute myeloid leukaemia (AML)

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#### **pandemic influenza vaccine (surface antigen, inactivated, adjuvanted) - EMEA/H/C/006052**

Active immunisation for the prevention of disease caused by the influenza A virus H5N1 subtype contained in the vaccine

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#### **germanium (68ge) chloride / gallium (68ga) chloride - EMEA/H/C/006053**

indicated for in vitro radiolabelling of specific carrier molecules to be used for positron emission tomography (PET) imaging

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#### **influenza virus a/turkey/turkey/1/2005 (h5n1) nibrg-23 strain, ha surface antigen - EMEA/H/C/006051**

Prophylaxis of influenza

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#### **omecamtiv mecarbil - EMEA/H/C/006112**

treatment of adult patients with symptomatic chronic heart failure and reduced ejection fraction less than 30%

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#### **bevacizumab - EMEA/H/C/005723**

Treatment of neovascular (wet) age-related macular degeneration (nAMD).

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#### **nintedanib - EMEA/H/C/006179**

treatment of non-small cell lung cancer (NSCLC)

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#### **omaveloxolone - EMEA/H/C/006084,**

#### **Orphan**

Reata Ireland Limited, Treatment of Friedreich's ataxia

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### **B.6.2. Start of procedure for Extension application according to Annex I of Reg. 1234/2008): timetables for information**

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#### **Azacitidine Accord - azacitidine -**

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**EMA/H/C/005147/X/0013**

Accord Healthcare S.L.U., Generic, Generic of Vidaza, Rapporteur: Hrefna Gudmundsdottir, PRAC Rapporteur: Menno van der Elst, "Extension application to introduce a new pharmaceutical form associated with a new strength (10 mg/ml powder for solution for infusion) and a new route of administration (intravenous use).

The RMP version 2 is updated in accordance."

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**Entyvio - vedolizumab -****EMA/H/C/002782/X/0075**

Takeda Pharma A/S, Rapporteur: Armando Genazzani

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**Kaftrio - ivacaftor / tezacaftor / elexacaftor - EMA/H/C/005269/X/0033, Orphan**

Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber, "Extension application to add a new pharmaceutical form (granules) associated with 2 new strengths (60 mg/40 mg/80 mg and 75 mg/50 mg/100 mg) to support a new indication in a combination regimen with ivacaftor for the treatment of cystic fibrosis (CF) in paediatric patients aged 2 to less than 6 years who have at least one F508del mutation in the CFTR gene (see section 5.1). The new indication is only applicable to the new granules pharmaceutical form. As a consequence of the line extension the PI for the film coated tablets is also updated to reflect the addition of a new pharmaceutical form. The RMP (version 6.2) has also been submitted."

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**Kalydeco - ivacaftor -****EMA/H/C/002494/X/0114/G**

Vertex Pharmaceuticals (Ireland) Limited, Co-Rapporteur: Robert Porszasz, PRAC Rapporteur: Monica Martinez Redondo, "Extension application to add a new strength (59.5 mg) of the granules pharmaceutical form grouped with C.I.6.a, to support a new indication in a combination regimen with ivacaftor/tezacaftor/elexacaftor for the treatment of cystic fibrosis (CF) in paediatric patients aged 2 to less than 6 years who have at least one F508del mutation in the CFTR gene (see section 5.1).

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The RMP (version 15.1) has also been submitted.

Type IB B.II.f.1.b The Product information has been updated accordingly.”

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### **B.6.3. Restart of procedure - responses received to Day 120 List of Questions timetables: for information**

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#### **enalapril maleate ph. eur. -**

**EMA/H/C/005731, PUMA**

treatment of heart failure

List of Questions adopted on 21.07.2022.

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#### **dabigatran etexilate - EMA/H/C/005922**

prevention of venous thromboembolic events

List of Questions adopted on 23.06.2022.

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#### **glofitamab - EMA/H/C/005751, Orphan**

Roche Registration GmbH, treatment of diffuse

large B-cell lymphoma

List of Questions adopted on 15.09.2022.

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#### **pirtobrutinib - EMA/H/C/005863, Orphan**

Eli Lilly Nederland B.V., treatment of mantle cell

lymphoma (MCL)

List of Questions adopted on 13.10.2022.

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#### **adagrasib - EMA/H/C/006013**

treatment of patients with advanced non-small

cell lung cancer (NSCLC) with KRAS G12C

mutation

List of Questions adopted on 15.09.2022.

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#### **lacosamide - EMA/H/C/006047**

treatment of epilepsy

List of Questions adopted on 15.09.2022.

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#### **futibatinib - EMA/H/C/005627, Orphan**

Taiho Pharma Netherlands B.V., treatment of

cholangiocarcinoma

List of Questions adopted on 15.09.2022.

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#### **Orkambi - lumacaftor / ivacaftor -**

**EMA/H/C/003954/X/0078/G**

Vertex Pharmaceuticals (Ireland) Limited,

Rapporteur: Armando Genazzani, Co-

Rapporteur: Finbarr Leacy, PRAC Rapporteur:

Rhea Fitzgerald, “Extension application to add a

new strength of 75 mg of lumacaftor and 94 mg

of ivacaftor fixed dose combination granules,

grouped with a type II variation (C.I.6.a).

C.I.6: Extension of indication to include

treatment of cystic fibrosis for children aged 1

to less than 2 years of age who are homozygous

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for the F508del mutation in the CFTR gene, based on final results from study 122, a 2-part study of CF subjects 1 to <2 years of age homozygous for F508del. As a consequence, sections 4.1, 4.2, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 11.2 of the RMP has also been submitted.”

List of Questions adopted on 13.10.2022.

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**eculizumab - EMEA/H/C/006036**

treatment of paroxysmal nocturnal haemoglobinuria

List of Questions adopted on 10.11.2022.

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**sugammadex - EMEA/H/C/006046**

reversal of neuromuscular blockade induced by rocuronium or vecuronium

List of Questions adopted on 15.09.2022.

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**Tenkasi - oritavancin -**

**EMEA/H/C/003785/X/0036**

Menarini International Operations Luxembourg S.A., Rapporteur: Janet Koenig, PRAC  
Rapporteur: Adam Przybylkowski, “Extension application to add a new strength of 1200 mg for powder for concentrate for solution for infusion. The RMP (version 4) is updated in accordance.”

List of Questions adopted on 21.07.2022.

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**B.6.4. Annual Re-assessments: timetables for adoption**

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**Defitelio - defibrotide -**

**EMEA/H/C/002393/S/0060, Orphan**

Gentium S.r.l., Rapporteur: Kristina Dunder, PRAC Rapporteur: Mari Thorn

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**Obizur - susoctocog alfa -**

**EMEA/H/C/002792/S/0050**

Baxalta Innovations GmbH, Rapporteur: Daniela Philadelphia, PRAC Rapporteur: Brigitte Keller-Stanislawski

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**B.6.5. Renewals of Marketing Authorisations: timetables for adoption provided only if the validation has been completed**

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**Defitelio - defibrotide -**

**EMEA/H/C/002393/R/0061, Orphan**

Gentium S.r.l., Rapporteur: Kristina Dunder, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Mari Thorn

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**Hulio - adalimumab -  
EMA/H/C/004429/R/0041**

Viatrix Limited, Rapporteur: Christophe Focke,  
Co-Rapporteur: Christian Gartner, PRAC  
Rapporteur: Ulla Wändel Liminga

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**Ilumetri - tildrakizumab -  
EMA/H/C/004514/R/0042**

Almirall S.A, Rapporteur: Jan Mueller-Berghaus,  
Co-Rapporteur: Finbarr Leacy, PRAC  
Rapporteur: Adam Przybylkowski

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**Kigabeq - vigabatrin -  
EMA/H/C/004534/R/0012**

ORPHELIA Pharma SAS, Rapporteur: Ewa  
Balkowiec Iskra, PRAC Rapporteur: Kirsti Villikka

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**Koselugo - selumetinib -  
EMA/H/C/005244/R/0010, Orphan**

AstraZeneca AB, Rapporteur: Alexandre Moreau,  
PRAC Rapporteur: Ulla Wändel Liminga

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**Lunsumio - mosunetuzumab -  
EMA/H/C/005680/R/0001, Orphan**

Roche Registration GmbH, Rapporteur: Aaron  
Sosa Mejia, PRAC Rapporteur: Ulla Wändel  
Liminga

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**Mepsevii - vestronidase alfa -  
EMA/H/C/004438/R/0033, Orphan**

Ultragenyx Germany GmbH, Rapporteur:  
Johann Lodewijk Hillege, Co-Rapporteur:  
Alexandre Moreau, PRAC Rapporteur: Maria del  
Pilar Rayon

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**Pelgraz - pegfilgrastim -  
EMA/H/C/003961/R/0040**

Accord Healthcare S.L.U., Rapporteur: Sol Ruiz,  
Co-Rapporteur: Ondřej Slanař, PRAC  
Rapporteur: Menno van der Elst

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**Slenyto - melatonin -  
EMA/H/C/004425/R/0021**

RAD Neurim Pharmaceuticals EEC SARL,  
Rapporteur: Kristina Dunder, Co-Rapporteur:  
Tomas Radimersky, PRAC Rapporteur: Ana Sofia  
Diniz Martins

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**Symkevi - tezacaftor / ivacaftor -  
EMA/H/C/004682/R/0038, Orphan**

Vertex Pharmaceuticals (Ireland) Limited,  
Rapporteur: Johann Lodewijk Hillege, Co-  
Rapporteur: Robert Porszasz, PRAC Rapporteur:  
Rhea Fitzgerald

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**Verzenios - abemaciclib -  
EMA/H/C/004302/R/0025**

Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Inês Ribeiro-Vaz

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**B.6.6. VARIATIONS – START OF THE PROCEDURE**

**Timetables for adoption** provided that the validation has been completed.

**B.6.7. Type II Variations scope of the Variations: Extension of indication**

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**Apexxnar - pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) -  
EMA/H/C/005451/II/0012**

Pfizer Europe MA EEIG, Rapporteur: Daniela Philadelphia, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Jean-Michel Dogné, "Extension of indication to include infants, children and adolescents from 6 weeks to less than 18 years of age for the prevention of invasive disease, pneumonia and acute otitis media caused by Streptococcus pneumoniae, based on final results from studies B7471003, B7471011, B7471012, B7471013 and B7471014. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.0 of the RMP has also been submitted."

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**Bylvay - odeixibat -  
EMA/H/C/004691/II/0011, Orphan**

Albireo, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski, "Extension of indication to include treatment of cholestasis and pruritus in Alagille syndrome (ALGS) in patients from birth and older for BYLVAY, based on final results from study A4250-012 and interim results from study A4250-015. Study A4250-012 is a 24-week, randomised, double-blind, placebo-controlled Phase III study conducted in 52 patients with a genetically confirmed diagnosis of ALGS and presence of pruritus and high serum bile acid levels at baseline. Study A4250-015 is an ongoing 72-week open-label extension trial for patients who completed study A4250-012 and evaluates the long-term safety and efficacy of Bylvay in patients with ALGS. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC

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are updated. The Package Leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted.”

Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

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**Enhertu - trastuzumab deruxtecan -  
EMA/H/C/005124/II/0027**

Daiichi Sankyo Europe GmbH, Rapporteur:  
Aaron Sosa Mejia, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Inês Ribeiro-Vaz, “Extension of indication to include the indication treatment of non-small cell lung cancer for Enhertu (trastuzumab deruxtecan), based on results from study DS8201-A-U204 (DESTINY-Lung01) and study DS8201-A-U206 (DESTINY-Lung02).

Study DESTINY-Lung01 is a phase 2, multicentre, open-label, 2-cohort study of trastuzumab deruxtecan (DS-8201a), an anti-HER2 antibody drug conjugate (ADC), for HER2-over-expressing or -mutated, unresectable and/or metastatic non-small cell lung cancer (NSCLC) conducted at sites in Japan, the United States and Europe.

Study DESTINY-Lung02 is an ongoing phase 2, multicentre, randomised study to evaluate the safety and efficacy of trastuzumab deruxtecan in subjects with HER2-mutated metastatic non-small cell lung cancer, conducted in North America, Europe and Asia-Pacific.

As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.

Version 2.2 of the RMP has also been submitted.”

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**Foclivia - pandemic influenza vaccine  
(surface antigen, inactivated, adjuvanted)  
- EMA/H/C/001208/II/0081**

Seqirus S.r.l, Rapporteur: Maria Grazia Evandri, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, “Extension of indication to include children from 6 months to less than 18 years of age for Foclivia, based on final results from study V87\_30; this is a phase 2, randomized, observer-blind, multicenter study to evaluate the immunogenicity and safety of several doses of antigen and MF59 adjuvant content in a monovalent H5N1

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pandemic influenza vaccine in healthy pediatric subjects 6 months to less than 9 years of age. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. Version 4.9 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and to bring it in line with the latest QRD template.”

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**Gazyvaro - obinutuzumab -  
EMA/H/C/002799/II/0052, Orphan**

Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ulla Wändel Liminga, “Extension of indication to include the pre-treatment to reduce the risk of cytokine release syndrome (CRS) induced by glofitamab for Gazyvaro, based on results from study NP30179; this is a multicenter, open-label, Phase I/II study evaluating the safety, efficacy, tolerability and pharmacokinetics of escalating doses of glofitamab as a single agent and in combination with obinutuzumab administered after a fixed, single dose pre-treatment of Gazyvaro in patients with relapsed/refractory B-cell NHL. As a consequence, sections 4.1, 4.2, 4.4, 5.1, 5.3 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 10.0 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version.”

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**Imfinzi - durvalumab -  
EMA/H/C/004771/II/0057**

AstraZeneca AB, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: David Olsen, “Extension of indication to include IMFINZI as treatment of adults with unresectable hepatocellular carcinoma (uHCC), based on final results from study D419CC00002 (HIMALAYA); this was a randomized, open-label, multi-center phase III study of durvalumab and tremelimumab as first-line treatment in patients with unresectable hepatocellular carcinoma (HIMALAYA). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 9, Succession 1

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of the RMP has also been submitted. In addition, the PI is brought in line with the latest QRD template version 10.3.”

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**Jardiance - empagliflozin -  
EMA/H/C/002677/II/0074**

Boehringer Ingelheim International GmbH,  
Rapporteur: Johann Lodewijk Hillege, Co-  
Rapporteur: Karin Janssen van Doorn, PRAC  
Rapporteur: Maria del Pilar Rayon, “Extension of indication to include treatment of chronic kidney disease (CKD) for JARDIANCE, based on final results from study EMPA-KIDNEY (1245-0137) listed as a category 3 study in the RMP; this is a Phase III, multicentre international randomised parallel group double-blind placebo controlled clinical trial of empagliflozin once daily to assess cardio-renal outcomes in patients with chronic kidney disease. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 19.0 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.3.”

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**Olumiant - baricitinib -  
EMA/H/C/004085/II/0037**

Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski, “Extension of indication to include the treatment of paediatric patients (from 2 years of age and older) with moderate to severe atopic dermatitis for OLUMIANT, based on the final results from study I4V-MC-JAIP; this is a Phase III, multicentre, randomised, double blind, placebo controlled, parallel-group, outpatient study evaluating the pharmacokinetics, efficacy, and safety of baricitinib in paediatric patients with moderate-to-severe atopic dermatitis. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet has been updated accordingly. Version 17.1 of the RMP has also been submitted”

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**Orencia - abatacept -  
EMA/H/C/000701/II/0152**

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Robert Porszasz, PRAC Rapporteur: Kimmo Jaakkola, “Extension of indication to include the

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prophylaxis of acute Graft versus Host Disease (aGvHD) in the adult and paediatric population for Orencia, based on final results from studies IM101311 - Abatacept Combined With a Calcineurin Inhibitor and Methotrexate for Graft Versus Host Disease Prophylaxis and IM101841 - Overall Survival In 7/8 HLA-Matched Hematopoietic Stem Cell Transplantation Patients Treated With Abatacept Combined With A Calcineurin Inhibitor And Methotrexate - An Analysis Of The Center For International Blood And Marrow Transplant Research (Cibmtr) Database. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 28.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI.”

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**Pepaxti - melphalan flufenamide -  
EMA/H/C/005681/II/0002**

Oncopeptides AB, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Elita Poplavska, PRAC Rapporteur: Martin Huber, “Extension of indication to include treatment of patients with Multiple Myeloma who have received at least two prior lines of therapies for PEPAXTI, based on final results from study OP-103 OCEAN; this is a randomized, open-label phase III study in patients with relapsed or refractory multiple myeloma following two to four lines of prior therapies and who were refractory to lenalidomide and the last line of therapy. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in the SmPC.”

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**Refixia - nonacog beta pegol -  
EMA/H/C/004178/II/0032**

Novo Nordisk A/S, Rapporteur: Daniela Philadelphia, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Extension of indication to include treatment and prophylaxis of bleeding in children below 12 years of age with haemophilia B including previously untreated patients for REFIXIA, based on interim results from studies NN7999-

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3774 and NN7999-3895. NN7999-3774 is a multicentre, open-label, non-controlled study evaluating the safety, efficacy and pharmacokinetics of nonacog beta pegol in previously treated children with haemophilia B, while NN7999-3895 is a multicentre, open-label, single-arm, non-controlled trial evaluating the safety and efficacy of nonacog beta pegol in previously untreated patients with haemophilia B. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated accordingly. Version 5.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI.”

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**Retsevmo - selpercatinib -  
EMA/H/C/005375/II/0021**

Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst, “Extension of indication to include the treatment of adults and adolescents 12 years and older with advanced RET fusion-positive thyroid cancer in the first-line setting for RETSEVMO based on interim data from studies LIBRETTO-001 (LOXO-RET-17001) and LIBRETTO-121; LIBRETTO-001 is an open-label, multicentre, global Phase 1/2 study of selpercatinib in patients with RET-altered advanced solid tumours. LIBRETTO-121 is a Phase 1/2 study of selpercatinib in paediatric patients with advanced RET-altered solid or primary central nervous system tumours. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.2 of the RMP has also been submitted.”

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**Retsevmo - selpercatinib -  
EMA/H/C/005375/II/0022**

Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst, “Extension of indication for RETSEVMO to include the treatment of adults with advanced or metastatic RET fusion-positive solid tumours with disease progression on or after prior systemic therapies or who have no satisfactory therapeutic options, based on interim data from study LIBRETTO-001 (LOXO-RET-17001); LIBRETTO-001 is an open-label, multicentre,

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global Phase 1/2 study of selpercatinib in adult and adolescent patients with advanced RET-altered tumours. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the SmPC.”

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**TRODELVY - sacituzumab govitecan -  
EMA/H/C/005182/II/0020**

Gilead Sciences Ireland UC, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, “Extension of indication to include treatment of adult patients with unresectable or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting, based on final results from study IMMU-132-09 (TROPICS-02); this is an open-label, randomized, multicenter phase 3 study of sacituzumab govitecan (IMMU-132) versus treatment of physician's choice (TPC) in subjects with hormonal receptor-positive (HR+) human epidermal growth factor receptor 2 (HER2) negative metastatic breast cancer (mBC) who have failed at least two prior chemotherapy regimens. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and to update the list of local representatives in the Package Leaflet.”  
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

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**Voxzogo - vosoritide -  
EMA/H/C/005475/II/0006, Orphan**

BioMarin International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Zane Neikena, “Extension of indication to include treatment of children less than 2 years of age for Voxzogo, based on final results from the category 1 study BMN 111-206 and interim results from its open-label extension study 111-208. 111-206 is a phase 2 randomized, double-blind, placebo-

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controlled, multicentre study to assess the safety and efficacy of BMN 111 in infants and young children with achondroplasia. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Annex II and Package Leaflet are updated in accordance. Version 3.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI.”

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#### **B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects**

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##### **COMIRNATY - tozinameran -**

**EMA/H/C/005735/II/0165/G**

BioNTech Manufacturing GmbH, Rapporteur:  
Filip Josephson

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##### **COMIRNATY - tozinameran -**

**EMA/H/C/005735/II/0167**

BioNTech Manufacturing GmbH, Rapporteur:  
Filip Josephson

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##### **Cyramza - ramucirumab -**

**EMA/H/C/002829/II/0051**

Eli Lilly Nederland B.V., Rapporteur: Paula  
Boudewina van Hennik

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##### **Dupixent - dupilumab -**

**EMA/H/C/004390/II/0069/G**

Sanofi Winthrop Industrie, Rapporteur: Jan  
Mueller-Berghaus

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##### **ECALTA - anidulafungin -**

**EMA/H/C/000788/II/0052/G**

Pfizer Europe MA EEIG, Rapporteur: Johann  
Lodewijk Hillege

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##### **EVUSHELD - tixagevimab / cilgavimab -**

**EMA/H/C/005788/II/0006/G**

AstraZeneca AB, Rapporteur: Jan Mueller-  
Berghaus

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##### **EXPAREL liposomal - bupivacaine -**

**EMA/H/C/004586/II/0011/G**

Pacira Ireland Limited, Rapporteur: Elita  
Poplavska

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##### **Hizentra - human normal immunoglobulin -**

**EMA/H/C/002127/II/0143**

CSL Behring GmbH, Rapporteur: Jan Mueller-  
Berghaus

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##### **Nucala - mepolizumab -**

**EMA/H/C/003860/II/0057/G**

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GlaxoSmithKline Trading Services Limited,  
Rapporteur: Finbarr Leacy

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**Privigen - human normal immunoglobulin -  
EMA/H/C/000831/II/0195**

CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

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**Sapropterin Dipharma - sapropterin -  
EMA/H/C/005646/II/0010**

Dipharma B.V., Generic, Generic of Kuvan,  
Rapporteur: Frantisek Drafi

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**Somavert - pegvisomant -  
EMA/H/C/000409/II/0106/G**

Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race

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**Spikevax - elasomeran -  
EMA/H/C/005791/II/0094/G**

Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus

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**Vaxelis - diphtheria, tetanus, pertussis  
(acellular, component), hepatitis B (rDNA),  
poliomyelitis (inact.) and haemophilus type  
b conjugate vaccine (adsorbed) -  
EMA/H/C/003982/II/0115**

MCM Vaccine B.V., Rapporteur: Christophe Focke

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**Vyvgart - efgartigimod alfa -  
EMA/H/C/005849/II/0004/G, Orphan**

Argenx, Rapporteur: Thalia Marie Estrup Blicher

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**WS2390**

**Januvia-**

**EMA/H/C/000722/WS2390/0080**

**Ristaben-**

**EMA/H/C/001234/WS2390/0074**

**Steglujan-**

**EMA/H/C/004313/WS2390/0019**

**TESAVEL-**

**EMA/H/C/000910/WS2390/0080**

**Xelevia-EMA/H/C/000762/WS2390/0088**

Merck Sharp & Dohme B.V., Lead Rapporteur:  
Kristina Dunder

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**WS2401/G**

**Hexacima-**

**EMA/H/C/002702/WS2401/0143/G**

**Hexyon-**

**EMA/H/C/002796/WS2401/0147/G**

Sanofi Pasteur, Lead Rapporteur: Jan Mueller-

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### **B.6.9. CHMP assessed procedures scope: Non-Clinical and Clinical aspects**

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#### **Cibinqo - abrocitinib -**

##### **EMA/H/C/005452/II/0007**

Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder, "To update section 5.1 of the SmPC in order to update long-term efficacy data based on the results from studies B7451012, B7451013, B7451015 and B7451029."

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#### **EVOTAZ - atazanavir / cobicistat -**

##### **EMA/H/C/003904/II/0044**

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, "Update of section 4.5 of the SmPC in order to update drug-drug interaction (DDI) information related to the co-administration with antiplatelet therapies classified as P2Y12 platelet inhibitors as well as the co-administration with dexamethasone and other corticosteroids. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

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#### **Keytruda - pembrolizumab -**

##### **EMA/H/C/003820/II/0132**

Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, "Update of section 4.8 of the SmPC in order to add optic neuritis to the list of adverse drug reactions (ADRs) with frequency rare based on literature review. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce editorial changes to the PI."

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#### **Lupkynis - voclosporin -**

##### **EMA/H/C/005256/II/0005**

Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Kristina Dunder, "Update of sections 4.5 and 5.2 of the SmPC in order to update safety information based on final results from study AUR-VCS-2021-02 / Statin-DDI listed as REC in the Letter of Recommendation and study AUR-VCS-2016-02. AUR-VCS-2021-02 / Statin-DDI is an in-vivo DDI study, investigating the effects of voclosporin on simvastatin and its active metabolite simvastatin acid as substrates for OATP1B1/OATP1B3 and AUR-VCS-2016-02 was to show long-term (3 years) safety data from subjects receiving voclosporin and concomitant

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statins.”

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**Methylthioninium chloride Proveblue -  
methylthioninium chloride -  
EMA/H/C/002108/II/0054**

Provepharm SAS, Rapporteur: Kristina Dunder, “Submission of the final report from studies PVP-2016003 and HQF-METHB-2018001. PVP-2016003 is an Open-label clinical study to evaluate the safety and efficacy of ProvayBlue (methylene blue) for the treatment of acquired methemoglobinemia (MEBIPAM); while HQF-METHB-2018001 is a prospective, observational registry designed to collect real world data regarding the safety and efficacy of ProvayBlue.”

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**Qutenza - capsaicin -  
EMA/H/C/000909/II/0057**

Grunenthal GmbH, Rapporteur: Bruno Sepodes, “Update of sections 4.4 and 4.8 of the SmPC in order to add ‘Third Degree Burn’ to the list of adverse drug reactions (ADRs) with frequency not known, based on a validated safety signal and post-marketing data; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes to the Package Leaflet.”

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**Reblozyl - luspaterecept -  
EMA/H/C/004444/II/0016, Orphan**

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Daniela Philadelphia, “Update of section 5.1 of the SmPC in order to reflect the correct values of late-reported transfusions and modifications of previously reported transfusions based on final results from study ACE-536-B-THAL-001 (BELIEVE), A Phase 3, Double-Blind, Randomized, Placebo-Controlled, Multicenter Study To Determine The Efficacy And Safety Of Luspaterecept (Ace-536) Versus Placebo In Adults Who Require Regular Red Blood Cell Transfusions Due To Beta-Thalassemia.”

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**Retsevmo - selpercatinib -  
EMA/H/C/005375/II/0023**

Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, “Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to introduce a new dose modification regimen in the event of ‘interstitial lung disease (ILD)/pneumonitis’ and to introduce it as a new warning and add it to the

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list of adverse drug reactions (ADRs) with frequency common, based on an internal safety review. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor formatting changes to the PI.”

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**Spikevax - elasmomeran -  
EMA/H/C/005791/II/0093**

Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, “Submission of the final report from study QHD00028 (NCT04969276), a Phase II, open-label study to ‘Assess the Safety and Immunogenicity of Fluzone High-Dose Quadrivalent (Influenza Vaccine), 2021-2022 Formulation and a Third Dose of Moderna COVID-19 Vaccine (mRNA-1273 Vaccine) Administered Either Concomitantly or Singly in Adults 65 Years of Age and Older Previously Vaccinated With a 2-dose Schedule of Moderna COVID-19 Vaccine’.”

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**Symtuza - darunavir / cobicistat /  
emtricitabine / tenofovir alafenamide -  
EMA/H/C/004391/II/0048**

Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, “Submission of the final report from study TMC114FD2HTX3002 (DIAMOND). This is a phase 3, single-arm, open-label study to evaluate the efficacy and safety of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) once daily fixed-dose combination (FDC) regimen in newly diagnosed, antiretroviral treatment-naïve human immunodeficiency virus type 1 (HIV-1) infected subjects receiving care in a test and treat model of care.”

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**Tecovirimat SIGA - tecovirimat -  
EMA/H/C/005248/II/0003/G**

SIGA Technologies Netherlands B.V., Rapporteur: Jayne Crowe, “Grouped application consisting of the submission of the final reports from the following five non-clinical studies: 9603766 (SG2 material), 9603767 (SG2 Dimer material), 9603768 (SG1 material), 9603769 (SG1 exo-isomer material) and 9603770 (Maleic Anhydride material). These are genotoxicity studies for active drug substance impurities/degradants.”

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**Ultomiris - ravulizumab -  
EMA/H/C/004954/II/0034**

Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study ALXN1210-PNH-302, a Phase III, randomised, open-label, active controlled study of ALXN1210 versus eculizumab in adult patients with paroxysmal nocturnal hemoglobinuria (PNH) currently treated with eculizumab, listed as a category 3 study in the RMP. The Package Leaflet is updated accordingly."

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**Veklury - remdesivir -  
EMA/H/C/005622/II/0045**

Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, "Update of section 5.1 of the SmPC in order to update clinical virology information based on results of the phenotypic analysis of the nsp12 substitutions that emerged post-treatment in study GS-US-540-5773, including T76I, A526V, A554V, E665K, and C697F."

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**Venclyxto - venetoclax -  
EMA/H/C/004106/II/0045**

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Submission of the final report from study M14-032 'A Phase 2 Open-Label Study of the Efficacy and Safety of Venetoclax ABT-199 (GDC-0199) in Chronic Lymphocytic Leukemia Subjects with Relapse of Refractory to B-Cell Receptor Signaling Pathway Inhibitor Therapy' listed as a category 3 study in the RMP"

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**Xolair - omalizumab -  
EMA/H/C/000606/II/0118**

Novartis Europharm Limited, Rapporteur: Kristina Dunder, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update long-term safety and efficacy based on results from XTEND study (ML29510), a Phase IV, multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of omalizumab through 48 weeks in patients with CSU."

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**WS2405  
BYANLI-  
EMA/H/C/005486/WS2405/0004  
Trevicta-**

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**EMA/H/C/004066/WS2405/0030**

**Xeplion-**

**EMA/H/C/002105/WS2405/0055**

Janssen-Cilag International N.V., Lead Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC for Xeplion and Trevicta in order to modify the frequencies of the list of adverse drug reactions (ADRs) to align with the Product Information of BYANLI. In addition, the MAH took the opportunity to introduce administrative corrections and minor editorial changes to the PI as well as to update the list of local representatives in the Package Leaflet."

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#### **B.6.10. CHMP-PRAC assessed procedures**

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**AUBAGIO - teriflunomide -**

**EMA/H/C/002514/II/0042**

Sanofi Winthrop Industrie, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Submission of the final report from study EFC11759 listed as a category 3 study in the RMP. This is a two-year, multicenter, randomized, double-blind, placebo-controlled, parallel group trial to evaluate efficacy, safety, tolerability and pharmacokinetics of teriflunomide administered orally once daily in paediatric patients with relapsing forms of multiple sclerosis (MS) followed by an open-label extension. The RMP version 8.0 has also been submitted."

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**AYVAKYT - avapritinib -**

**EMA/H/C/005208/II/0022, Orphan**

Blueprint Medicines (Netherlands) B.V., Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations and to update pharmacokinetic information for use in patients with severe hepatic impairment based on the final results from study BLU-285-0107 listed as a category 3 study in the RMP; this is a phase 1, open-label, single-dose study to investigate the influence of severe hepatic impairment on the pharmacokinetics of avapritinib. The package leaflet is updated accordingly. The RMP version 3.0 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest

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**GAVRETO - pralsetinib -  
EMA/H/C/005413/II/0010**

Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Ulla Wändel Liminga, “Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update efficacy and safety information in the treatment of adult patients with RET fusion-positive advanced NSCLC based on final results (NSCLC indication) from study ARROW/BO42863, a Phase 1/2 Study of the Highly-selective RET Inhibitor, BLU 667, in Patients With Thyroid Cancer, Non-Small Cell Lung Cancer (NSCLC), and Other Advanced Solid Tumours listed as a specific obligation in the Annex II.  
The RMP version 1.5 has also been submitted.”

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**Lumykras - sotorasib -  
EMA/H/C/005522/II/0007**

Amgen Europe B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Marie Louise Schougaard Christiansen, “Update of sections 4.2 and 5.2 of the SmPC in order to update recommendations for patients with moderate to severe hepatic impairment following final results from study 20200362 listed as a category 3 PASS study in the EU RMP; this is a Phase I clinical study to evaluate the pharmacokinetics (PK) of a single oral dose of sotorasib administered in subjects with moderate or severe hepatic impairment compared with subjects who have normal hepatic function. The EU RMP version 1.0 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.3.”

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**MINJUVI - tafasitamab -  
EMA/H/C/005436/II/0008, Orphan**

Incyte Biosciences Distribution B.V., Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Ulla Wändel Liminga, “Update of section 4.4 of the SmPC in order to add a new warning on Progressive Multifocal Leukoencephalopathy (PML) based on post-marketing data; the Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in the SmPC and to bring the PI in line with the

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**Piqray - alpelisib -**

**EMA/H/C/004804/II/0018**

Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst, “Update of sections 4.5 and 5.2 of the SmPC in order to update drug-drug interaction information, based on final results from study BYL719A2111; this is a phase 1, open-label, fixed-sequence, two-period drug-drug interaction (DDI) study evaluating the PK probe substrates for CYP3A4, CYP2B6, CYP2C8, CYP2C9, and CYP2C19 when administered either alone or in combination with repeated doses of alpelisib. The Annex II and Package Leaflet are updated accordingly. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI.”

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**Polivy - polatuzumab vedotin -**

**EMA/H/C/004870/II/0020, Orphan**

Roche Registration GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ulla Wändel Liminga, “To submit the updated final OS CSR for study GO39942 - A Phase III, multicenter, randomized, double-blind, placebo-controlled trial comparing the efficacy and safety of polatuzumab vedotin in combination with R-CHP versus R-CHOP in previously untreated patients with DLBCL (POLARIX) listed as a Category 3 study in the RMP. This submission will address the missing information of "long-term safety" in patients treated with polatuzumab vedotin. An updated RMP version 4.0 has also been submitted to remove the commitment for this study along with the missing information of "long-term safety".”

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**TUKYSA - tucatinib -**

**EMA/H/C/005263/II/0010**

Seagen B.V., Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Jean-Michel Dogné, “Submission of the final report from study SGNTUC-017 (MOUNTAINEER) listed as a category 3 study in the RMP. This is a Phase 2, Open Label Study of Tucatinib Combined with Trastuzumab in Patients with HER2+ Metastatic Colorectal Cancer. Primary objective is to determine the antitumor activity of tucatinib

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given in combination with trastuzumab. The RMP version 1.1 has also been submitted.”

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**Vabysmo - faricimab -**

**EMA/H/C/005642/II/0002**

Roche Registration GmbH, Rapporteur: Jayne Crowe, PRAC Rapporteur: Inês Ribeiro-Vaz, “Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information and to update the warnings and the list of adverse drug reactions (ADRs), based on longer-term results from studies GR40306 (TENAYA) and GR40844 (LUCERNE); these are phase 3, multicenter, randomized, double-masked, active comparator-controlled, 112-week studies to evaluate the efficacy and safety of faricimab in patients with neovascular age-related macular degeneration (nAMD); the Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI.”

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**Veklury - remdesivir -**

**EMA/H/C/005622/II/0044/G**

Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, PRAC Rapporteur: Eva Jirsová, “Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to change posology recommendations for patients with renal impairment, remove an existing warning on renal impairment and update the safety and efficacy information based on final results from studies GS US 540 5912 and GS-US-540-9015, listed as category 3 studies in the RMP. Study GS US 540 5912 is a phase 3 randomized, double-blind, placebo-controlled, parallel group, multicenter study evaluating the efficacy and safety of remdesivir in participants with severely reduced kidney function who were hospitalised for COVID-19, while study GS-US-540-9015 is a phase 1, multicenter, open-label, single-dose study to evaluate the single-dose PK of remdesivir in participants with normal and impaired renal function. The Package Leaflet is updated accordingly. The RMP version 5.1 has also been submitted. In addition, the MAH took the opportunity to introduce minor edits to the PI.”

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**Veklury - remdesivir -**

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**EMA/H/C/005622/II/0046**

Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, PRAC Rapporteur: Eva Jirsová, "Update of sections 4.6 and 5.1 of the SmPC in order to update information on pregnancy and breast-feeding based on final results from study IMPAACT 2032 listed as a category 3 study in the RMP; this is a phase 4, prospective, open-label, non-randomized study to address PK and safety of remdesivir in pregnant women. The Package Leaflet is updated accordingly. The RMP version 5.2 has also been submitted."

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**B.6.11. PRAC assessed procedures**

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PRAC Led

**Brukinsa - zanubrutinib -****EMA/H/C/004978/II/0008**

BeiGene Ireland Ltd, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Paula Boudewina van Hennik, "Submission of the updated RMP (Version 3.0) on the dates of submission of information to the ongoing study BGB-3111-LTE1."

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PRAC Led

**Coagadex - human coagulation factor x -****EMA/H/C/003855/II/0046, Orphan**

BPL Bioproducts Laboratory GmbH, Rapporteur: Daniela Philadelphia, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report from study TEN06 - NCT03161626 (REC EMA/H/C/003855). This is a non-interventional, multicenter, post-marketing registry study in three patients with moderate or severe hereditary FX deficiency, to assess Coagadex administered peri-operatively for haemostatic cover in major surgery during routine post-marketing use. The primary objective is to collect additional surgical data on the clinical effectiveness of Coagadex, in a post-marketing environment, for peri-operative haemostatic cover during major surgery in patients with moderate or severe hereditary factor X (FX) deficiency. The RMP version 3.0 has also been submitted."

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PRAC Led

**Myozyme - alglucosidase alfa -****EMA/H/C/000636/II/0093**

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Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Nathalie Gault, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final non-interventional Pompe Registry Report 2022 (MEA024 and MEA025)."

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PRAC Led

**Ocaliva - obeticholic acid -**

**EMA/H/C/004093/II/0039, Orphan**

Advanz Pharma Limited, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 2.0 in order to change to EU Qualified Person for Pharmacovigilance (QPPV), update the list of safety concerns and study data for 747-302 and 747-401."

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PRAC Led

**OPDIVO - nivolumab -**

**EMA/H/C/003985/II/0127**

Bristol-Myers Squibb Pharma EEIG, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from the post-authorisation safety study (PASS) CA209835: A registry study in patients who underwent post-nivolumab allogeneic haematopoietic stem-cell transplantation (HSCT). This study is listed as a Category 3 study in the RMP. An updated RMP version 31.0 has also been submitted."

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PRAC Led

**Ozurdex - dexamethasone -**

**EMA/H/C/001140/II/0044**

AbbVie Deutschland GmbH & Co. KG, PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of an updated Annex II and RMP version 11 in order to remove additional risk minimisation measure: Patient guide, audio CD (where required)."

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PRAC Led

**Parsabiv - etelcalcetide -**

**EMA/H/C/003995/II/0021**

Amgen Europe B.V., PRAC Rapporteur: Valentina Di Giovanni, PRAC-CHMP liaison: Armando Genazzani, "Submission of the final report from study 20170561 listed as a category 3 study in the RMP. This is an observational PASS to evaluate the potential association

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between Parsabiv and gastrointestinal bleeding.”

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PRAC Led

**Simponi - golimumab -  
EMA/H/C/000992/II/0111**

Janssen Biologics B.V., PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, “Update of section 4.6 of the SmPC in order to update information on pregnancy based on final results from PASS study CNTO148ART4001 listed as a category 3 study in the RMP; this is an observational prospective cohort study to collect and analyse information pertaining to pregnancy outcomes of women exposed to golimumab during pregnancy. The RMP version 23.2 has also been submitted.”

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PRAC Led

**Simponi - golimumab -  
EMA/H/C/000992/II/0112**

Janssen Biologics B.V., PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, “Submission of the final report from study P04480 (RABBIT) listed as a category 3 study in the RMP. This is an observational prospective cohort study to evaluate the long-term safety of treatment with biologics in rheumatoid arthritis. The RMP version 23.3 has also been submitted.”

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PRAC Led

**Symkevi - tezacaftor / ivacaftor -  
EMA/H/C/004682/II/0039, Orphan**

Vertex Pharmaceuticals (Ireland) Limited, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, “Submission of the final report from PASS study VX17-661-117 listed as a category 3 study in the RMP. This is an Observational Study to Evaluate the Utilization Patterns and Real-World Effects of Tezacaftor and Ivacaftor Combination Therapy (TEZ/IVA) in Patients With Cystic Fibrosis (CF). The RMP version 3.4 has also been submitted.”

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PRAC Led

**Vimizim - elosulfase alfa -  
EMA/H/C/002779/II/0040, Orphan**

BioMarin International Limited, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, “Submission of an updated RMP version 6.0 in order to correct the

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objectives of MARS in RMP to be consistent with version 6 of the protocol and to update the "Method used to calculate exposure" due to GDPR restrictions following the assessment of procedures PSA/S/0062 and PSUSA/00010218/202102."

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PRAC Led

**XOSPATA - gilteritinib -**

**EMA/H/C/004752/II/0012, Orphan**

Astellas Pharma Europe B.V., PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of the final report from study 2215-PV-0001 - Evaluation of the effectiveness of the Xospata Routine Risk Minimisation Measures (RMMs) and an additional Risk Minimisation Measure (aRMM): A Cross sectional study among Healthcare Professionals to assess awareness and knowledge, listed as a category 3 study in the RMP. The RMP version 3.0 has also been submitted."

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PRAC Led

**Zavesca - miglustat -**

**EMA/H/C/000435/II/0076**

Janssen-Cilag International N.V., PRAC Rapporteur: Mari Thorn, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 15.1 in order to remove risks in line with GVP module V revision 2. The MAH has also taken the opportunity to introduce minor changes, such as update of the post marketing exposure data and alignment with the latest Company EU-RMP Template."

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PRAC Led

**WS2402**

**Advagraf-**

**EMA/H/C/000712/WS2402/0069**

**Modigraf-**

**EMA/H/C/000954/WS2402/0045**

Astellas Pharma Europe B.V., Lead PRAC Rapporteur: Ronan Grimes, PRAC-CHMP liaison: Jayne Crowe, "C.I.11.z - To update the EU Risk Management Plan with the new TPRI final study submission milestone, related to procedure EMA/H/C/000712/MEA030 and EMA/H/C/000954/MEA022 (Study F506-PV-0001)."

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PRAC Led

**WS2430**

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**Exviera-EMEA/H/C/003837/WS2430/0056**

**Viekirax-**

**EMEA/H/C/003839/WS2430/0068**

AbbVie Deutschland GmbH & Co. KG, Lead PRAC  
Rapporteur: Maria del Pilar Rayon, PRAC-CHMP  
liaison: Maria Concepcion Prieto Yerro, "C.I.11.z  
- To update the RMP for Viekirax and Exviera to include the completion of studies B16-959, B20-146, M14-423 (TOPAZ-I) and M14-222 (TOPAZ-II), following the outcome of EMEA/H/C/PSR/J/0038, EMEA/H/C/WS2216 and EMEA/H/C/WS2304, respectively. The MAH proposes to remove the emergence and recurrence of hepatocellular carcinoma as potential risks and update the related pharmacovigilance activities and other sections of the RMPs."

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PRAC Led

**WS2434**

**Entresto-**

**EMEA/H/C/004062/WS2434/0049**

**Neparvis-**

**EMEA/H/C/004343/WS2434/0047**

Novartis Europharm Limited, Lead PRAC  
Rapporteur: Anette Kirstine Stark, PRAC-CHMP  
liaison: Thalia Marie Estrup Blicher, "C.I.11.z -  
To amend the RMP for Ernestro and its duplicate marketing authorisation Neparvis to update the milestones for MEA 002 (study CLCZ696B2014) and MEA 004 (study CLCZ696B2015) ."

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PRAC Led

**WS2435**

**Entresto-**

**EMEA/H/C/004062/WS2435/0048**

**Neparvis-**

**EMEA/H/C/004343/WS2435/0046**

Novartis Europharm Limited, Lead PRAC  
Rapporteur: Anette Kirstine Stark, PRAC-CHMP  
liaison: Thalia Marie Estrup Blicher, "Submission of the final report from study CLCZ696B2013 listed as a category 3 study in the RMP. Study CLCZ696B2013 is a non-interventional, post-authorization, database cohort study to assess the risk of serious angioedema in association with LCZ696 (sacubitril/valsartan; Entresto) use in Black patients with heart failure in the United States."

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#### **B.6.12. CHMP-CAT assessed procedures**

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**Abecma - idecabtagene vicleucel -  
EMA/H/C/004662/II/0022/G, Orphan,  
ATMP**

Bristol-Myers Squibb Pharma EEIG, Rapporteur:  
Rune Kjekken, CHMP Coordinator: Ingrid Wang

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**Breyanzi - lisocabtagene maraleucel /  
lisocabtagene maraleucel -  
EMA/H/C/004731/II/0013/G, ATMP**

Bristol-Myers Squibb Pharma EEIG, Rapporteur:  
Concetta Quintarelli, CHMP Coordinator:  
Armando Genazzani

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**WS2389/G**

**Tecartus-**

**EMA/H/C/005102/WS2389/0031/G**

**Yescarta-**

**EMA/H/C/004480/WS2389/0059/G**

Kite Pharma EU B.V., Lead Rapporteur: Jan  
Mueller-Berghaus, CHMP Coordinator: Jan  
Mueller-Berghaus

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#### **B.6.13. CHMP-PRAC-CAT assessed procedures**

#### **B.6.14. PRAC assessed ATMP procedures**

#### **B.6.15. Unclassified procedures and worksharing procedures of type I variations**

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**WS2410**

**Glyxambi-**

**EMA/H/C/003833/WS2410/0050**

**Jardiance-**

**EMA/H/C/002677/WS2410/0077**

**Synjardy-**

**EMA/H/C/003770/WS2410/0069**

Boehringer Ingelheim International GmbH, Lead  
Rapporteur: Johann Lodewijk Hillege

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**WS2411/G**

**Copalia HCT-**

**EMA/H/C/001159/WS2411/0104/G**

**Dafiro HCT-**

**EMA/H/C/001160/WS2411/0106/G**

**Exforge HCT-**

**EMA/H/C/001068/WS2411/0103/G**

Novartis Europharm Limited, Lead Rapporteur:  
Thalia Marie Estrup Blicher

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**WS2413/G**

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**Axura-**

**EMA/H/C/000378/WS2413/0083/G**

**Memantine Merz-**

**EMA/H/C/002711/WS2413/0019/G**

Merz Pharmaceuticals GmbH, Lead Rapporteur:  
Maria Concepcion Prieto Yerro

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**WS2417/G**

**Ongentys-**

**EMA/H/C/002790/WS2417/0055/G**

**Ontilyv-**

**EMA/H/C/005782/WS2417/0010/G**

Bial - Portela & Ca, S.A., Lead Rapporteur:  
Martina Weise

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**WS2420**

**Nuwiq-EMA/H/C/002813/WS2420/0052**

**Vihuma-**

**EMA/H/C/004459/WS2420/0034**

Octapharma AB, Lead Rapporteur: Jan Mueller-  
Berghaus

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## **B.7. DOCUMENTS TABLED IN MMD AFTER THE CHMP PLENARY**

### **B.7.1. Yearly Line listing for Type I and II variations**

### **B.7.2. Monthly Line listing for Type I variations**

### **B.7.3. Opinion on Marketing Authorisation transfer (MMD only)**

### **B.7.4. Notifications in accordance with Article 61(3) of Council Directive 2001/83/EC (MMD only)**

### **B.7.5. Request for supplementary information relating to Notification of Type I variation (MMD only)**

### **B.7.6. Notifications of Type I Variations (MMD only)**

## **C. Annex C - Post-Authorisation Measures (PAMs), (Line listing of Post authorisation measures with a description of the PAM. Procedures starting in that given month with assessment timetabled)**

## **D. Annex D - Post-Authorisation Measures (PAMs), (Details on PAMs including description and conclusion, for adoption by CHMP in that given month, or finalised ones with PRAC recommendation and no adoption by CHMP needed)**

## **E. Annex E - EMA CERTIFICATION OF PLASMA MASTER FILES**

Information related to plasma master files cannot be released at the present time as these contain commercially confidential information.

### **E.1. PMF Certification Dossiers:**

#### **E.1.1. Annual Update**

#### **E.1.2. Variations:**

#### **E.1.3. Initial PMF Certification:**

### **E.2. Time Tables – starting & ongoing procedures: For information**

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PMF timetables starting and ongoing procedures Tabled in MMD and sent by post mail (folder E).

## **F. ANNEX F - Decision of the Granting of a Fee Reduction/Fee Waiver**

### **F.1. Parallel Distribution - Pursuant to Article 9 of Council Regulation (EC) No. 2743/98 of 14 December 1998, as amended**

### **F.2. Request for scientific opinion on justification of exceptional circumstance and for imperative grounds of public health**

## **G. ANNEX G**

### **G.1. Final Scientific Advice (Reports and Scientific Advice letters):**

Information related to Scientific Advice cannot be released at the present time as these contain commercially confidential information.

### **G.2. PRIME**

Some information related to PRIME cannot be released at the present time as these contain commercially confidential information.

#### **G.2.1. List of procedures concluding at 23-26 January 2023 CHMP plenary:**

#### **G.2.2. List of procedures starting in January 2023 for February 2023 CHMP adoption of outcomes**

## **H. ANNEX H - Product Shared Mailboxes – e-mail address**