



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

22 October 2018  
EMA/743328/2018 Corr.2<sup>1</sup>  
Inspections, Human Medicines Pharmacovigilance and Committees Division

## Committee for medicinal products for human use (CHMP) Draft agenda for the meeting on 15-18 October 2018

Chair: Harald Enzmann – Vice-Chair: TBC

15 October 2018, 13:00 – 19:30, room 2A

16 October 2018, 08:30 – 19:30, room 2A

17 October 2018, 08:30 – 19:30, room 2A

18 October 2018, 08:30 – 13:00, room 2A

### 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 on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

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<sup>1</sup> Correction in section 9.1.3 and 14.1.3



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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 15-18 October 2018. See October 2018 CHMP minutes (to be published post November 2018 CHMP meeting).

### 1.2. Adoption of agenda

CHMP agenda for 15-18 October 2018

### 1.3. Adoption of the minutes

CHMP minutes for 17-20 September 2018

## 2. Oral Explanations

### 2.1. Pre-authorisation procedure oral explanations

#### 2.1.1. glycopyrronium / formoterol fumarate dihydrate - EMEA/H/C/004245

indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD)

Scope: Oral explanation

**Action:** Oral explanation to be held on 16 October 2018 at time 09:00

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 09.11.2017.

#### 2.1.2. dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171

indicated for the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4

Scope: Possible oral explanation

**Action:** Possible oral explanation to be held on 16 October 2018 at time 11:00

List of Outstanding Issues adopted on 20.09.2018, 26.04.2018, 23.03.2017. List of Questions adopted on 21.07.2016.

## 2.2. Re-examination procedure oral explanations

No items

## 2.3. Post-authorisation procedure oral explanations

### 2.3.1. Caprelsa - vandetanib - EMEA/H/C/002315/II/0028

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Genzyme Europe BV

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: Oral explanation to be held on 16 October 2018 at time 16:00

**Action:** For adoption

Request for Supplementary Information adopted on 26.04.2018, 14.12.2017.

See 9.1

## 2.4. Referral procedure oral explanations

No items

## 3. Initial applications

### 3.1. Initial applications; Opinions

#### 3.1.1. influenza vaccine surface antigen inactivated prepared in cell cultures - Article 28 - EMEA/H/C/004814

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prophylaxis of influenza in adults and children from 4 years of age

Scope: Opinion

**Action:** For adoption

List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 22.03.2018.

#### 3.1.2. mexiletine hcl - Orphan - EMEA/H/C/004584

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LUPIN (EUROPE) LIMITED; Treatment of myotonic disorders

Scope: Opinion

**Action:** For adoption

Oral explanation held on 18.09.2018. List of Outstanding Issues adopted on 31.05.2018.

List of Questions adopted on 14.12.2017.



### 3.1.3. trastuzumab - EMEA/H/C/004916

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treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)

Scope: Opinion

**Action:** For adoption

List of Outstanding Issues adopted on 20.09.2018. List of Questions adopted on 22.03.2018.

### 3.1.4. lanadelumab - Orphan - EMEA/H/C/004806

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Accelerated assessment

Shire Pharmaceuticals Ireland Limited; treatment of angioedema attacks, prevention of angioedema attacks

Scope: Opinion

**Action:** For adoption

List of Outstanding Issues adopted on 18.09.2018. List of Questions adopted on 26.06.2018.

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

### 3.2.1. dapivirine - Article 58 - EMEA/H/W/002168

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Reducing the risk of HIV-1 infection via vaginal intercourse in sexually active HIV-uninfected women

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 09.11.2017.

### 3.2.2. zanamivir - EMEA/H/C/004102

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treatment of influenza A or B virus infection

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 26.04.2018.

### 3.2.3. lorlatinib - EMEA/H/C/004646

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treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-

small cell lung cancer (NSCLC)

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 31.05.2018.

#### **3.2.4. lusutrombopag - EMEA/H/C/004720**

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treatment of thrombocytopenia

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 31.05.2018.

#### **3.2.5. botulinum toxin type a - EMEA/H/C/004587**

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temporary improvement in the appearance of moderate to severe vertical lines between the eyebrows

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 09.11.2017.

#### **3.2.6. treosulfan - Orphan - EMEA/H/C/004751**

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medac Gesellschaft für klinische Spezialpräparate mbH; conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT)

Scope: List of outstanding issues

**Action:** For adoption

List of Questions adopted on 31.05.2018.

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

#### **3.3.1. angiotensin II - EMEA/H/C/004930**

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treatment of hypotension in adults with distributive or vasodilatory shock who remain hypotensive despite fluid and vasopressor therapy

Scope: List of questions

**Action:** For adoption

#### **3.3.2. enasidenib - Orphan - EMEA/H/C/004324**

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Celgene Europe Limited; treatment of acute myeloid leukaemia (AML)

Scope: List of questions

**Action:** For adoption

### 3.3.3. L-lysine hydrochloride / L-arginine hydrochloride - EMEA/H/C/004541

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reduction of renal radiation exposure during Peptide-Receptor Radionuclide Therapy (PRRT) with lutetium (<sup>177</sup>Lu) oxodotreotide

Scope: List of questions

**Action:** For adoption

### 3.3.4. posaconazole - EMEA/H/C/005028

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treatment of fungal infections in adults

Scope: List of questions

**Action:** For adoption

### 3.3.5. rituximab - EMEA/H/C/004807

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treatment of Non-Hodgkin's lymphoma (NHL), Chronic lymphocytic leukaemia (CLL) and Rheumatoid arthritis

Scope: List of questions

**Action:** For adoption

### 3.3.6. tobramycin - EMEA/H/C/005086

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management of chronic pulmonary infection due to *Pseudomonas aeruginosa* in patients aged 6 years and older with cystic fibrosis (CF)

Scope: List of questions

**Action:** For adoption

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

### 3.4.1. viable T-cells - Orphan - ATMP - EMEA/H/C/002397

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Kiadis Pharma Netherlands B.V.; adjunctive treatment in haematopoietic stem cell transplantation (HSCT) for a malignant disease

Scope: Request by the applicant for an extension to the clock stop to respond to the List of Outstanding Issues adopted on 14.09.2018

**Action:** For adoption

List of Outstanding Issues adopted on 14.09.2018, 25.05.2018. List of Questions adopted on 08.09.2017.

### 3.4.2. sotagliflozin - EMEA/H/C/004889

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indicated as an adjunct to insulin therapy to improve glycaemic control in adults with type 1 diabetes mellitus

Scope: List of questions to the Ad Hoc Expert Group

**Action:** For adoption

List of Questions adopted on 26.07.2018.

### 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

#### 3.6.1. Symkevi - tezacaftor / ivacaftor - Orphan - EMEA/H/C/004682

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Vertex Pharmaceuticals (Europe) Ltd.; treatment of cystic fibrosis

Scope: Final similarity assessment report.

**Action:** For information

New active substance (Article 8(3) of Directive No 2001/83/EC)

Opinion adopted 26.07.2018. List of Outstanding Issues adopted on 28.06.2018, 31.05.2018, 22.03.2018. List of Questions adopted on 14.12.2017.

### 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. Vihuma - simoctocog alfa - EMEA/H/C/004459/X/0006/G

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Octapharma AB

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add new strengths of 2500 IU, 3000 IU and 4000 IU, powder and solvent for solution for injection.

The above line extension is grouped with the following variations:

- C.I.4 - to update sections 4.2, 4.8 and 5.1 of the SmPC to reflect available data from Previously Untreated Patients (PUP) from GENA-05 (interim report) study
- C.I.11.b - to update the Risk Management Plan (version 10) to align the content in a single harmonised worldwide version for simocotocg alfa (rFVIII).
- C.I.1.b - to update the Product Information with the wording agreed in the Art. 31 referral (EMA/H/A-31/1448)."

**Action:** For adoption

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

No items

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

No items

#### **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. Hemlibra - emicizumab - EMA/H/C/004406/II/0002**

Roche Registration GmbH

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of Indication to include routine prophylaxis of bleeding episodes in

patients with hemophilia A without factor VIII inhibitors, for Hemlibra. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated with efficacy and safety information of the pivotal trials:

- Study BH30071 (HAVEN 3) - an ongoing, multicenter, open-label, randomized Phase III clinical study evaluating the efficacy, safety and PK of emicizumab prophylaxis at doses of 1.5 mg/kg/week (QW) and 3 mg/kg/every 2 weeks (Q2W) versus no prophylaxis in adults and adolescent patients (age of 12 or above) with haemophilia A without inhibitors against factor VIII (FVIII).

- Study BO39182 (HAVEN 4) - an ongoing multicenter, open-label, non-randomized Phase III study evaluating the efficacy, safety and PK of emicizumab given as the dose of 6 mg/kg/every 4 weeks (Q4W) in adults and adolescent patients (age of 12 or above) with hemophilia A with or without FVIII inhibitors.

- Study BH29992 (HAVEN 2) - a multicenter, open-label, non-randomized Phase III study evaluating the efficacy, safety and PK of emicizumab at the QW dose in pediatric patients (<12 years old or 12-17 years old and <40kg) with hemophilia A with FVIII inhibitors. The Package Leaflet and the Risk Management Plan (v.2.0) is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor corrections and clarity to sections 4.4, 4.5 and 4.6 of the SmPC."

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 26.07.2018.

Letter from third party

### 5.1.2. Imnovid - pomalidomide - Orphan - EMEA/H/C/002682/II/0031/G

Celgene Europe Limited

Rapporteur: Robert James Hemmings, Co-Rapporteur: Jorge Camarero Jiménez, PRAC  
Rapporteur: Patrick Batty

Scope: "Extension of indication to include treatment with Imnovid in combination with bortezomib and dexamethasone of adult patients with multiple myeloma who have received at least one prior treatment regimen including lenalidomide; as a result, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.

As a consequence the MAH submitted a request to add 14-capsule pack sizes for the 1 mg, 2 mg, 3 mg and 4 mg Imnovid strengths to support the proposed posology and pomalidomide dose modification. The SmPC, Labelling and Package leaflet are updated in accordance.

Update of section 5.1 of the SmPC in order to update the information on pomalidomide mechanism of action based on literature data."

**Action:** For adoption

### 5.1.3. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/II/0069

Vertex Pharmaceuticals (Europe) Ltd.

Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Maria del Pilar Rayon

Scope: "Extension of Indication to include treatment of cystic fibrosis in children age 12 to less than 24 months who have one of the currently approved gating mutations in the CFTR gene for Kalydeco 50 mg & 75 mg Granules; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. Relevant consequential changes are made to the Kalydeco 150 mg film-coated tablet Product Information. The Package Leaflet is updated in accordance.

The RMP version 7.2 has also been submitted."

**Action:** For adoption

Request for Supplementary Information adopted on 20.09.2018, 28.06.2018.

#### 5.1.4. [Keytruda - pembrolizumab - EMEA/H/C/003820/II/0047](#)

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Merck Sharp & Dohme B.V.

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of Indication to include (as monotherapy) adjuvant treatment of melanoma in adults with lymph node involvement who have undergone complete resection, based on study KEYNOTE-054; a randomized, double-blind, phase 3 study conducted in collaboration with the European Organisation for Research and Treatment of Cancer (EORTC), undertaken to evaluate adjuvant therapy with pembrolizumab compared to placebo in patients with resected high-risk melanoma (Stage IIIA [ $> 1$  mm lymph node metastasis], IIIB and IIIC). As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC have been updated and the Package Leaflet has been updated accordingly. An updated RMP version 17.1 was provided as part of the application."

**Action:** For adoption

Request for Supplementary Information adopted on 26.07.2018.

#### 5.1.5. [Keytruda - pembrolizumab - EMEA/H/C/003820/II/0057](#)

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Merck Sharp & Dohme B.V.

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of Indication to include 1st line treatment of locally advanced or metastatic non-small cell lung cancer tumours expressing PD-L1 with a  $\geq 1\%$  tumour proportion score (TPS), based on data from study KEYNOTE-042; an international, randomized, open-label Phase 3 study investigating KEYTRUDA monotherapy compared to standard of care platinum-based chemotherapy in patients with locally advanced or metastatic PD-L1 positive (TPS  $\geq 1\%$ ) NSCLC, and on supportive data from the final planned analysis of KEYNOTE-024; a Phase 3 randomized open-label study of KEYTRUDA monotherapy compared to platinum-based chemotherapy in metastatic NSCLC with PD-L1 TPS  $\geq 50\%$ . As a result, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC have been updated. An updated RMP version 18.1 was provided as part of the application."

**Action:** For adoption

#### 5.1.6. NovoSeven - eptacog alfa (activated) - EMEA/H/C/000074/II/0104

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Novo Nordisk A/S

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Nithyanandan Nagercoil

Scope: "Extension of Indication to extend patient population of NovoSeven for use in patients with Glanzmann's thrombasthenia without antibodies to platelets, or where platelets are not readily available, based on a prospective observational registry and literature references. As a consequence, sections 4.1 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in section 4.8 of the SmPC and in Package Leaflet."

**Action:** For adoption

Request for Supplementary Information adopted on 26.07.2018.

#### 5.1.7. Praluent - alirocumab - EMEA/H/C/003882/II/0042

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sanofi-aventis groupe

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include the prevention of cardiovascular events in patients with established atherosclerotic cardiovascular disease for Praluent based on the final study report of EFC11570; as a consequence, sections, 4.1, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and RMP v4, have been updated accordingly."

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

**Action:** For adoption

#### 5.1.8. Rapiscan - regadenoson - EMEA/H/C/001176/II/0027

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GE Healthcare AS

Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty

Scope: "Extension of Indication to include use in the measurement of fractional flow reserve (FFR) during invasive coronary angiography (ICA) in patients presenting a coronary artery stenosis for Rapiscan based on study 060912001: Comparison of Regadenoson (RAPISCAN) and Central Intravenous Adenosine for Measurement of Fractional Flow Reserve and data from published literature. 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. An updated RMP version 10.0 was provided as part of this extension of indication."

**Action:** For adoption

Request for Supplementary Information adopted on 28.06.2018.



5.1.9. [WS1344](#)  
[Edistride - dapagliflozin - EMEA/H/C/004161/WS1344/0025](#)  
[Forxiga - dapagliflozin - EMEA/H/C/002322/WS1344/0044](#)

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AstraZeneca AB

Lead Rapporteur: Kristina Dunder, Lead Co-Rapporteur: Martina Weise, PRAC Rapporteur: Annika Folin

Scope: "Extension of Indication to include new indication for the treatment of insufficiently controlled type 1 diabetes mellitus as an adjunct to insulin, when insulin does not provide adequate glycaemic control, for Forxiga and Edistride; 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. The updated RMP version 16 has also been submitted.

In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor editorial changes to SmPC and Package Leaflet."

**Action:** For adoption

Request for Supplementary Information adopted on 31.05.2018.

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](#)

5.3.1. [WS1278](#)  
[OPDIVO - nivolumab - EMEA/H/C/003985/WS1278/0042](#)  
[Yervoy - ipilimumab - EMEA/H/C/002213/WS1278/0053](#)

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Bristol-Myers Squibb Pharma EEIG

Scope: "Extension of indication to include the combination treatment with nivolumab and ipilimumab of adult patients with intermediate/poor-risk advanced renal cell carcinoma. As a consequence sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the Opdivo and Yervoy SmPCs are updated. The Package Leaflet and the Risk Management Plan (version 19.0 for Yervoy and version 13.0 for Opdivo) are updated in accordance. In addition, the Worksharing applicant (WSA) took the opportunity to correct some typos throughout the Yervoy and Opdivo product information."

List of questions to the SAG

**Action:** For adoption

Opinion adopted on 26.07.2018. An oral Explanation was held on 25.07.2018.

## 6. Ancillary medicinal substances in medical devices

### 6.1. Ancillary medicinal substances in medical devices; Opinions/ Day 180 list of outstanding issues / Day 120 list of questions

No items

### 6.2. Update of Ancillary medicinal substances in medical devices

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. fenfluramine hcl - Orphan - H0003933

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Zogenix International Ltd; treatment of seizures associated with Dravet syndrome.

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

**Action:** For adoption

#### 8.1.2. cilastatin sodium, imipenem monohydrate, relebactam - H0004808

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indicated for the treatment of bacterial infections due to gram-negative microorganisms in patients 18 years of age and older with limited treatment options.

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

**Action:** For adoption

#### 8.1.3. potassium bicarbonate, potassium citrate monohydrate - H0004460

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treatment of distal Renal Tubular Acidosis (dRTA)

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

**Action:** For adoption

## 8.2. Priority Medicines (PRIME)

Disclosure of 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. Caprelsa - vandetanib - EMEA/H/C/002315/II/0028

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Genzyme Europe BV

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: "Update of sections 4.1, 4.4 and 5.1 of the SmPC in order to delete the information regarding Rearranged during Transfection (RET) mutation. The application addresses SOB 001 and the MAH proposes to revert from conditional marketing authorisation to standard marketing authorisation. Annex II and Package Leaflet are updated accordingly. The RMP version 12.2 has also been submitted.

In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10."

**Action:** For adoption

Request for Supplementary Information adopted on 26.04.2018, 14.12.2017.

See 2.3

#### 9.1.2. Evoltra - clofarabine - EMEA/H/C/000613/S/0059

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Genzyme Europe BV

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: Request for Supplementary Information/Opinion

**Action:** For discussion

### 9.1.3. IONSYS - fentanyl - EMEA/H/C/002715

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MAH: Incline Therapeutics Europe Ltd, treatment of acute moderate to severe post-operative pain

Rapporteur: Greg Markey, Co-Rapporteur: Outi Mäki-Ikola,

Scope: Letter from the applicant dated 4 September 2018 informing EMA about the withdrawal of the marketing authorisation on commercial reasons

**Action:** For information

### 9.1.4. Isentress - raltegravir - EMEA/H/C/000860/II/0073

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Merck Sharp & Dohme Limited

Rapporteur: Greg Markey

Scope: PRAC Recommendation/Opinion

**Action:** For discussion

### 9.1.5. VELCADE - bortezomib - EMEA/H/C/000539/II/0088

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Janssen-Cilag International NV

Rapporteur: Daniela Melchiorri

Scope: "Update of sections 4.2 and 5.1 of the SmPC in order to add a new dosing schedule for VELCADE (bortezomib) in combination with melphalan and prednisone (VMP) for the treatment of patients with newly diagnosed multiple myeloma who are not eligible for high-dose chemotherapy with hematopoietic stem cell transplant. The proposed new dosing schedule is supported by analyses comparing the current approved VcMP schedule (from 26866138MMY3002 [VISTA] study) with pooled modified less intensive ("once-weekly") VcMP schedules (from 54767414MMY3007 [ALCYONE], GIMENA MM-03-05 [GIMENA]). Additional supportive efficacy and safety data come from GEM2005MAS65 [PETHEMA]. The PL (section 3) is amended accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the PL."

**Action:** For adoption

Request for Supplementary Information adopted on 26.07.2018, 22.03.2018.

## 10. Referral procedures

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

No items

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

### 10.2.1. Gentamicin – EMEA/H/A-5(3)/1468

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MAHs: various

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Jorge Camarero Jiménez

Scope: Update on procedure

**Action:** For discussion

Review of histamine levels in Gentamicin-containing solutions for injection/infusion

### 10.2.2. Norethisterone and Ethinylestradiol – EMEA/H/A-5(3)/1470

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MAH various

Rapporteur: Paula Boudewina van Hennik, Co-rapporteur: Kristina Dunder

Scope: List of outstanding Issues/Opinion

**Action:** For adoption

Request from UK for a CHMP opinion on a recently published study using the zebrafish model for studying the developmental effect of norethisterone acetate and ethinylestradiol and any potential clinical implications on the human foetus

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

No items

## 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

### 10.4.1. Paclitaxel Hetero - EMEA/H/A-29(4)/1256

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Hetero Europe S.L.

Rapporteur: Fátima Ventura, Co-Rapporteur: Paula Boudewina van Hennik

Scope: Opinion

**Action:** For adoption

Decentralised Procedure number: PT/H/1256/001/DC, notification by the Portuguese Agency dated 29 March 2018 notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC.

#### 10.4.2. [Perlinring 0.120mg/0.015mg per 24 hours Vaginal Delivery System - Etonogestrel and Ethinylestradiol - EMEA/H/A-29/1473](#)

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MAH: Actavis Group PTC EHF

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Paula B van Hennik

Scope: Opinion

**Action:** For adoption

UK/H/6234/001/DC; Disagreement on the proposed deviations from the recommended posology

#### 10.4.3. [Diotop 75mg/20mg modified-release capsules, hard - Diclofenac/Omeprazole – EMEA/H/A29\(4\)/1474](#)

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MAH: Temmler Pharma GmbH

Rapporteur: TBC, Co-Rapporteur: TBC

Scope: Appointment of rapporteurs, Draft timetable

**Action:** For adoption

MRP Procedure number: UK/H/6135/001/E/001, notification by the Medicines and Healthcare products Regulatory Agency dated 28 September 2018 notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC.

#### 10.4.4. [Diclofenac Sodium Spray Gel 4% cutaneous spray, solution and associated names– EMEA/H/A-29\(4\)/1467](#)

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MAHs: various

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Harald Enzmann

Scope: Updated timetable was adopted via written procedure on 2 October 2018

**Action:** For information

Submission of responses: 11.10.2018

Re-start of the procedure: 18.10.2018

Rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 31.10.2018

Comments: 05.11.2018

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 08.11.2018

CHMP Opinion: November 2018 CHMP

### 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. Bacterial lysates-containing based medicinal products for respiratory conditions - EMEA/H/A-31/1465

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MAH various

Rapporteur: Daniela Melchiorri, Co-rapporteur: Jan Mueller-Berghaus

Scope: List of outstanding Issues

**Action:** For adoption

Review of the benefit-risk balance following notification by AIFA in Italy on 22 May 2018 of a referral under Article 31 of Directive 2001/83/EC.

### 10.6.2. Omega-3-acid-ethyl esters- containing medicinal products for oral use – EMEA/H/A-31/1464

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MAHs: various

Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise

Scope: List of outstanding Issues/SAG Report from meeting held 10 October 2018

Updated list of experts to the SAG CVS was adopted via written procedure on 8 October 2018.

**Action:** For adoption

Review of the benefit-risk balance following notification by the MPA in Sweden on 15 March 2018 of a referral under Article 31 of Directive 2001/83/EC.

### 10.6.3. Gadolinium-containing contrast agents (GdCA): Gadobenate dimeglumine; gadobutrol; gadodiamide; gadopentetic acid dimeglumine, gadoteric acid (intra articular formulation); gadoteric acid (intravenous and intravascular formulations); gadoteridol; gadoxetic acid disodium (NAP)

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Lead Rapporteur: Patrick Batty

Scope: Annual cumulative reviews on NSF cases submission as a post-authorisation measure resulting from the 2010 Article 20 and Article 31 referral procedures for gadolinium-containing contrast agents

**Action:** For adoption

## 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

October 2018 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

Information related to briefing meetings taking place with applicants cannot be released at the present time as it is deemed to contain commercially confidential information

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. Election of new CHMP vice-chairperson

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Further to the election of Harald Enzmann as new CHMP Chairperson, the election of a new Vice-Chairperson will take place at the October 2018 CHMP meeting.

**Action:** For adoption

#### 14.1.2. EMA-FDA analysis on marketing authorisations

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**Action:** For discussion

## 14.2. Coordination with EMA Scientific Committees

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

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Summary of recommendations and advice of PRAC meeting held on 01-04 October 2018

**Action:** For information

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for October 2018

**Action:** For adoption

List of questions from PRAC to Safety Working Party (SWP) on dolutegravir

**Action:** For adoption

### 14.2.2. Committee for Advanced Therapies (CAT)

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CAT draft minutes of meeting held on 10-12 October 2018

**Action:** For information

### 14.2.3. Committee for Herbal Medicinal Products (HMPC)

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Report from the HMPC meeting held on 24-27 September 2018

**Action:** For information

### 14.2.4. Paediatric Committee (PDCO)

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PIPs reaching D30 at October 2018 PDCO

**Action:** For information

Report from the PDCO meeting held on 18-21 September 2018

**Action:** For information

Joint CHMP-PDCO session

**Action:** For discussion

FINAL reflection paper on the use of extrapolation in the development of medicines for paediatrics

CHMP: Rob Hemmings

**Action:** For adoption

Follow-up from October ORGAM

#### 14.2.5. Committee for Orphan Medicinal Products (COMP)

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Report from the COMP meeting held on 09-11 October 2018

**Action:** For information

#### 14.2.6. Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh)

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Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 15-17 October 2018

**Action:** For information

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

#### 14.3.1. Quality Working Party (QWP)

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Chair: Keith Pugh/Blanka Hirschlerova

Small Volume Q&A (EMA/CHMP/QWP/672418/2018)

Rapporteur Diana van Riet (via TC)

**Action:** For adoption

Enteral feeding tubes Q&A

Rapporteur Abigail Moran (via TC)

**Action:** For adoption

Guideline of quality and equivalence of topical products (EMA/678311/2018)

Presented by Sean Jones

**Action:** For adoption for public consultation

Follow-up from October ORGAM

Quality data requirements to demonstrate suitability of multidose containers for preservative free eye drops (EMA/CHMP/QWP/677572/2018)

Presented by Blanka Hirschlerova

**Action:** For adoption

Follow-up from October ORGAM

Guideline on Active Substance Master File Procedure – corrections to the GL

Presented by Blanka Hirschlerova

**Action:** For adoption

Follow-up from October ORGAM

QWP letter to EDQM (Ph Eur chapter 2.2.46)

Presented by Blanka Hirschlerova

**Action:** For adoption

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

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Chair: Robert Hemmings

Report from the SAWP meeting held on 01-04 October 2018. Table of conclusions

**Action:** For information

Scientific advice letters: Disclosure of information related to scientific advice letters cannot be released at present time as these contain commercially confidential information.

#### 14.3.3. Geriatric Expert Group (GEG)

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Chair: Katarina Vučić

Outcome of geriatric pilot on 10 products

**Action:** For discussion

#### 14.3.4. Safety Working Party (SWP)

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Summary report of EMA workshop on non-animal approaches in support of medicinal product development – challenges and opportunities for use of micro-physiological systems held on 5 October 2017 (EMA/CHMP/SWP/250438/2018)

**Action:** For adoption

Election of SWP Chair

**Action:** For adoption

#### 14.3.5. Name Review Group (NRG)

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Table of Decisions of the NRG meeting held on 26 September 2018.

**Action:** For adoption

#### 14.3.6. Biologics Working Party (BWP)

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Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP October 2018 meeting to CHMP for adoption:

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

**Action:** For adoption

Questions and answers on Bovine Spongiform Encephalopathies (BSE) and vaccines (EMA/CHMP/BWP/192228/2017)

**Action:** For adoption

- Overview of comments received on 'Questions and Answers on Bovine Spongiform Encephalopathies (BSE) and vaccines' (EMA/CHMP/642937/2018)

**Action:** For information

Follow-up from October ORGAM

Questions and answers on the Haemagglutination Inhibition (HI) test for qualification of influenza vaccine (inactivated) seed preparations (EMA/CHMP/642937/2018)

**Action:** For adoption

- Overview of comments received on "Questions and answers on the Haemagglutination Inhibition (HI) test for qualification of influenza vaccine (inactivated) seed preparations" (EMA/CHMP/642937/2018)

**Action:** For information

Follow-up from October ORGAM

Guideline on quality aspects included in the product information for vaccines for human use (EMA/CHMP/642937/2018)

**Action:** For adoption

- Overview of comments received on 'Guideline on quality aspects included in the product information for vaccines for human use' (EMA/CHMP/642937/2018)

**Action:** For information

Follow-up from October ORGAM

Revision of the CHMP position statement on Creutzfeldt-Jakob disease and plasma-derived and urine-derived medicinal products (EMA/CHMP/BWP/303353/2010 Rev 1)

**Action:** For adoption for public consultation

Follow-up from October ORGAM

#### 14.3.7. Vaccines Working Party (VWP)

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Chair: Mair Powell/Svein Rune Andersen

Final joint guideline with IDWP on the clinical evaluation of medicinal products indicated for the prophylaxis or treatment of respiratory syncytial virus (RSV) disease.

**Action:** For adoption

Follow-up from October ORGAM

#### 14.3.8. Cardiovascular Working Party (CVSWP)

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Chair: Kristina Dunder/Alar Irs

Paediatric addendum to CHMP guidelines on the clinical investigations of medicinal products for the prevention and treatment of thromboembolic disease (EMA/CHMP/763438/2017)

**Action:** For adoption for 6-month public consultation

Follow-up from October ORGAM

Concept Paper on the revision of the Guideline on clinical investigation of medicinal products for the treatment of peripheral arterial occlusive disease (CPMP/EWP/714/98 rev.1)  
(EMA/CHMP/78339/2018)

**Action:** For adoption for 6-month public consultation

Follow-up from October ORGAM

#### 14.3.9. Pharmacokinetics Working Party (PKWP)

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Chair: Jan Welink/Henrike Potthast

Guideline on equivalence studies for the demonstration of therapeutic equivalence for locally acting products in the gastrointestinal tract (CPMP/EWP/239/95 Rev. 1)

Rapporteur: Alfredo Garcia-Arieta

**Action:** For adoption

- Overview of comments received on 'Guideline on equivalence studies for the demonstration of therapeutic equivalence for products that are locally applied, locally acting in the gastrointestinal tract (EMA/CPMP/EWP/239/95 Rev.1)

**Action:** For information

Follow-up from October ORGAM

#### 14.3.10. Excipients Drafting Group

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Chair: Dominique Masset

Nomination of new member Fokaline Vroom to replace Diana van Riet–Nales

**Action:** For information

#### 14.3.11. Joint CVMP/CHMP ad-hoc expert group on the application of the 3Rs (replacement, reduction and refinement) in the regulatory testing of medicinal products (J 3RsWG)

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Chair: Ellen-Margrethe Vestergaard, CoChair: Susanne Brendler-Schwaab

Reflection paper providing an overview of the current regulatory testing requirements for medicinal products for human use and opportunities for implementation of the 3Rs (EMA/CHMP/CVMP/3Rs/742466/2015)

**Action:** For adoption

### 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**

No items



## 16. 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/)



15 October 2018  
EMA/652433/2018

## Annex to 15-18 October 2018 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  
October 2018: **For adoption**

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#### **Appointment of Rapporteur / Co-Rapporteur Full Applications**

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Final Outcome of Rapporteurship allocation for  
October 2018: **For adoption**

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#### A.2. 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

#### Annual re-assessment outcomes

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

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**Evoltra - clofarabine -** For discussion  
**EMA/H/C/000613/S/0059**  
Genzyme Europe BV, Rapporteur: Alexandre  
Moreau, PRAC Rapporteur: Ghania Chamouni

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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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**Entyvio - vedolizumab -**  
**EMA/H/C/002782/R/0032**  
Takeda Pharma A/S, Rapporteur: Greg Markey,  
Co-Rapporteur: Daniela Melchiorri, PRAC  
Rapporteur: Adam Przybylkowski  
Request for Supplementary Information adopted  
on 20.09.2018.

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**Pregabalin Pfizer - pregabalin -**  
**EMA/H/C/003880/R/0025**  
Pfizer Europe MA EEIG, Rapporteur: Johann  
Lodewijk Hillege, Co-Rapporteur: Bruno  
Sepodes, PRAC Rapporteur: Liana  
Gross-Martirosyan

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**Thymanax - agomelatine -**  
**EMA/H/C/000916/R/0040**  
Servier (Ireland) Industries Ltd., Duplicate,

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Duplicate of Valdoxan, Rapporteur: Svein Rune Andersen, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Karen Pernille Harg  
Request for Supplementary Information adopted on 20.09.2018.

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**Valdoxan - agomelatine -  
EMA/H/C/000915/R/0042**

Les Laboratoires Servier, Rapporteur: Svein Rune Andersen, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Karen Pernille Harg  
Request for Supplementary Information adopted on 20.09.2018.

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**Vokanamet - canagliflozin / metformin -  
EMA/H/C/002656/R/0039**

Janssen-Cilag International NV, Rapporteur: Martina Weise, Co-Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Menno van der Elst

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

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**Granupas - para-aminosalicylic acid -  
EMA/H/C/002709/R/0026, Orphan**

Eurocept International B.V., Rapporteur: Greg Markey, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Patrick Batty

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**Holoclar - ex vivo expanded autologous human corneal epithelial cells containing stem cells - EMA/H/C/002450/R/0021, Orphan, ATMP**

Chiesi Farmaceutici S.p.A., Rapporteur: Egbert Flory, PRAC Rapporteur: Julie Williams

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**Jardiance - empagliflozin -  
EMA/H/C/002677/R/0040**

Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Eva A. Segovia

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**Mepact - mifamurtide -  
EMA/H/C/000802/R/0047, Orphan**

Takeda France SAS, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst

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**Ulunar Breezhaler - indacaterol / glycopyrronium -  
EMA/H/C/003875/R/0028**

Novartis Europharm Limited, Rapporteur: Mark Ainsworth, Co-Rapporteur: Jayne Crowe, PRAC

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Rapporteur: Anette Kirstine Stark

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**Vimizim - elosulfase alfa -**

**EMA/H/C/002779/R/0024, Orphan**

BioMarin Europe Ltd, Rapporteur: Johann  
Lodewijk Hillege, Co-Rapporteur: Harald  
Enzmann, PRAC Rapporteur: Patrick Batty  
Request for Supplementary Information adopted  
on 20.09.2018.

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

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**Caprelsa - vandetanib -**

**EMA/H/C/002315/R/0032**

Genzyme Europe BV, Rapporteur: Alexandre  
Moreau, PRAC Rapporteur: Ghania Chamouni

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**OCALIVA - obeticholic acid -**

**EMA/H/C/004093/R/0009, Orphan**

Intercept Pharma Ltd, Rapporteur: Jorge  
Camarero Jiménez, PRAC Rapporteur: Menno van  
der Elst  
Request for Supplementary Information adopted  
on 20.09.2018.

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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 01-04 October 2018 PRAC:

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**Signal of dysglycaemia: Direct Acting  
Antivirals**

**Daklinza – DACLATASVIR –**

**EMA/H/C/003768**

Bristol-Myers Squibb Pharma EEIG,  
Rapporteur: Filip Josephson, Co-Rapporteur:  
Robert James Hemmings

**Epclusa – SOFOSBUVIR/VELPATASVIR -**

**EMA/H/C/004210**

Gilead Sciences Ireland UC, Rapporteur: Filip  
Josephson, Co-Rapporteur: Alar Irs

**Harvoni – LEDIPASVIR/SOFOSBUVIR -**

**EMA/H/C/003850**

Gilead Sciences Ireland UC, Rapporteur: Filip  
Josephson, Co-Rapporteur: Joseph Emmerich

**Sovaldi – SOFOSBUVIR -**

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**EMEA/H/C/002798**

Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, Co-Rapporteur: Alar Irs

**Vosevi – SOFOSBUVIR/VELPATASVIR/**

**VOXILAPREVIR - EMEA/H/C/004350**

Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, Co-Rapporteur: Greg Markey

**Zepatier – ELBASVIR/GRAZOPREVIR -  
EMEA/H/C/004126**

Rapporteur: Greg Markey, Co-Rapporteur:  
Johann Lodewijk Hillege

**Exviera – DASABUVIR -  
EMEA/H/C/003837**

AbbVie Deutschland GmbH & Co. KG,  
Rapporteur: Filip Josephson, Co-Rapporteur:  
Johann Lodewijk Hillege

**Maviret – GLECAPREVIR/PIBRENTASVIR -  
EMEA/H/C/004430**

AbbVie Deutschland GmbH & Co. KG,  
Rapporteur: Joseph Emmerich, Co-Rapporteur:  
Filip Josephson

**Viekirax –  
OMBITASVIR/PARITAPREVIR/RITONAVI  
R - EMEA/H/C/003839**

Rapporteur: Filip Josephson, Co-Rapporteur:  
Johann Lodewijk Hillege

PRAC recommendation on a variation: **For  
adoption**

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**Signal of suicidality with hormonal  
contraceptives following a recent  
publication:** Hormonal Contraceptives

**EVRA -  
ETHINYLESTRADIOL/NORELGESTROMIN  
– EMEA/H/C/000410**

Janssen-Cilag International NV, Rapporteur:  
Paula B. van Hennik, Co-Rapporteur:  
Concepcion Prieto Yerro

**ZOELY - NOMEGESTROL  
ACETATE/ESTRADIOL –  
EMEA/H/C/001213**

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Teva B.V., Rapporteur: Joseph Emmerich,  
Co-Rapporteur: Agnes Gyurasics

PRAC recommendation on a variation: **For adoption**

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**Signal of dyslipidaemia**

**AUBAGIO -Teriflunomide –  
EMA/H/C/002514**

sanofi-aventis groupe, Rapporteur: Martina  
Weise, Co-Rapporteur: Johann Lodewijk Hillege

PRAC recommendation on a variation: **For adoption**

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**Signal on evaluation of preliminary data  
from an observational study on birth  
outcomes in human immunodeficiency  
virus (HIV)-infected women**

Dolutegravir; abacavir sulfate, dolutegravir  
sodium, lamivudine; rilpivirine –

**TIVICAY – DOLUTEGRAVIR -  
EMA/H/C/002753**

ViiV Healthcare B.V., Rapporteur: Filip  
Josephson, Co-Rapporteur: Joseph Emmerich

**TRIUMEQ –  
DOLUTEGRAVIR/ABACAVIR/LAMIVUDINE  
- EMA/H/C/002754**

ViiV Healthcare UK Limited, Rapporteur: Filip  
Josephson, Co-Rapporteur: Johann Lodewijk  
Hillege

**JULUCA - DOLUTEGRAVIR/RILPIVIRINE –  
EMA/H/C/004427**

ViiV Healthcare UK Limited, Rapporteur:  
Martina Weise, Co-Rapporteur: Johann  
Lodewijk Hillege

PRAC recommendation on a variation: **For adoption**

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PSUR procedures for which PRAC adopted a  
recommendation for variation of the terms of  
the MA at its October 2018 meeting:

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**EMA/H/C/PSUSA/00002330/201802**

(pemetrexed)

CAPS:

**Alimta** (EMA/H/C/000564) (pemetrexed), Eli

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Lilly Nederland B.V., Rapporteur: Alexandre Moreau  
**Armisarte** (EMA/H/C/004109) (pemetrexed),  
Actavis Group PTC ehf, Rapporteur: Alar Irs  
NAPS:  
**NAPs - EU**  
, PRAC Rapporteur: Ghania Chamouni,  
"05-Feb-2015 - 04-Feb-2018"

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**EMA/H/C/PSUSA/00003127/201802**  
(voriconazole)  
CAPS:  
**Vfend** (EMA/H/C/000387) (voriconazole),  
Pfizer Limited, Rapporteur: Johann Lodewijk Hillege  
NAPS:  
**VORICONAZOL ARISTO - ARISTO PHARMA IBERIA, S.L., ARISTO PHARMA GMBH (ART 57)**  
**VORICONAZOLE ARISTO - ARISTO PHARMA GMBH (ART 57)**  
, PRAC Rapporteur: Liana Gross-Martirosyan,  
"01-Mar-2017 to 28-Feb-2018"

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**EMA/H/C/PSUSA/00010317/201803**  
(naloxegol)  
CAPS:  
**Moventig** (EMA/H/C/002810) (naloxegol),  
Kyowa Kirin Holdings B.V., Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Rhea Fitzgerald, "September 2017 to 15 March 2018"

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**EMA/H/C/PSUSA/00010338/201803**  
(apremilast)  
CAPS:  
**Otezla** (EMA/H/C/003746) (apremilast),  
Celgene Europe BV, Rapporteur: Peter Kiely,  
PRAC Rapporteur: Eva A. Segovia, "21 March 2017 - 20 March 2018"

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**EMA/H/C/PSUSA/00010403/201803**  
(pembrolizumab)  
CAPS:  
**Keytruda** (EMA/H/C/003820)  
(pembrolizumab), Merck Sharp & Dohme B.V.,  
Rapporteur: Daniela Melchiorri, PRAC  
Rapporteur: Menno van der Elst, "04/09/2017 - 03/03/2018"

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#### **B.4. EPARs / WPARs**

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**Alunbrig - brigatinib - EMA/H/C/004248** For information only. Comments can be sent to

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Takeda Pharma A/S, treatment of anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC), New active substance (Article 8(3) of Directive No 2001/83/EC)	the EPL in case necessary.
<b>Apealea - paclitaxel - EMEA/H/C/004154</b> Oasmia Pharmaceutical AB, treatment of ovarian cancer, Known active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
<b>Buvidal - buprenorphine - EMEA/H/C/004651</b> Camurus AB, treatment of opioid dependence within a framework of medical, social and psychological treatment, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
<b>Delstrigo - doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746</b> Merck Sharp & Dohme B.V., treatment of adults infected with HIV-1 without past or present evidence of viral resistance to doravirine, lamivudine, or tenofovir, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
<b>Emgality - galcanezumab - EMEA/H/C/004648</b> Eli Lilly Nederland B.V., prophylaxis of migraine, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
<b>Exondys - eteplirsen - EMEA/H/C/004355, Orphan</b> AVI Biopharma International Ltd, treatment of Duchenne muscular dystrophy, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
<b>Fulphila - pegfilgrastim - EMEA/H/C/004915</b> MYLAN S.A.S, treatment of neutropenia, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
<b>Jivi - damoctocog alfa pegol - EMEA/H/C/004054, Orphan</b> Bayer AG, Treatment and prophylaxis of haemophilia A, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
<b>Luxturna - voretigene neparvovec - EMEA/H/C/004451, Orphan, ATMP</b> Spark Therapeutics Ireland Ltd, treatment of patients with vision loss due to Leber congenital	For information only. Comments can be sent to the EPL in case necessary.

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amaurosis or retinitis pigmentosa inherited  
retinal dystrophy, New active substance (Article  
8(3) of Directive No 2001/83/EC)

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**Pelmeg - pegfilgrastim -  
EMA/H/C/004700**

Cinfa Biotech S.L., treatment of neutropenia,  
Similar biological application (Article 10(4) of  
Directive No 2001/83/EC)

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

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**Pifeltro - doravirine - EMA/H/C/004747**

Merck Sharp & Dohme B.V., treatment of adults  
infected with HIV-1 without past or present  
evidence of viral resistance to treatment of adults  
infected with HIV-1 without past or present  
evidence of viral resistance to doravirine, New  
active substance (Article 8(3) of Directive No  
2001/83/EC)

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

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**POTELIGEO - mogamulizumab -  
EMA/H/C/004232, Orphan**

Kyowa Kirin Holdings B.V., treatment of  
cutaneous T-cell lymphoma, New active  
substance (Article 8(3) of Directive No  
2001/83/EC)

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

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**Vabomere - meropenem / vaborbactam -  
EMA/H/C/004669**

Rempex London Ltd, treatment of urinary tract  
infection (cUTI), including pyelonephritis,  
intra-abdominal infection (cIAI),  
hospital-acquired pneumonia (HAP), including  
ventilator associated pneumonia (VAP) including  
ventilator associated pneumonia (VAP), New  
active substance (Article 8(3) of Directive No  
2001/83/EC)

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

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**Ziextenzo - pegfilgrastim -  
EMA/H/C/004802**

Sandoz GmbH, treatment of neutropenia, Similar  
biological application (Article 10(4) of Directive  
No 2001/83/EC)

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

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## **B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES**

Scopes related to Chemistry, Manufacturing, and Controls cannot be released at the present time as  
these contain commercially confidential information.

### **B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects**

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**Ceprotrin - human protein C -  
EMA/H/C/000334/II/0106/G**

Baxter AG, Rapporteur: Jan Mueller-Berghaus

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**Ceprotin - human protein C -**  
**EMEA/H/C/000334/II/0107/G**

Baxter AG, Rapporteur: Jan Mueller-Berghaus

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**Entecavir Accord - entecavir -**  
**EMEA/H/C/004458/II/0001**

Accord Healthcare Limited, Generic, Generic of  
Baraclude, Rapporteur: Ewa Balkowiec Iskra

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**Fabrazyme - agalsidase beta -**  
**EMEA/H/C/000370/II/0107**

Genzyme Europe BV, Rapporteur: Johann  
Lodewijk Hillege

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**Flixabi - infliximab -**  
**EMEA/H/C/004020/II/0031**

Samsung Bioepis UK Limited, Rapporteur: Jan  
Mueller-Berghaus  
Request for Supplementary Information adopted  
on 27.09.2018.

Request for supplementary information adopted  
with a specific timetable.

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**Fuzeon - enfuvirtide -**  
**EMEA/H/C/000514/II/0051/G**

Roche Registration GmbH, Rapporteur: Kristina  
Dunder  
Opinion adopted on 27.09.2018.  
Request for Supplementary Information adopted  
on 26.07.2018.

Positive Opinion adopted by consensus on  
27.09.2018. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**HBVAXPRO - hepatitis B vaccine (rDNA) -**  
**EMEA/H/C/000373/II/0064**

MSD Vaccins, Rapporteur: Jan Mueller-Berghaus

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**Lemtrada - alemtuzumab -**  
**EMEA/H/C/003718/II/0025/G**

Sanofi Belgium, Duplicate, Duplicate of Lemtrada  
(WD), Rapporteur: Mark Ainsworth  
Request for Supplementary Information adopted  
on 13.09.2018.

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**Levemir - insulin detemir -**  
**EMEA/H/C/000528/II/0089**

Novo Nordisk A/S, Rapporteur: Sinan B. Sarac  
Request for Supplementary Information adopted  
on 27.09.2018.

Request for supplementary information adopted  
with a specific timetable.

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**NovoEight - turoctocog alfa -**  
**EMEA/H/C/002719/II/0026/G**

Novo Nordisk A/S, Rapporteur: Jan  
Mueller-Berghaus  
Request for Supplementary Information adopted

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Request for supplementary information adopted  
with a specific timetable.

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on 27.09.2018, 19.07.2018.

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**Orencia - abatacept -**

**EMA/H/C/000701/II/0120/G**

Bristol-Myers Squibb Pharma EEIG, Rapporteur:  
Outi Mäki-Ikola  
Opinion adopted on 27.09.2018.

Positive Opinion adopted by consensus on  
27.09.2018. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**Orphacol - cholic acid -**

**EMA/H/C/001250/II/0025, Orphan**

Laboratoires CTRS, Rapporteur: Robert James  
Hemmings

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**Respreeza - human alpha1-proteinase**

**inhibitor - EMA/H/C/002739/II/0024**

CSL Behring GmbH, Rapporteur: Kristina Dunder  
Opinion adopted on 04.10.2018.

Positive Opinion adopted by consensus on  
04.10.2018. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**Thyrogen - thyrotropin alfa -**

**EMA/H/C/000220/II/0099/G**

Genzyme Europe BV, Rapporteur: Peter Kiely

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**Vimpat - lacosamide -**

**EMA/H/C/000863/II/0074/G**

UCB Pharma S.A., Rapporteur: Filip Josephson

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**Xofigo - radium-223 -**

**EMA/H/C/002653/II/0034**

Bayer AG, Rapporteur: Harald Enzmann

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**Yargesa - miglustat -**

**EMA/H/C/004016/II/0004**

JensonR+ Limited, Generic, Generic of Zavesca,  
Rapporteur: Milena Stain  
Opinion adopted on 04.10.2018.

Positive Opinion adopted by consensus on  
04.10.2018. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**WS1393/G**

**Hexacima-EMA/H/C/002702/WS1393/00  
80/G**

**Hexaxim-EMA/H/W/002495/WS1393/00  
85/G**

**Hexyon-EMA/H/C/002796/WS1393/008  
4/G**

Sanofi Pasteur Europe, Duplicate, Duplicate of  
Hexacima, Lead Rapporteur: Jan  
Mueller-Berghaus  
Request for Supplementary Information adopted  
on 19.07.2018.

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**WS1404**

**Nuwiq-EMA/H/C/002813/WS1404/0022**

**Vihuma-EMA/H/C/004459/WS1404/000  
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Octapharma AB, Lead Rapporteur: Jan  
Mueller-Berghaus

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Request for Supplementary Information adopted on 13.09.2018, 05.07.2018.

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**WS1438/G**

**Hexacima-EMEA/H/C/002702/WS1438/0083/G**

**Hexaxim-EMEA/H/W/002495/WS1438/0088/G**

**Hexyon-EMEA/H/C/002796/WS1438/0087/G**

Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

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**WS1462**

**Rixathon-EMEA/H/C/003903/WS1462/0014**

**Riximyo-EMEA/H/C/004729/WS1462/0014**

Sandoz GmbH, 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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**Adenuric - febuxostat - EMEA/H/C/000777/II/0051**

Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop, "Update of section 5.1 of the SmPC in order to include the results of the clinical safety study CARES (TMX-67\_301), to compare the cardiovascular outcomes of febuxostat and allopurinol in subjects with gout and cardiovascular comorbidities; this is a Multicenter, Randomized, Active-Control, Phase 3B Study.

In addition, the Marketing authorisation holder (MAH) took the opportunity to provide a consolidated Module 2.7.6 in order to list all the synopsis of individual studies in a unique tabular format."

Request for Supplementary Information adopted on 04.10.2018.

Request for supplementary information adopted with a specific timetable.

**Brineura - cerliponase alfa - EMEA/H/C/004065/II/0007, Orphan**

BioMarin International Limited, Rapporteur: Martina Weise, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update the safety information of Brineura in relation to device-related complications and meningitis, and to include meningitis as a possible adverse reaction, based on data collected from clinical trials and post-marketing experience. The

Request for supplementary information adopted with a specific timetable.

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package leaflet is updated accordingly.”  
Request for Supplementary Information adopted  
on 04.10.2018.

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**Brineura - cerliponase alfa -  
EMA/H/C/004065/II/0011, Orphan**

BioMarin International Limited, Rapporteur:  
Martina Weise, “Update of section 4.4 of the  
SmPC to include a warning in relation to the  
access device use life following a review of the  
global safety database for all device-related  
events. The PL is updated accordingly.”

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**Cayston - aztreonam -  
EMA/H/C/000996/II/0073, Orphan**

Gilead Sciences Ireland UC, Rapporteur: Johann  
Lodewijk Hillege, “Submission of the final report  
from study GX US 205-0128, listed as a category  
3 study in the RMP. This is a prospective,  
observational, 5 year registry study carried out to  
monitor the susceptibility to aztreonam of  
Pseudomonas aeruginosa isolates from patients  
with Cystic Fibrosis in the US. The population  
eligible for the registry included paediatric  
subjects, and the final study population included  
approximately 26% of subjects of less than 18  
years of age.

No changes to the SmPC are proposed based on  
the results from this non-interventional, registry  
study.”

Request for Supplementary Information adopted  
on 19.07.2018.

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**Cetrotide - cetrorelix -  
EMA/H/C/000233/II/0068**

Merck Europe B.V., Rapporteur: Martina Weise,  
“Update of section 4.2 of the SmPC based on  
literature review to add an alternative option for  
the treatment initiation to start once the leading  
follicle(s) reach a size that could lead to  
premature LH (Luteinizing Hormone) surge and  
ovulation.

The Package Leaflet (PL) is updated in  
accordance. Correction in section 3 of the PL to  
regarding the timing of ovulation induction.

In addition, the Marketing authorisation holder  
(MAH) took the opportunity to delete the list of  
local representatives in the Package Leaflet.

Furthermore, the PI is brought in line with the  
latest QRD template version 10.0.”

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**Darzalex - daratumumab -  
EMA/H/C/004077/II/0019, Orphan**

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Janssen-Cilag International NV, Rapporteur:  
Sinan B. Sarac, "Update of sections 4.2, 4.8 and 5.2 of the SmPC in order to include the possibility for a split first dose for the treatment of patients with multiple myeloma, based on the Phase 1b open-label, nonrandomized, multicenter Study 54767414MMY1001. The package leaflet is updated accordingly."

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**IBRANCE - palbociclib -  
EMA/H/C/003853/II/0011**

Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC to update the clinical efficacy data from pivotal Phase 3 Study A5481008 (PALOMA-2), a study of IBRANCE in combination with letrozole, to include the results from recent analyses of the study with a data cutoff date of 31 May 2017. In addition, the MAH took the opportunity to update section 4.2 to include that when coadministered with an aromatase inhibitor, the later should be administered according to the dose schedule reported in the Summary of Product Characteristics."

Request for Supplementary Information adopted on 27.09.2018, 26.07.2018, 17.05.2018.

Request for supplementary information adopted with a specific timetable.

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**ISENTRESS - raltegravir -  
EMA/H/C/000860/II/0073**

Merck Sharp & Dohme B.V., Rapporteur: Greg Markey, "Update of sections 4.6 and 5.3 of the SmPC, upon request by PRAC following the assessment of the latest PSUR (PSUSA/00010373/201703), to include revised safety information about pregnancy and risk of malformative or foetal toxicity (LEG). The Package Leaflet has been updated accordingly." Request for Supplementary Information adopted on 26.07.2018, 12.04.2018.

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**Ivemend - fosaprepitant -  
EMA/H/C/000743/II/0040**

Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "Update of sections 4.4 of the SmPC in order to update the safety information related to Infusion Site Reactions (ISR) based on reports of post-marketing experience resulting the cumulative search of the company global safety data base for serious adverse events (interventional, spontaneous, literature and non-interventional study reports) which led to a

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safety labelling change notification issued by the FDA on the 23rd January 2018; the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include edits in the SmPC previously and in the Package Leaflet.”

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**Kuvan - sapropterin -  
EMA/H/C/000943/II/0060, Orphan**

BioMarin International Limited, Rapporteur:  
Peter Kiely, “Update of the section 4.8 of the Summary of Product Characteristics (SmPC) to add oesophagitis as a new adverse drug reaction with a frequency unknown. The Package Leaflet (PL) is updated accordingly and editorial changes are made in section 4 of the PL.”

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**Kuvan - sapropterin -  
EMA/H/C/000943/II/0061, Orphan**

BioMarin International Limited, Rapporteur:  
Peter Kiely, “Update of section 5.2 of the Summary of Product Characteristics (SmPC) for Kuvan in order to update the information related to the interaction with digoxin (P-gp) when administered concomitantly based on pharmacokinetic study in healthy volunteers.”

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**Latuda - lurasidone -  
EMA/H/C/002713/II/0021**

Aziende Chimiche Riunite Angelini Francesco S.p.A., Rapporteur: Filip Josephson, “Update of section 5.1 of the SmPC to add new paediatric data available in children and adolescent patients (10-17 years of age) with bipolar I disorder, upon request by CHMP following the assessment of the paediatric study D1050326 submitted according to Art. 46 procedure (no. EMA/H/C/002713/P46/008).”  
Request for Supplementary Information adopted on 20.09.2018.

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**Lokelma - sodium zirconium cyclosilicate -  
EMA/H/C/004029/II/0003/G**

AstraZeneca AB, Rapporteur: Romaldas Mačiulaitis, “1) type II (C.I.4): Update of sections 4.8 and 5.1 of the SmPC in order to update the information based on final results from study ZS-005 (category 3 PASS study in the RMP). This is an open-label, multicentre, multi-dose, prospective maintenance study to investigate the long-term safety and efficacy of Lokelma (sodium zirconium cyclosilicate) in subjects with hyperkalaemia.

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Request for supplementary information adopted with a specific timetable.

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2) type II (C.I.4): Update of section 4.5 of the SmPC in order to add information regarding the use with drugs that have the potential for drug-drug interaction based on an increase in gastric PH.

The Package Leaflet has been updated accordingly.”

Request for Supplementary Information adopted on 04.10.2018, 28.06.2018.

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**Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) -**

**EMA/H/W/002300/II/0035**

GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus, “Submission of the final report from study MALARIA-071. This is a phase IIA, open-label, controlled, single-centre, single-country study, to evaluate efficacy, safety, reactogenicity and immunogenicity of GSK Biologicals’ candidate malaria vaccine in healthy malaria-naïve adults.”

Opinion adopted on 04.10.2018.

Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine -**

**EMA/H/C/002226/II/0083**

Pfizer Europe MA EEIG, Rapporteur: Greg Markey, “Update of section 4.4 of the SmPC in order to include a safety warning of the risk for invasive disease caused by Meningococcal polysaccharide serogroups A, C, W-135 and Y because of the use of Nimenrix with concomitant treatment of eculizumab.”

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**Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine -**

**EMA/H/C/002226/II/0084**

Pfizer Europe MA EEIG, Rapporteur: Greg Markey, “Update of section 4.2 of the SmPC in order to update the posology information in infants, following the final results from study MenACWY-TT-087 (Study 087); this is a phase IIIb, controlled, randomised, open study aimed to demonstrate the immunogenicity and safety of Nimenrix in healthy infants, given on a 3+1 primary and booster (2, 4, 6 and 15-18 months of age), a 1+1 primary and booster (6 and 15-18 months of age) or as a single dose at 15-18 months of age. The Package Leaflet is updated accordingly.

The MAH took the opportunity to include editorial

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changes in sections 4.4 and 4.8 of the SmPC.”

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**Ozempic - semaglutide -**

**EMA/H/C/004174/II/0001**

Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, “Update of section 5.1 of the SmPC in order to reflect final results from the SUSTAIN 7 trial (NN9535-4216), a 40-week open-label trial comparing the safety and efficacy of 0.5 mg of Ozempic to 0.75 mg of dulaglutide and 1 mg of Ozempic to 1.5 mg of dulaglutide in patients on metformin with type-2 diabetes.”

Request for Supplementary Information adopted on 13.09.2018, 26.07.2018, 25.05.2018.

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**RAVICTI - glycerol phenylbutyrate -**

**EMA/H/C/003822/II/0023, Orphan**

Horizon Pharma Ireland Limited, Rapporteur: Greg Markey, “Update of section 5.1 of the Summary of Product Characteristics (SmPC) in order to update the efficacy and safety information based on study HPN-100-011, a non randomised, open-label safety extension study on the long term use of HPN-100 in Urea Cycle Disorders. In addition, QRD changes are made in Annex IIIA related to the addition of section 17 and 18 and in line with the QRD template version 10.0”

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**Revolade - eltrombopag / eltrombopag  
olamine - EMA/H/C/001110/II/0046**

Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, “Update of the PI to align with the company's Core Safety Data Sheet:

- Update of information related to liver function tests, thrombotic and thromboembolic complications, MDS in the section 4.4;
- Update of DDI and food interaction information in the sections 4.5 and 5.2;
- Update of the section 4.8 by: inclusion and removal of ADRs, changes in some ADRs frequencies following pooling of safety data;
- Reorganisation of the section 5.1 in relation to severe aplastic anaemia;
- Update of the section 5.3 with information related to Juvenile animal studies.

The MAH took the opportunity to make some editorial changes throughout the PI. The Package leaflet is updated accordingly.”

Request for Supplementary Information adopted on 03.05.2018.

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**Rubraca - rucaparib -****EMA/H/C/004272/II/0002, Orphan**

Clovis Oncology UK Limited, Rapporteur: Jorge Camarero Jiménez, "Submission of the final study report (QS-CLV-010) on the exploratory population pharmacokinetic analysis of rucaparib undertaken to test additional semi-mechanistic absorption and distribution models."

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**Stelara - ustekinumab -****EMA/H/C/000958/II/0066**

Janssen-Cilag International NV, Rapporteur: Greg Markey, "Update of section 4.8 of the SmPC to add allergic alveolitis and eosinophilic pneumonia as rare adverse reaction. The PL is updated accordingly."

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**Stribild - elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil -****EMA/H/C/002574/II/0097**

Gilead Sciences Ireland UC, Rapporteur: Robert James Hemmings, "Submission of the final report from study GS-US-236-0112, a phase 2/3, open-label study of the pharmacokinetics, safety and antiviral activity of the elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate single tablet regimen (STR) in HIV-1 infected antiretroviral treatment-naïve adolescents. This submission fulfils the post-authorisation measures MEA 019 and P46 020."

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**Sutent - sunitinib -****EMA/H/C/000687/II/0070**

Pfizer Limited, Rapporteur: Daniela Melchiorri, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to include paediatric study results (from studies A6181196 and ACNS1021) performed in compliance with a paediatric investigation plan (PIP)."

Request for Supplementary Information adopted on 27.09.2018.

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Request for supplementary information adopted with a specific timetable.

**TECFIDERA - dimethyl fumarate -****EMA/H/C/002601/II/0054/G**

Biogen Idec Ltd, Rapporteur: Martina Weise, "Type II grouped variation (3xC.I.13) for the submission of results of the below listed studies in order to fulfil LEG 004:

1. RSCH-2018-30: In vitro transcriptional profiling feasibility pilot study to determine the mechanism of action for lymphopenia in dimethyl
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fumarate-treated patients.

2. DMF-109MS301: Ex vivo transcriptional profiling study to assess the transcriptional changes induced by DMF in whole blood in 109MS301 and 109MS302 cohorts.

3. NLD-BGT-15-10945 (kinetic study): Characterisation of the immune-modulatory effects of Tecfidera in multiple sclerosis patients: exploration of drug mechanism and methodological feasibility.”

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**VELCADE - bortezomib -**

See 9.1

**EMA/H/C/000539/II/0088**

Janssen-Cilag International NV, Rapporteur: Daniela Melchiorri, “Update of sections 4.2 and 5.1 of the SmPC in order to add a new dosing schedule for VELCADE (bortezomib) in combination with melphalan and prednisone (VMP) for the treatment of patients with newly diagnosed multiple myeloma who are not eligible for high-dose chemotherapy with hematopoietic stem cell transplant.

The proposed new dosing schedule is supported by analyses comparing the current approved VcMP schedule (from 26866138MMY3002 [VISTA] study) with pooled modified less intensive (“once-weekly”) VcMP schedules (from 54767414MMY3007 [ALCYONE], GIMENA MM-03-05 [GIMENA]). Additional supportive efficacy and safety data come from GEM2005MAS65 [PETHEMA].

The PL (section 3) is amended accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the PL.”

Request for Supplementary Information adopted on 26.07.2018, 22.03.2018.

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**Viekirax - ombitasvir / paritaprevir / ritonavir - EMA/H/C/003839/II/0048**

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, “Submission of the final report from study M13-101 listed as a category 3 study in the RMP. This is an open-label study to examine the safety, antiviral activity and pharmacokinetics of 12 weeks of paritaprevir/ritonavir/ombitasvir in combination with Peginterferon  $\alpha$ -2a and Ribavirin (PegIFN/RBV) in Chronic Hepatitis C Virus (HCV) infected patients who had experienced virologic failure while participating in a previous MAH

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combination study.”

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**Xadago - safinamide -**

**EMA/H/C/002396/II/0027**

Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.4 and 4.5 of the SmPC in order to implement information regarding interaction of safinamide and rosuvastatin, following results from study CRO-PK-17-318. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Ireland in the Package Leaflet and to include editorial changes in the English, German and Spanish product information.”

Request for Supplementary Information adopted on 13.09.2018.

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**WS1371**

**Rasilez-EMA/H/C/000780/WS1371/0119**

**Rasilez**

**HCT-EMA/H/C/000964/WS1371/0086**

Noden Pharma DAC, Lead Rapporteur: Daniela Melchiorri, “Update of section 4.8 and 5.1 of the Rasilez SmPC and section 4.8 of the Rasilez/HCTZ SmPC in order to reflect the results from paediatric study CSPP100A2365E2 (a multicenter, 52 to 104 week extension study to evaluate the long term growth and development of pediatric hypertensive patients 6–17 years of age treated previously with aliskiren) provided as per the requirement of article 46.”

Request for Supplementary Information adopted on 20.09.2018, 31.05.2018.

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**WS1392**

**ProQuad-EMA/H/C/000622/WS1392/012**

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MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus, “Update of section 4.8 of the SmPC in order to add the adverse reaction (ADR) meningitis with a frequency “not known” and to add a clarifying foot note for immunocompromised or immunocompetent individuals applicable to the ADR meningitis, herpes zoster and encephalitis. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to make some editorial changes in the product information and to update the list of local representatives in the package leaflet.”

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Request for Supplementary Information adopted on 13.09.2018, 05.07.2018.

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**WS1401**

**Genvoya-EMEA/H/C/004042/WS1401/0047**

**Stribild-EMEA/H/C/002574/WS1401/0094**

**Tybost-EMEA/H/C/002572/WS1401/0044**

Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings, "Update of section 4.6 the SmPC for Tybost, Stribild and Genvoya based on pharmacokinetics data in pregnancy from IMPAACT study P1026s (ClinicalTrials.gov ID NCT00042289); this is an ongoing, nonrandomized, open-label, parallel-group, multi-centre phase 4 prospective study of antiretroviral (ARV) pharmacokinetics (PK) and safety in HIV-1 infected pregnant women that includes an arm for EVG/COBI. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 12.07.2018.

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**WS1454**

**Zypadhera-EMEA/H/C/000890/WS1454/0035**

**Zyprexa-EMEA/H/C/000115/WS1454/0127**

**Zyprexa**

**Velotab-EMEA/H/C/000287/WS1454/0095**

Eli Lilly Nederland B.V., Duplicate, Duplicate of Olansek (SRD), Lead Rapporteur: Outi Mäki-Ikola, "Update section 4.8 of the SmPC to add stuttering as adverse drug reaction based on data from clinical trials and spontaneous reporting. PL is updated accordingly. In addition, the MAH took this opportunity to revised wording of section 5.2 for smokers to improve clarity."

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**WS1472**

**Exviera-EMEA/H/C/003837/WS1472/0040**

**Viekirax-EMEA/H/C/003839/WS1472/0049**

AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Filip Josephson, "Submission of the final report from study M12-999 listed as a category 3 study in the RMP. This is an open-label, phase 2 study to evaluate the safety

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and efficacy of the combination of ombitasvir/paritaprevir/ritonavir with or without dasabuvir and with or without ribavirin (RBV) in adult liver or renal transplant recipients with Hepatitis C Virus (HCV) GT1 or GT4 infection (CORAL I).”

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**WS1473**

**Exviera-EMEA/H/C/003837/WS1473/0041**

**Viekirax-EMEA/H/C/003839/WS1473/0050**

AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Filip Josephson, “Submission of the final report from study M14-004 listed as a category 3 study in the RMP. This is a multipart, open-label study to evaluate the safety and efficacy of ombitasvir/paritaprevir/ritonavir with or without dasabuvir coadministered with and without ribavirin in adults with Genotype 1 or 4 Chronic Hepatitis C Virus infection and Human Immunodeficiency Virus, Type 1 co-infection (TURQUOISE-I).”

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**WS1474/G**

**Prezista-EMEA/H/C/000707/WS1474/0098/G**

**8/G**

**Rezolsta-EMEA/H/C/002819/WS1474/0027/G**

**7/G**

**Symtuza-EMEA/H/C/004391/WS1474/0011/G**

**1/G**

Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege, “C.I.4 Update sections 4.3 and 4.5 of the SmPC of Prezista, Rezolsta and Symtuza to implement a new contraindication for the concomitant use with dabigatran and to add information regarding potential interaction with the edoxaban and dabigatran. The Package Leaflets are updated accordingly.

C.I.4 Update section 4.5 of of the SmPC of Prezista, Rezolsta and Symtuza to add information regarding potential interaction with Hepatitis C virus direct-acting antivirals: glecaprevir/pibrentasvir (concomitant administration not recommended). The Package Leaflets are updated accordingly.”

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

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**Avastin - bevacizumab -**

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**EMEA/H/C/000582/II/0106/G**

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "1) Type II Variation (C.I.4): Update of section 5.1 of the SmPC to reflect final overall survival data from the long-term follow-up study JO25567 in order to fulfil ANX 085 for study JO29424.

2) Type IB Variation (C.I.11.z): Change in the deadline for the fulfilment of ANX 086 from Q4 2018 to Q2 2019.

Annex II.D and the RMP (ver 29.0) have been updated accordingly. The RMP is submitted according to template Rev 2 and consolidates the approved versions (27.1 & 28.1)."

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**Caprelsa - vandetanib -****EMEA/H/C/002315/II/0028**

Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of sections 4.1, 4.4 and 5.1 of the SmPC in order to delete the information regarding Rearranged during Transfection (RET) mutation. The application addresses SOB 001 and the MAH proposes to revert from conditional marketing authorisation to standard marketing authorisation. Annex II and Package Leaflet are updated accordingly. The RMP version 12.2 has also been submitted.

In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10."

Request for Supplementary Information adopted on 26.04.2018, 14.12.2017.

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**Dacogen - decitabine -****EMEA/H/C/002221/II/0033, Orphan**

Janssen-Cilag International N.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of section sections 4.2, 4.8, 5.1 and 5.2 of the SmPC to reflect the results from paediatric study DACOGENAML2004 titled 'Phase 1-2 Safety and Efficacy Study of DACOGEN in sequential administration with Cytarabine in children with relapsed or refractory acute myeloid leukemia', provided as per the requirement of article 46. The RMP version 3.1 (in line with the revision 2 of the RMP template) has also been submitted.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.4 of the SmPC to align the safety warning related to sodium excipient with the Annex to the revised

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European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. The Package Leaflet is updated in accordance. Moreover, the contact details of the local representative in Slovenia have been updated in the Package Leaflet." Request for Supplementary Information adopted on 26.07.2018, 31.05.2018.

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**ELOCTA - efmoroctocog alfa -  
EMEA/H/C/003964/II/0026**

Swedish Orphan Biovitrum AB (publ),  
Rapporteur: Jan Mueller-Berghaus, PRAC  
Rapporteur: Julie Williams, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to add a statement for a once-weekly prophylaxis dose and to update the safety information based on the final results from study 8HA01EXT listed as a category 3 study in the RMP; this is a interventional study that evaluated the long-term safety (particularly immunogenicity) and efficacy of ELOCTA in the prevention and treatment of bleeding episodes and for perioperative management. This variation is a follow-up of P46/005 submitted on 16.04.18 RMP version 2.1 was submitted and followed revision 2 of the template."

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**Entyvio - vedolizumab -  
EMEA/H/C/002782/II/0034**

Takeda Pharma A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Adam Przybylkowski, "Update of section 5.1 of the SmPC in order to provide the final efficacy results up to week 348 regarding clinical study c13008, listed as a category 3 study in the RMP. This is a Phase 3, Open-label Study to Determine the Long-term Safety and Efficacy of Vedolizumab in subjects with Ulcerative Colitis and Crohn's Disease. The RMP version 4 has also been submitted." Request for Supplementary Information adopted on 04.10.2018.

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Request for supplementary information adopted with a specific timetable.

**Erbix - cetuximab -  
EMEA/H/C/000558/II/0082**

Merck KGaA, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "C.I.4) To update sections 4.4 and 4.8. of the SmPC regarding the existing warning on Interstitial lung disease (ILD), by specifying potentially fatal ILD outcome, patients with contributory factors at

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risk of fatal events and need for close monitoring of these patients.

RMP version 19.0 has been submitted in relation to the above changes and also to include changes recommended in latest PSUSA.

MAH also took the opportunity to update Annex II-D to delete an obsolete sentence which refers to an RMP to be submitted in 2014.”

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**IMVANEX - modified vaccinia ankara virus - EMEA/H/C/002596/II/0035**

Request for supplementary information adopted with a specific timetable.

Bavarian Nordic A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, “Update of sections 4.4., 4.8 and 5.1 of the SmPC in order to update the safety information and to add urticaria as an adverse reaction following the final results from study POX-MVA-037 (phase II, randomized, open-label, multicenter trial designed to evaluate the safety and immunogenicity of IMVANEX (MVA-BN smallpox vaccine) when increasing the dose or the number of injections compared with the standard 2-dose regimen in a population of adult, vaccinia naive, immunocompromised subjects with human immunodeficiency virus (HIV) infection) listed as a category 3 study in the RMP (described as post authorisation MEA 007); The RMP version 7.1 has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.”

Request for Supplementary Information adopted on 04.10.2018.

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**IMVANEX - modified vaccinia ankara virus - EMEA/H/C/002596/II/0036**

Request for supplementary information adopted with a specific timetable.

Bavarian Nordic A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, “Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update the safety information and to provide confirmation in terms of immunogenicity based on the results from study (POX-MVA-006) (a randomized, open-label phase III non-inferiority trial to compare indicators of efficacy for smallpox vaccine to the US licensed replicating smallpox vaccine in 18-42 year old healthy vaccinia-naïve subjects) listed as an obligation in the Annex II (ANX 004); the Package Leaflet is updated accordingly. The RMP version 7.2 has also been submitted.”

Request for Supplementary Information adopted on 04.10.2018.

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**Keytruda - pembrolizumab -**

Positive Opinion adopted by consensus on

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**EMA/H/C/003820/II/0058**

Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Menno van der Elst, "Update of section 4.4 of the SmPC, to include in the existing warning regarding immune-related adverse reactions the fact that these reactions may be fatal in patients treated with pembrolizumab, as well as minor consequential amendments to increase consistency. The Package Leaflet is being updated accordingly, and for consistency with the already existing statement in the SmPC section 4.4, the Package Leaflet is also being updated to include the fact that immune-related adverse reactions can occur after discontinuation of pembrolizumab treatment. An updated RMP version 20.0 was agreed during the procedure."  
Opinion adopted on 04.10.2018.

04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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**Mircera - methoxy polyethylene glycol-epoetin beta -****EMA/H/C/000739/II/0068**

Roche Registration GmbH, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "Submission of the final report from study BH21260 listed as a category 3 study in the RMP (MEA008.5). This is a randomized, controlled, open-label, multicenter, parallel-group study to assess all-cause mortality and cardiovascular morbidity in patients with chronic kidney disease on dialysis and those not on renal replacement therapy under treatment with Mircera® or reference ESAs. The RMP (version 12.0) is updated accordingly and transitioned to the new EU RMP template in line with the revised Good Pharmacovigilance Practice (GVP) Module V (Revision 2) guideline."  
Request for Supplementary Information adopted on 04.10.2018.

Request for supplementary information adopted with a specific timetable.

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**Oncaspar - pegaspargase -****EMA/H/C/003789/II/0016/G**

Baxalta Innovations GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Patrick Batty, "Update of sections 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC based on the final results from studies DFCI 11-001 and AALL07P4 listed as category 3 studies in the Risk Management Plan: Study DFCI 11-001 is a Phase 2, open-label, randomized, multicenter study to determine the safety and feasibility of administering an

Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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investigational asparaginase product (asparaginase formulation) compared with Oncaspar in subjects aged 1 to <22 years with newly diagnosed Acute Lymphoblastic Leukaemia (ALL) and lymphoblastic lymphoma.

Study AALL07P4 is a multicenter, open label, randomized, active-controlled, parallel design clinical pilot study conducted to evaluate the pharmacokinetics, pharmacodynamics, safety, immunogenicity and efficacy of an investigational asparaginase product in comparison with Oncaspar in patients aged 1 to <31 years newly diagnosed with high risk B-precursor ALL.

The Package Leaflet has been updated accordingly.

The RMP version 3.0 has also been submitted."

Opinion adopted on 04.10.2018.

Request for Supplementary Information adopted on 06.09.2018, 17.05.2018.

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**Onivyde - irinotecan hydrochloride trihydrate - EMEA/H/C/004125/II/0008, Orphan**

Baxalta Innovations GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: David Olsen, "Update of sections 1, 2, 4.2, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC in order to reflect the expression of strength based on irinotecan anhydrous free-base. The Labelling and Package Leaflet are updated accordingly. In addition the MAH took the opportunity to introduce minor editorial changes. The updated RMP version 2.1 has also been submitted."

Request for Supplementary Information adopted on 20.09.2018.

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**Plegridy - peginterferon beta-1a - EMEA/H/C/002827/II/0046**

Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Julie Williams, "Update of sections 4.4 and 4.8 of the SmPC in order to add new warning and safety information about anaphylaxis. RMP version 3.3 was also approved."

Opinion adopted on 04.10.2018.

Request for Supplementary Information adopted on 06.09.2018.

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Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Remicade - infliximab - EMEA/H/C/000240/II/0214**

Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga,

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“Update of the RMP (v 17.0) and Annex II-D of the Product Information to remove the Educational material for health care professionals. In addition, the MAH is taking the opportunity to update the package leaflet with some missing warnings and ADRs already reflected in the SmPC, as requested by CHMP, and to introduce some minor QRD related changes.”

Request for Supplementary Information adopted on 20.09.2018, 26.07.2018.

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**Reyataz - atazanavir / atazanavir sulfate - EMEA/H/C/000494/II/0117**

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Adrien Inoubli, “Submission of the final reports from studies AI424397 (PRINCE I) and AI424451 (PRINCE II) listed as a category 3 studies in the RMP. These studies were phase IIIb, prospective, single arm, open-label, international, multicentre studies to evaluate the safety, efficacy and pharmacokinetics of atazanavir powder boosted with ritonavir and administered with an optimised NRTI background therapy, in HIV infected paediatric patients.

The RMP version 15.0 has also been submitted to reflect on the final data from these two paediatric studies. In addition, the MAH took the opportunity to introduce the new RMP template Rev. 2.”

Request for Supplementary Information adopted on 04.10.2018.

Request for supplementary information adopted with a specific timetable.

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**Sivextro - tedizolid phosphate - EMEA/H/C/002846/II/0027**

Merck Sharp & Dohme B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maria del Pilar Rayon, “Submission of the final results from Bayer study 16099, a prospective, randomised, open-label, active-controlled, multicentre study to evaluate the efficacy and safety of tedizolid in Japanese patients with MRSA infections (skin and soft tissue infection [SSTI] and SSTI-related bacteraemia) listed as a Post-Authorisation Efficacy Study (PAES) in the RMP. The MAH obligations with regard to this PAES are considered fulfilled. The updated RMP version 5.0, implementing Revision 2 of the RMP template, is adopted.”

Opinion adopted on 04.10.2018.

Request for Supplementary Information adopted

Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.



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on 14.06.2018.

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**Vimpat - lacosamide -**

**EMA/H/C/000863/II/0073/G**

UCB Pharma S.A., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.4, 4.5 and 4.8 of the SmPC in order to include new safety information on cardiac arrhythmias based on safety signal assessment report (SSAR). Update of section 4.8 of the SmPC to update the frequency of some adverse events (AEs) based on data obtained from the updated safety pool analysis (Pool DBC-1). The Package Leaflet is updated accordingly. The RMP version 13 has also been submitted."

Request for Supplementary Information adopted on 04.10.2018.

Request for supplementary information adopted with a specific timetable.

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**Xolair - omalizumab -**

**EMA/H/C/000606/II/0092**

Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of sections 4.2, 4.4, 4.6 and 6.6 of the Xolair solution for injection in pre-filled syringe SmPC to allow for home use in severe allergic asthma and chronic spontaneous urticaria. Consequential updates are applied to the SmPC for powder and solvent for solution for injection. Artwork for the outer box, the blister and the syringe label for Xolair solution for injection in pre-filled syringe have been updated to ensure that patients/lay caregiver can more easily distinguish the 2 strengths of Xolair PFS. The Package Leaflet and Labelling are updated accordingly. The RMP version 13 has also been submitted."

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**B.5.4. PRAC assessed procedures**

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PRAC Led

**Aclasta - zoledronic acid -**

**EMA/H/C/000595/II/0069**

Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final 5-year report from study (ZOL446H2422) listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study using health registries to compare safety of Aclasta against

Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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oral bisphosphonates and untreated population controls.”  
Opinion adopted on 04.10.2018.  
Request for Supplementary Information adopted on 11.01.2018, 06.07.2017.

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PRAC Led  
**Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0148**  
Amgen Europe B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, “Update of annex IID to implement information on education material proposal to address the incorrect self-administration of Aranesp via the SureClick pre-filled pen and associated dosing errors. The RMP (version 9.1) is updated accordingly and aligned to the latest revision 2.”  
Request for Supplementary Information adopted on 04.10.2018.

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Request for supplementary information adopted with a specific timetable.

PRAC Led  
**Betmiga - mirabegron - EMEA/H/C/002388/II/0030**  
Astellas Pharma Europe B.V., Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Concepcion Prieto Yerro, “Submission of the final report of the Drug Utilization Study of mirabegron using real-word healthcare databases from the NL, UK and FI (study 178-PV-002), as agreed via MEA 009.2.”  
Request for Supplementary Information adopted on 04.10.2018.

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Request for supplementary information adopted with a specific timetable.

PRAC Led  
**Bosulif - bosutinib - EMEA/H/C/002373/II/0030**  
Pfizer Europe MA EEIG, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, “Submission of an updated RMP version 4.3 in line with changes requested by the CHMP following variation II/25/G in fulfilment of PAM (REC 014). In addition, the MAH took the opportunity to extend due date of SOB (Specific Obligation). Annex II has been updated accordingly.”  
Request for Supplementary Information adopted on 26.07.2018.

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Request for supplementary information adopted with a specific timetable.

PRAC Led  
**Evicel - human fibrinogen / human**

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**thrombin - EMEA/H/C/000898/II/0063**

Omrix Biopharmaceuticals N. V., PRAC  
Rapporteur: Brigitte Keller-Stanislawski,  
PRAC-CHMP liaison: Jan Mueller-Berghaus,  
"C.I.11: Submission of an updated RMP version  
14.2 in order to transition to RMP version 2,  
updated exposure data, updates following PRAC  
request in accordance to PSUSA/00010297  
(removal of lack of efficacy as identified risk),  
reclassification and/or removal of risk from the  
safety specification."

Request for Supplementary Information adopted  
on 04.10.2018.

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PRAC Led

**Farydak - panobinostat -  
EMEA/H/C/003725/II/0013, Orphan**

Novartis Europharm Limited, Rapporteur: Paula  
Boudewina van Hennik, PRAC Rapporteur:  
Patrick Batty, PRAC-CHMP liaison: Greg Markey,  
"Submission of an updated RMP version 5.0 in  
order to remove the commitment to conduct a  
non-interventional PASS study (LBH589D2408)  
of panobinostat use in relapsed or  
relapsed/refractory multiple myeloma patients  
who have received at least two prior regimens  
including bortezomib and an immunomodulatory  
agent in a real-world setting according to the  
current EU prescribing information and document  
adherence to dosing regimen (including the  
dosing card, blister pack) by describing clinical  
characteristics, frequency and severity of the  
medication error events; listed as a category 3  
study in the RMP."

Request for Supplementary Information adopted  
on 04.10.2018.

Request for supplementary information adopted  
with a specific timetable.

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PRAC Led

**ReFacto AF - moroctocog alfa -  
EMEA/H/C/000232/II/0147**

Pfizer Europe MA EEIG, Rapporteur: Mark  
Ainsworth, PRAC Rapporteur: Doris Stenver,  
PRAC-CHMP liaison: Sinan B. Sarac, "Submission  
of the final report from study B1831007  
(previously referred to as Study  
3082B2-4435-WW) listed as a category 3 study  
in the RMP. This is a post authorization safety  
surveillance registry in previously untreated  
patients with severe hemophilia A in usual care  
settings, in order to fulfil the post-approval  
commitment MEA 115."

Positive Opinion adopted by consensus on  
04.10.2018. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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Opinion adopted on 04.10.2018.

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PRAC Led

**Repatha - evolocumab -  
EMA/H/C/003766/II/0028**

Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Tuomo Lapveteläinen, "Submission of an updated RMP version 5.0 in order to provide the final results of study 20120332 (GAUSS-3, part C), listed as a category 3 study in the RMP. This is a 3-part, phase 3, multicenter, randomized, double-blind, ezetimibe-controlled, parallel-group study. Part C was a 2-year, open-label extension that evaluated the long-term safety and efficacy of evolocumab in hypercholesterolemic subjects unable to tolerate an effective dose of a statin. The MAH has consequentially proposed to remove missing information of use in patients with severe hepatic impairment (Child-Pugh class C) and use in patients with hepatitis C." Request for Supplementary Information adopted on 04.10.2018.

Request for supplementary information adopted with a specific timetable.

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PRAC Led

**Thalidomide Celgene - thalidomide -  
EMA/H/C/000823/II/0056, Orphan**

Celgene Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Update of the RMP version 19 in line with the updated Guideline on Good Pharmacovigilance Practices (GVP) Module V to propose the reclassification and/or renaming of known safety concerns associated with the use of thalidomide. Consequently, Annex IID, SmPC section 4.4 and 4.6 and PL have been updated accordingly." Request for Supplementary Information adopted on 04.10.2018.

Request for supplementary information adopted with a specific timetable.

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PRAC Led

**Votrient - pazopanib -  
EMA/H/C/001141/II/0049**

Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final report from the non-interventional post-authorisation safety study PZP034AKR02 to monitor the safety and effectiveness of Votrient in Korea. This study is listed as a category 3 study in the RMP."

Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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Opinion adopted on 04.10.2018.

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PRAC Led

**Votrient - pazopanib -  
EMA/H/C/001141/II/0050**

Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final report from the observational study PZP034A2401 'A prospective observational study of real world treatment patterns and treatment outcomes in patients with advanced or metastatic renal cell carcinoma receiving pazopanib. This study is listed as a category 3 study in the RMP.'" Opinion adopted on 04.10.2018.

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Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Led

**WS1364**

**Lyrica-EMA/H/C/000546/WS1364/0092  
Pregabalin**

**Pfizer-EMA/H/C/003880/WS1364/0021**

Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 12.0 in order to include the changes proposed by

EMA/H/C/PSUSA/00002511/201701, updating the safety specifications and risk minimisation measures. The pharmacovigilance plan has also been updated. The draft protocol for non-interventional non-imposed PASS (A0081359) titled "A population-based cohort study of Pregabalin to characterize pregnancy outcomes" has been submitted.

The MAH has taken the opportunity to include minor updates and to align the RMP to template revision 2."

Request for Supplementary Information adopted on 04.10.2018, 17.05.2018.

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Request for supplementary information adopted with a specific timetable.

PRAC Led

**WS1441**

**Descovy-EMA/H/C/004094/WS1441/003  
4**

**Genvoya-EMA/H/C/004042/WS1441/005  
1**

**Odefsey-EMA/H/C/004156/WS1441/003  
5**

**Vemlidy-EMA/H/C/004169/WS1441/001  
6**

Gilead Sciences Ireland UC, Lead Rapporteur:

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Positive Opinion adopted by consensus on 04.10.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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Robert James Hemmings, Lead PRAC  
Rapporteur: Amelia Cupelli, PRAC-CHMP liaison:  
Daniela Melchiorri, "Submission of an updated  
RMP version 3.1 for Vemlidy, Descovy and  
Odefsey, as well as version 3.3 for Genvoya  
according to GVP Module V (revision 2) in order to  
revise the safety concerns in alignment with the  
approved RMP for Biktarvy. In addition, the MAH  
took the opportunity to update category 3 studies  
and the address of the MAH."  
Opinion adopted on 04.10.2018.

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

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

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

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

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##### **WS1387**

##### **Infanrix**

##### **hexa-EMEA/H/C/000296/WS1387/0242**

GlaxoSmithkline Biologicals SA, Lead  
Rapporteur: Bart Van der Schueren  
Request for Supplementary Information adopted  
on 19.07.2018.

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##### **WS1394**

##### **Hexacima-EMEA/H/C/002702/WS1394/0082**

##### **Hexaxim-EMEA/H/W/002495/WS1394/0087**

##### **Hexyon-EMEA/H/C/002796/WS1394/0086**

Sanofi Pasteur Europe, Duplicate, Duplicate of  
Hexacima, Lead Rapporteur: Jan  
Mueller-Berghaus  
Opinion adopted on 27.09.2018.

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Positive Opinion adopted by consensus on  
27.09.2018. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

##### **WS1421**

##### **Infanrix**

##### **hexa-EMEA/H/C/000296/WS1421/0244**

GlaxoSmithkline Biologicals SA, Lead  
Rapporteur: Bart Van der Schueren  
Opinion adopted on 04.10.2018.

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Positive Opinion adopted by consensus on  
04.10.2018. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

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**WS1430**  
**Descovy-EMEA/H/C/004094/WS1430/003**  
**3**  
**Genvoya-EMEA/H/C/004042/WS1430/004**  
**9**  
**Odefsey-EMEA/H/C/004156/WS1430/003**  
**4**  
**Vemlidy-EMEA/H/C/004169/WS1430/001**  
**4**  
Gilead Sciences Ireland UC, Lead Rapporteur:  
Robert James Hemmings  
Opinion adopted on 04.10.2018.

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**WS1435/G**  
**Infanrix**  
**hexa-EMEA/H/C/000296/WS1435/0245/**  
**G**  
GlaxoSmithkline Biologicals SA, Lead  
Rapporteur: Bart Van der Schueren

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**WS1442**  
**Infanrix**  
**hexa-EMEA/H/C/000296/WS1442/0246**  
GlaxoSmithkline Biologicals SA, Lead  
Rapporteur: Bart Van der Schueren

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**WS1445**  
**Kispilyx-EMEA/H/C/004224/WS1445/0017**  
**Lenvima-EMEA/H/C/003727/WS1445/002**  
**0**  
Eisai Europe Ltd., Lead Rapporteur: Bart Van der  
Schueren

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**WS1446**  
**Kispilyx-EMEA/H/C/004224/WS1446/0016**  
**Lenvima-EMEA/H/C/003727/WS1446/001**  
**9**  
Eisai Europe Ltd., Lead Rapporteur: Bart Van der  
Schueren  
Opinion adopted on 04.10.2018.

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**WS1447**  
**Atripla-EMEA/H/C/000797/WS1447/0132**  
**Eviplera-EMEA/H/C/002312/WS1447/009**  
**3**  
**Stribild-EMEA/H/C/002574/WS1447/0096**  
**Truvada-EMEA/H/C/000594/WS1447/015**  
**0**  
**Viread-EMEA/H/C/000419/WS1447/0192**  
Gilead Sciences Ireland UC, Lead Rapporteur:  
Greg Markey  
Opinion adopted on 04.10.2018.

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**WS1457/G****Fertavid-EMEA/H/C/001042/WS1457/004  
0/G****Puregon-EMEA/H/C/000086/WS1457/009  
8/G**

Merck Sharp & Dohme B.V., Informed Consent of  
Puregon, Lead Rapporteur: Nithyanandan  
Nagercoil

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**WS1458****Cervarix-EMEA/H/C/000721/WS1458/009  
7****Fendrix-EMEA/H/C/000550/WS1458/006  
5**

GlaxoSmithkline Biologicals SA, Lead  
Rapporteur: Bart Van der Schueren

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**WS1465/G****Abseamed-EMEA/H/C/000727/WS1465/0  
075/G****Binocrit-EMEA/H/C/000725/WS1465/007  
5/G****Epoetin alfa****Hexal-EMEA/H/C/000726/WS1465/0074/  
G**

Sandoz GmbH, Lead Rapporteur: Alexandre  
Moreau

Opinion adopted on 04.10.2018.

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Positive Opinion adopted by consensus on  
04.10.2018. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

**WS1470****Abseamed-EMEA/H/C/000727/WS1470/0  
076****Binocrit-EMEA/H/C/000725/WS1470/007  
6****Epoetin alfa****Hexal-EMEA/H/C/000726/WS1470/0075**

Medice Arzneimittel Pütter GmbH & Co. KG,  
Duplicate, Duplicate of Epoetin alfa Hexal, Lead  
Rapporteur: Alexandre Moreau

Opinion adopted on 04.10.2018.

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Positive Opinion adopted by consensus on  
04.10.2018. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

**Mosquirix-EMEA/H/W/002300/WS1434/0  
034****Shingrix-EMEA/H/C/004336/WS1434/000  
8**

GlaxoSmithkline Biologicals SA, Lead  
Rapporteur: Jan Mueller-Berghaus

Opinion adopted on 27.09.2018.

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Positive Opinion adopted by consensus on  
27.09.2018. The Icelandic and Norwegian CHMP  
Members were in agreement with the CHMP  
recommendation.

**Mosquirix-EMEA/H/W/002300/WS1450/0  
037****Shingrix-EMEA/H/C/004336/WS1450/001  
0**



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

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

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**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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**bortezomib - EMEA/H/C/005074**

, treatment of multiple myeloma, Generic,  
Generic of VELCADE

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**clopidogrel / acetylsalicylic acid -  
EMEA/H/C/004996**

, indicated for the secondary prevention of  
atherothrombotic  
indicated for the secondary prevention of  
atherothrombotic events, Generic, Generic of  
DuoPlavin

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**dolutegravir / lamivudine -  
EMEA/H/C/004909**

, treatment of Human Immunodeficiency Virus  
type 1 (HIV-1)

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**fostamatinib - EMEA/H/C/005012**

, indicated for the treatment of thrombocytopenia

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**autologous cd34+ cell enriched population      Accelerated review  
that contains hematopoietic stem cells  
transduced with lentiglobin bb305 lentiviral  
vector encoding the beta-a-t87q-globin  
gene - EMEA/H/C/003691, Orphan, ATMP**

bluebird bio GmbH, treatment of  
transfusion-dependent  $\beta$ -thalassaemia (TDT)

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**clofarabine - EMEA/H/C/005039**

, treatment of acute lymphoblastic leukaemia,  
Generic, Generic of Evoltra

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**siponimod - EMEA/H/C/004712**

, treatment of secondary progressive multiple  
sclerosis (SPMS), treatment of secondary  
progressive multiple sclerosis (SPMS)  
treatment of secondary progressive multiple  
sclerosis (SPMS)  
treatment of secondary progressive multiple

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sclerosis (SPMS)

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**omadacycline tosylate - EMEA/H/C/004715**

, treatment of community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI) in adults, treatment

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**netarsudil - EMEA/H/C/004583**

, indicated for the reduction of elevated intraocular pressure (IOP) in adults with open-angle glaucoma or ocular hypertension.

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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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**Nucala - mepolizumab -**

**EMEA/H/C/003860/X/0018**

GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension application to introduce a new pharmaceutical form, solution for injection (in pre-filled syringe or in pre-filled pen)."

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**Pemetrexed Fresenius Kabi - pemetrexed - EMEA/H/C/003895/X/0009**

Fresenius Kabi Deutschland GmbH, Generic, Generic of Alimta, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ghania Chamouni, "Extension application to introduce a new pharmaceutical form (concentrate for solution for infusion) associated with new strength 25 mg/ml."

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**Tecentriq - atezolizumab -**

**EMEA/H/C/004143/X/0017**

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Extension application to add a new strength of 840 mg (60 mg/ml) for Tecentriq concentrate for solution for infusion in a vial and a new indication (metastatic triple-negative breast cancer (TNBC)). The new indication applies only to the 840mg strength." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

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

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

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

**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**

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

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**ATryn - antithrombin alfa -**

**EMA/H/C/000587/II/0036**

Laboratoire Francais du Fractionnement et des Biotechnologies, Rapporteur: Alexandre Moreau

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**Bexsero - meningococcal group B vaccine (recombinant, component, adsorbed) -**

**EMA/H/C/002333/II/0069**

GSK Vaccines S.r.l, Rapporteur: Kristina Dunder

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**Fulvestrant Mylan - fulvestrant -**

**EMA/H/C/004649/II/0005**

Mylan S.A.S, Generic, Generic of Faslodex, Rapporteur: Natalja Karpova

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**Humira - adalimumab -**

**EMA/H/C/000481/II/0184/G**

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder

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**InductOs - dibotermin alfa -**

**EMA/H/C/000408/II/0093**

Medtronic BioPharma B.V., Rapporteur: Johann Lodewijk Hillege

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**KANJINTI - trastuzumab -**

**EMA/H/C/004361/II/0006/G**

Amgen Europe B.V., BREDA, Rapporteur: Jan Mueller-Berghaus

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**Kevzara - sarilumab -**

**EMA/H/C/004254/II/0010/G**

sanofi-aventis groupe, Rapporteur: Jan

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Mueller-Berghaus

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**Metalyse - tenecteplase -**

**EMA/H/C/000306/II/0057**

Boehringer Ingelheim International GmbH,

Rapporteur: Harald Enzmann

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**MVASI - bevacizumab -**

**EMA/H/C/004728/II/0005/G**

Amgen Europe B.V., Duplicate, Duplicate of

KYOMARC, Rapporteur: Svein Rune Andersen

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**Nimenrix - meningococcal group A, C, W135  
and Y conjugate vaccine -**

**EMA/H/C/002226/II/0086/G**

Pfizer Europe MA EEIG, Rapporteur: Greg Markey

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**Obizur - susoctocog alfa -**

**EMA/H/C/002792/II/0022/G**

Baxalta Innovations GmbH, Rapporteur:

Nithyanandan Nagercoil

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**Ocrevus - ocrelizumab -**

**EMA/H/C/004043/II/0007**

Roche Registration GmbH, Rapporteur: Mark

Ainsworth

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**Omidria - phenylephrine / ketorolac -**

**EMA/H/C/003702/II/0008/G**

Omeros London Limited, Rapporteur: Jayne

Crowe

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**Pheburane - sodium phenylbutyrate -**

**EMA/H/C/002500/II/0019**

Lucane Pharma, Rapporteur: Jayne Crowe

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**Stelara - ustekinumab -**

**EMA/H/C/000958/II/0070/G**

Janssen-Cilag International NV, Rapporteur:

Greg Markey

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**Vizarsin - sildenafil -**

**EMA/H/C/001076/II/0029**

KRKA, d.d., Novo mesto, Generic, Generic of

Viagra, Rapporteur: Alexandre Moreau

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**Zinplava - bezlotoxumab -**

**EMA/H/C/004136/II/0013**

Merck Sharp & Dohme B.V., Rapporteur: Jan

Mueller-Berghaus

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**WS1478**

**Saxenda-EMA/H/C/003780/WS1478/001**

**9**

**Victoza-EMA/H/C/001026/WS1478/0048**

**Xultophy-EMA/H/C/002647/WS1478/00**

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Novo Nordisk A/S, Lead Rapporteur: Johann  
Lodewijk Hillege

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**WS1479/G**

**Halimatoz-EMEA/H/C/004866/WS1479/0  
001/G**

**Hefiya-EMEA/H/C/004865/WS1479/0001  
/G**

**Hyrimoz-EMEA/H/C/004320/WS1479/000  
1/G**

Sandoz GmbH, Lead Rapporteur: Milena Stain,  
Lead PRAC Rapporteur: Ulla Wändel Liminga

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**WS1480**

**Rixathon-EMEA/H/C/003903/WS1480/00  
15**

**Riximyo-EMEA/H/C/004729/WS1480/001  
5**

Sandoz GmbH, Lead Rapporteur: Jan  
Mueller-Berghaus

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**WS1499**

**Fluenz**

**Tetra-EMEA/H/C/002617/WS1499/0085**

**Pandemic influenza vaccine H5N1**

**AstraZeneca-EMEA/H/C/003963/WS1499/  
0018**

AstraZeneca AB, Lead Rapporteur: Jan  
Mueller-Berghaus

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**WS1502**

**Fertavid-EMEA/H/C/001042/WS1502/004  
2**

**Puregon-EMEA/H/C/000086/WS1502/010  
0**

Merck Sharp & Dohme B.V., Lead Rapporteur:  
Nithyanandan Nagercoil

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

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**Alprolix - eftrenonacog alfa -**

**EMEA/H/C/004142/II/0021, Orphan**

Swedish Orphan Biovitrum AB (publ),

Rapporteur: Andrea Laslop, PRAC Rapporteur:

Brigitte Keller-Stanislawski, "Update of sections  
4.8 and 5.1 of the SmPC to include new clinical  
efficacy and safety data on long-term treatment  
with Alprolix. The submission includes integrated  
evaluation of data from the extension study

(9HB01EXT (BYOND) which was submitted in a

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previous P46 procedure) and the pivotal parent studies. The PIL is updated accordingly. In addition, the MAH took the opportunity to update the product information to comply with the latest version of the "Excipients in the labelling and package leaflet of medicinal products for human use" guideline. The list of local representatives has been updated and other minor editorial changes have been included in the PIL."

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**AUBAGIO - teriflunomide -  
EMA/H/C/002514/II/0020**

sanofi-aventis groupe, Rapporteur: Martina Weise, "Submission of the final report from study LTS 6050. This is a phase 3 long term interventional study to document the safety of two doses of teriflunomide (7 and 14 mg) in patients with multiple sclerosis with relapses."

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**Epivir - lamivudine -  
EMA/H/C/000107/II/0108**

ViiV Healthcare UK Limited, Rapporteur: Joseph Emmerich, "Update of section 4.2 of the SmPC in order to correct the posology of paediatric patients at least 3 months of age and weighting less than 25 kg with renal impairment."

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the PI in relation to sodium and propylene glycol content in line with QRD. The package leaflet is updated in accordance."

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**Ferriprox - deferiprone -  
EMA/H/C/000236/II/0128**

Apotex Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update section 4.4 of the SmPC and the patient/carer reminder card in order to update and change the recommended frequency of ANC monitoring throughout Ferriprox treatment from a weekly basis to every week for the first six months of Ferriprox therapy, once every two weeks after six months of Ferriprox therapy, and to monthly after one year of therapy. The package leaflet has been updated accordingly. The RMP version 13.2 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update minor linguistic amendments in the HU and MT product information."

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**Halaven - eribulin -**

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**EMEA/H/C/002084/II/0047**

Eisai GmbH, Rapporteur: Filip Josephson,  
"Update of section 4.8 of the SmPC in order to add Hypocalcaemia as new adverse reaction with frequency 'common' as a result of a cumulative review on the matter requested during EMEA/H/C/PSUSA/00001254/201711 procedure (LEG 021). The Package Leaflet is updated accordingly."

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**Kadcyla - trastuzumab emtansine -  
EMEA/H/C/002389/II/0042/G**

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver,  
"Submission of an updated RMP version 8 in order to remove MoTHER pharmacovigilance activities [MEA 011] from the European Union Risk Management Plan (EU RMP) and use the Global Enhanced Pharmacovigilance (PV) Pregnancy Program to fulfil the commitment (c.1.11.b) and to change the due date of final results for the provision of the final study report for BO27938 (KATHERINE), a category 3 study in the RMP (c.1.11.z).

A randomized, multicenter, open label Phase III study to evaluate the efficacy and safety of Trastuzumab emtansine versus trastuzumab as adjuvant therapy for patients with Her2-positive primary breast cancer who have residual tumor present pathologically in the breast or axillary lymph nodes following preoperative therapy to address the following safety concerns: Left ventricular dysfunction, safety in elderly patients, immunogenicity (Anti-therapeutic Antibodies [ATAs])

In addition, the MAH takes the opportunity to update the RMP in line with the version 2.0 or new GVP Module V. and include an update of Kadcyla Educational Material to reflect changes in the Prescribing information following the renewal of the marketing authorisation."

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**Latuda - lurasidone -  
EMEA/H/C/002713/II/0022**

Aziende Chimiche Riunite Angelini Francesco S.p.A., Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to update the safety information following literature review regarding drug interaction between a strong CYP3A4 inhibitor (i.e. posaconazole) and

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lurasidone.”

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**Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) -**

**EMA/H/W/002300/II/0038**

GlaxoSmithKline Biologicals SA, Rapporteur: Jan Mueller-Berghaus, “Submission of the final report from study Malaria-063; this is a phase III randomized, open, controlled study to evaluate the long term immune response to the hepatitis B antigen of the RTS,S/AS01E candidate vaccine, when administered as primary vaccination integrated into an Expanded Program on Immunization (EPI) regimen to infants living in sub-Saharan Africa.”

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**Resolor - prucalopride -**

**EMA/H/C/001012/II/0046**

Shire Pharmaceuticals Ireland Limited, Rapporteur: Greg Markey, “Update of section 4.8 of the SmPC in order to add migraine and vertigo as uncommon adverse events, based on a reanalysis of the integrated safety information of 16 double-blind, placebo-controlled studies.

In addition, the Marketing authorisation holder (MAH) made editorial revision proposals for sections 4.4, 4.6 and 5.2 for alignment with Company Core Data Sheet version 12 and QRD templated wording.

The MAH also took the opportunity to propose minor editorial changes to Package Leaflet and sections 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC.”

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**Tyverb - lapatinib -**

**EMA/H/C/000795/II/0057**

Novartis Europharm Limited, Rapporteur: Filip Josephson, “Update of section 4.6 of the SmPC in order to update the safety information on pregnancy and breast-feeding following review of the company Core Data Sheet (CDS).The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Estonia and Lithuania in the Package Leaflet. Moreover, the MAH took the opportunity to make minor editorial changes/clarification in labelling for bottle presentations.”

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**Vosevi - sofosbuvir / velpatasvir /**

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**voxilaprevir - EMEA/H/C/004350/II/0018**

Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC based on final results from study GS-US-367-4181. This is an open-label study to evaluate the safety and efficacy of sofosbuvir/velpatasvir/voxilaprevir fixed-dose combination for 12 weeks in subjects who participated in a prior Gilead-sponsored HCV treatment study."

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**Zykadia - ceritinib -****EMEA/H/C/003819/II/0027**

Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, "C.I.13: Submission of the final Biomarker annual update report from phase II studies (A2201 and Study A2203) in order to fulfil the following Post-Marketing Measure identified by the CHMP: To submit a yearly update of the biomarker program for ceritinib."

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**WS1488****Segluromet-EMEA/H/C/004314/WS1488/0004****Steglatro-EMEA/H/C/004315/WS1488/0004****Steglujan-EMEA/H/C/004313/WS1488/0006**

Merck Sharp & Dohme B.V., Lead Rapporteur: Kristina Dunder, "Submission of the final CSR for Study P007/1017 - a Phase 3, randomized, double-blind, placebo-controlled, 26-week multicenter study with a 78-week extension to evaluate the efficacy and safety of ertugliflozin in subjects with type 2 Diabetes Mellitus and inadequate glycaemic control on metformin monotherapy - together with the final summarized data of all adjudicated confirmed fractures from the broad pool and pooled 2-year safety data from the 7 completed Phase 3 studies, including both 2-year studies P007/1017 and P002/1013."

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**WS1495****Lyrica-EMEA/H/C/000546/WS1495/0096  
Pregabalin****Pfizer-EMEA/H/C/003880/WS1495/0026**

Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect information from study A0081042 A Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter

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Study of the Efficacy and Safety of Pregabalin as Adjunctive Therapy in Children 1 Month through less than 4 Years of Age with Partial Onset Seizures. This submission relates to paediatric studies submitted according to Article 46 of the paediatric regulation (EC) No 1901/2006.”

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#### **B.6.10. CHMP-PRAC assessed procedures**

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##### **Darzalex - daratumumab -**

##### **EMA/H/C/004077/II/0020, Orphan**

Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Submission of study report of trial SMM2001 - A randomised Phase 2 trial to evaluate 3 daratumumab dose schedules in smouldering multiple myeloma. Consequently, the RMP is updated (version 4.1) in order to remove QTc prolongation as an Important Potential Risk from the RMP.”

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##### **Darzalex - daratumumab -**

##### **EMA/H/C/004077/II/0021, Orphan**

Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Update of section 5.2 of the SmPC to remove the following a sentence from the Immunogenicity subsection regarding the assay detecting anti daratumumab antibodies. With this submission the MAH considers MEA-005 to be fulfilled. The RMP is updated accordingly.”

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##### **Entyvio - vedolizumab -**

##### **EMA/H/C/002782/II/0035**

Takeda Pharma A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Adam Przybylkowski, “Update of sections 4.2, 4.4, 4.6, 5.1 and 5.3 of the SmPC in order to update the safety information following review of Company Core Data Sheet and literature review. Update of sections 4.6 and 5.3. is proposed with regards to the information on lactation, based on findings from non-Takeda, recently published data. In addition, the MAH proposed clarifications to other sections of the SmPC.

The Package Leaflet is updated accordingly.

The MAH also took the opportunity to correct

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typographical errors, spelling mistakes and other minor updates to the local languages Product Information.”

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**MabThera - rituximab -  
EMA/H/C/000165/II/0157**

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, “Update of Annex II section D of the product information, resulting from the obligation fulfilment for the rituximab subcutaneous formulation at a dose of 1400 mg by the submission of the final clinical study report for study BO22334 (SABRINA, category 1) including reports on long-term safety in relation to body surface area (BSA) (as a measure for exposure variation) and to gender. SABRINA is a two-stage Phase III, international, multi-centre, randomized, controlled, open-label study investigating the pharmacokinetics (PK), efficacy and safety of rituximab SC in combination with cyclophosphamide, doxorubicin, vincristine, prednisolone (CHOP) chemotherapy or cyclophosphamide, vincristine, prednisolone (CVP) chemotherapy versus rituximab IV in combination with CHOP or CVP chemotherapy followed by maintenance treatment with either rituximab SC or rituximab IV.)

Furthermore, the RMP version 19.0 has also been updated accordingly to reflect the removal this commitment. In addition, the Marketing authorisation holder (MAH) took the opportunity to include other changes to the RMP including the fulfilment of the previous information on concluded commitments such as the prolonged B-cell depletion and immunogenicity associated with the subcutaneous formulation.”

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**MabThera - rituximab -  
EMA/H/C/000165/II/0158**

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, “Update of Annex II section D of the product information, resulting from the obligation fulfilment for the rituximab subcutaneous formulation at a dose of 1400 mg by the submission of the final clinical study report for study BO25341 (SAWYER, category 1) including reports on long-term safety in relation to body surface area (BSA) (as a measure for exposure variation) and to gender. SAWYER is a Phase Ib adaptive, comparative, randomized, parallel-group, multi-center study of

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subcutaneous (SC) rituximab versus intravenous (IV) rituximab both in combination with chemotherapy (fludarabine and cyclophosphamide), in patients with previously untreated CLL.

Furthermore, the RMP version 19.0 has also been updated accordingly to reflect the removal this commitment. In addition, the Marketing authorisation holder (MAH) took the opportunity to include the changes on the concluded commitment such as the prolonged B-cell depletion and immunogenicity associated with the subcutaneous formulation.”

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**Mimpara - cinacalcet -**

**EMA/H/C/000570/II/0062/G**

Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “Update to Section 4.4 of the SmPC to provide additional information on switching from etelcalcetide to Mimpara (cinacalcet), upon request by PRAC following the assessment of the etelcalcetide PSUR (dated 14 June 2018). Further, the term ‘silica, dental type’ has been replaced by ‘Amorphous silicon dioxide’ in SmPC section 6.1.

An updated RMP version 9.0 was provided as part of the application in order to align the RMP with the GVP Module V (template Rev 2) with consequential reclassification of existing safety concerns.”

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**Parsabiv - etelcalcetide -**

**EMA/H/C/003995/II/0010**

Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, “Update of sections 4.8 to add convulsions secondary to hypocalcaemia as uncommon adverse reactions and further information on reports related to hypersensitivity reactions. Editorial correction is made to section 7. The Package Leaflet is update accordingly. Consequentially, RMP (version 2) has been submitted to reclassify some of the existing safety concerns.”

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**Tremfya - guselkumab -**

**EMA/H/C/004271/II/0005**

Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Update of sections 4.4 and 4.8 of the SmPC in order to add hypersensitivity

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and rash as adverse drug reactions with the frequency uncommon, together with a statement describing the characteristics of the serious hypersensitivity events. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted.”

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**XGEVA - denosumab -  
EMA/H/C/002173/II/0065**

Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “Update of section 4.8 of the SmPC to modify the frequency category of the ADR Atypical Femoral Fracture (AFF) from “rare” to “uncommon” and to add descriptive language regarding latency observed in clinical studies. The Package Leaflet has been updated accordingly. In addition, the MAH is taking the opportunity to remove the black triangle and corresponding text from the Annexes as Xgeva is no longer under additional monitoring, to implement editorial changes in the annexes and to update the contact details of the local representative in Ireland in the Package Leaflet.

An updated RMP (version 33) was provided as part of the application.”

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**Zejula - niraparib -  
EMA/H/C/004249/II/0006, Orphan**

Tesaro UK Limited, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Patrick Batty, “Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to optimise the starting dose of niraparib and clarify dose modification information, modify the existing warning on haematologic adverse reactions, amend the description of thrombocytopenia and amend existing efficacy and pharmacokinetics information, respectively. The changes are based on the integrated Population clinical report that contains information from the completed Phase 3 NOVA, study submitted as part of the initial MAA, as well as supportive information from the ongoing phase 2 PR-30-5020-C (QUADRA) and phase 1 / 2 300-PN-162-01-001 (TOPACIO) studies. The update of the SmPC posology is based on exposure response study reports to propose alternative dosing strategies that aim to reduce Grade 3/4 thrombocytopenia; the Package Leaflet is updated accordingly. The RMP version 1.1 has also been submitted to reflect the new EU RMP format. Furthermore, the core sections of

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the RMP have been updated to: align with niraparib PSUR 1, reflect post-authorization experience, inclusion of embolic and thrombotic events as important potential risks and to optimize the starting dose of niraparib to reduce adverse events.”

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**Zykadia - ceritinib -**

**EMA/H/C/003819/II/0026**

Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Annika Folin, “Update of section 4.5 of the SmPC in order to update the safety information based on final results from study CLDK378A2103, a Post Authorisation Measure Study (MEA 002) which evaluated the effects of ceritinib daily dosing on the pharmacokinetics of the probe drugs midazolam and warfarin, which are metabolised by CYP3A4 and CYP2C9 respectively, in patients with ALK-positive advanced tumors including NSCLC. The Package Leaflet is updated accordingly. The RMP version 14 has also been submitted.”

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**WS1461**

**Glyxambi-EMA/H/C/003833/WS1461/0017**

**Jentadueto-EMA/H/C/002279/WS1461/0047**

**Trajenta-EMA/H/C/002110/WS1461/0035**

Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, “Update of sections 4.4 , 4.8 and 5.1 of the SmPC to update the warnings related to acute pancreatitis and bullous pemphigoid and the efficacy and safety information based on final results from study listed as a category 3 in the RMP “A multicenter, international, randomized, parallel group, double blind, placebo-controlled Cardiovascular Safety & Renal Microvascular outcome study with LINAgliptin, 5 mg once daily in patients with type 2 diabetes mellitus at high vascular risk (CARMELINA)”. The RMP have also been updated accordingly for all products (Trajenta and Jentadueto version 12, Glyxambi version 4.0) and to be in accordance with the revision 2 of the RMP template.”

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**WS1476**

**Epclusa-EMA/H/C/004210/WS1476/002**

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**Harvoni-EMEA/H/C/003850/WS1476/007**

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**Sovaldi-EMEA/H/C/002798/WS1476/0052**

**Vosevi-EMEA/H/C/004350/WS1476/0016**

Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, "Submission of the final report from study GS-US-334-0154, listed as a category 3 study in the RMP. This is a phase 2b randomized, open-label study of 200mg or 400mg sofosbuvir + ribavirin for 24 Weeks in genotype 1 or 3 HCV-infected subjects with renal insufficiency. The RMPs have also been submitted for each of the products in this work-sharing procedure."

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#### **B.6.11. PRAC assessed procedures**

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PRAC Led

**alli - orlistat - EMEA/H/C/000854/II/0058**

Glaxo Group Ltd, Informed Consent of Xenical, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "Submission of the final report for non-interventional PASS study 204675 "Evaluating the effectiveness of the revised alli pack information in helping pharmacy staff within the EU supply alli appropriately" listed as a category 3 study in the RMP.

In addition, the MAH took the opportunity to update the RMP template in accordance to GVP module V Rev 2 (RMP version 17)."

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PRAC Led

**Emtriva - emtricitabine - EMEA/H/C/000533/II/0127**

Gilead Sciences Ireland UC, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "C.I.11: Submission of an updated RMP version 9.1 in order to implement Revision 2 of the EU-RMP template and update the safety concerns accordingly. In addition, updates have been made to the Antiretroviral Pregnancy Registry and the Mitochondrial Collaborative Committee (MITOC) study (A Cross-Sectional Study of HIV Negative Children Aged 18-24 Months Born to HIV-1 Infected Mothers in Europe: A European Study Sponsored by the Collaborative Committee

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for Mitochondrial Toxicity in Children (MITOC)).  
Finally, the RMP is also updated to reflect the approved transfer of the Marketing Authorisation from Gilead Sciences International Ltd, Cambridge (GSIL) to Gilead Sciences Ireland UC, Cork (GSIUC).”

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PRAC Led

**Invokana - canagliflozin -**

**EMA/H/C/002649/II/0039**

Janssen-Cilag International NV, Rapporteur:  
Martina Weise, PRAC Rapporteur: Martin Huber,  
PRAC-CHMP liaison: Martina Weise, “Provision of final Study Report for non-interventional PASS Study RRA-21430; Acute Pancreatitis Retrospective Observational Epidemiology Cohort Study: Acute pancreatitis in patients with T2DM who are new users of canagliflozin as compared with new users of other AHAs: a retrospective cohort study using large claims databases in the US.”

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PRAC Led

**JETREA - ocriplasmin -**

**EMA/H/C/002381/II/0042/G**

Oxurion NV, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, “C.I.13z: Submission of the final report from ‘ORBIT study (TG-MV-018): Ocriplasmin Research to Better Inform Treatment (ORBIT)’. This is a multicenter, prospective, observational study which assesses clinical outcomes and safety of JETREA® administered in a real-world setting for the treatment of symptomatic VMA.

C.I.13z: Submission of the final report from ‘Use of Intravitreal JETREA® in Clinical Practice: A European Prospective Drug Utilisation Study (TG-MV-017)’ listed as a category 3 study in the RMP. This study is a European, multicentre, observational study. The study includes two parts, a drug utilisation study (DUS) and the Patient Educational Material Evaluation Survey (PEMES). The main objective of the DUS is to document JETREA utilisation patterns in real-life clinical practice. The objective of the PEMES is to assess the effectiveness of the risk minimisation measures (i.e. the patient educational material [PEM] provided to patients prior to the injection of JETREA).

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C.I.13z: Submission of the final report from 'INJECT: INvestigation of JETREA® in Patients with Confirmed Vitreomacular Traction'. This is a non-interventional, multi-centre, worldwide study in patients treated with JETREA® (ocriplasmin) for the approved indication in their country. The aim of the study is to evaluate safety, clinical effectiveness, and HRQoL outcomes in a real world setting among a large population of patients exposed to ocriplasmin across different countries according to country's approved indications.

In addition, RMP V7.2 has been updated accordingly and the second revision of the RMP template has been implemented as well."

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PRAC Led

**Onglyza - saxagliptin -  
EMA/H/C/001039/II/0048**

AstraZeneca AB, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 14 in order to introduce the new template (EMA/PRAC/613102/2015, GVP Module V, revision 2) and to reclassify or remove some of the safety concerns."

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PRAC Led

**Vokanamet - canagliflozin / metformin -  
EMA/H/C/002656/II/0040**

Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Provision of final Study Report for non-interventional PASS Study RRA-21430; Acute Pancreatitis Retrospective Observational Epidemiology Cohort Study: Acute pancreatitis in patients with T2DM who are new users of canagliflozin as compared with new users of other AHAs: a retrospective cohort study using large claims databases in the US."

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## **B.6.12. CHMP-CAT assessed procedures**

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**talimogene laherparepvec -  
EMA/H/C/002771/II/0027, ATMP**

, "Update of section 4.8 of the SmPC in order to add granulomatous dermatitis as new adverse drug reaction with an uncommon frequency and to update the adverse reaction dyspnoea from

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dyspnoea exertional to dyspnoea under common frequency.”

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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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**WS1460**

**Viagra-EMEA/H/C/000202/WS1460/0099**

Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, “To update Section 4.7 “Effects on the ability to drive and use machines “ of the current Viagra, Verventi and sildenafil Pfizer (sildenafil citrate) Summaries of Product Characteristics (SmPCs), to align the content of the SmPC with the requirement of the current European Union (EU) Quality Review of Documents (QRD) template. The package leaflet (PL) has already been updated accordingly.”

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**WS1466/G**

**Atripla-EMEA/H/C/000797/WS1466/0133 /G**

**Biktarvy-EMEA/H/C/004449/WS1466/000 2/G**

**Descovy-EMEA/H/C/004094/WS1466/003 5/G**

**Emtriva-EMEA/H/C/000533/WS1466/012 6/G**

**Eviplera-EMEA/H/C/002312/WS1466/009 4/G**

**Genvoya-EMEA/H/C/004042/WS1466/005 2/G**

**Odefsey-EMEA/H/C/004156/WS1466/003 6/G**

**Stribild-EMEA/H/C/002574/WS1466/0098 /G**

**Truvada-EMEA/H/C/000594/WS1466/015 2/G**

Gilead Sciences Ireland UC, Lead Rapporteur:  
Robert James Hemmings

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**WS1481**

**Mircera-EMEA/H/C/000739/WS1481/0071**

**NeoRecormon-EMEA/H/C/000116/WS148 1/0100**

Roche Registration GmbH, Lead Rapporteur:

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**WS1486**

**Aluvia-EMEA/H/W/000764/WS1486/0106**

**Kaletra-EMEA/H/C/000368/WS1486/0173**

**Norvir-EMEA/H/C/000127/WS1486/0151**

AbbVie Deutschland GmbH & Co. KG, Lead  
Rapporteur: Joseph Emmerich, "To update  
sections 4.4 Special warnings and precautions for  
use and 4.8 Undesirable effects of the SmPC with  
the risk of autoimmune hepatitis as  
recommended by PRAC (EPITT no: 18956)."

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**WS1487**

**Blitzima-EMEA/H/C/004723/WS1487/001**

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**Ritemvia-EMEA/H/C/004725/WS1487/00**

**17**

**Rituzena-EMEA/H/C/004724/WS1487/00**

**18**

**Truxima-EMEA/H/C/004112/WS1487/001**

**9**

Celltrion Healthcare Hungary Kft., Duplicate,  
Duplicate of Truxima, Lead Rapporteur: Sol Ruiz

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**WS1507**

**Abseamed-EMEA/H/C/000727/WS1507/0**  
**078**

**Binocrit-EMEA/H/C/000725/WS1507/007**

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**Epoetin alfa**

**Hexal-EMEA/H/C/000726/WS1507/0077**

Sandoz GmbH, Lead Rapporteur: Alexandre  
Moreau, "To align the Instruction For Use (IFU) to  
include additional information concerning  
myelodysplastic syndromes (MDS). The annexes  
are also brought in line with the QRD general  
principles regarding the SmPC information for a  
generic/hybrid/biosimilar product"

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## **DOCUMENTS TABLED IN MMD AFTER THE CHMP PLENARY**

**B.6.16. Yearly Line listing for Type I and II variations**

**B.6.17. Monthly Line listing for Type I variations**

**B.6.18. Opinion on Marketing Authorisation transfer (MMD only)**

**B.6.19. Notifications in accordance with Article 61(3) of Council Directive 2001/83/EC (MMD only)**

**B.6.20. Request for supplementary information relating to Notification of Type I variation (MMD only)**

**B.6.21. 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 - EMEA 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:**

**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**

**Parallel Distribution - Pursuant to Article 9 of Council Regulation (EC) No. 2743/98 of 14 December 1998, as amended**

**F.1. 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.

### **Qualification of Biomarkers:**

**HTA:**

**Ongoing procedures**

**G.2. PRIME**

Some information related to PRIME cannot be released at the present time as these contain commercially confidential information.

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**G.2.1. List of procedures concluding at 15-18 October 2018 CHMP plenary:**

**G.2.2. List of procedures starting in October 2018 for November 2018 CHMP adoption of outcomes**

**H. ANNEX H - Product Shared Mailboxes – e-mail address**