07 February 2019
EMA/CHMP/44613/2019 Corr.2[1]
Inspections, Human Medicines Pharmacovigilance and Committees Division

# Committee for medicinal products for human use (CHMP)

## Draft agenda for the meeting on 28-31 January 2019

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

28 January 2019, 13:00 – 19:30, room 2A

29 January 2019, 08:30 – 19:30, room 2A

30 January 2019, 08:30 – 19:30, room 2A

31 January 2019, 08:30 – 15:00, 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).

[1] Correction in section 3.4.4 and in section 10.2.1

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
**Telephone** +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
**Send a question via our website** www.ema.europa.eu/contact

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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 28-31 January 2019. See January 2019 CHMP minutes (to be published post February 2019 CHMP meeting).

## 1.2. Adoption of agenda

CHMP agenda for 28-31 January 2019

## 1.3. Adoption of the minutes

CHMP minutes for 10-13 December 2018.

# 2. Oral Explanations

## 2.1. Pre-authorisation procedure oral explanations

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

; treatment of influenza A or B virus infection

Scope: Oral explanation, Report from SAG HIV/viral diseases meeting held on 21 January 2019

**Action**: Oral explanation to be held on 29 January 2019 at time 16:00

List of Outstanding Issues adopted on 13.12.2018, 18.10.2018. List of Questions adopted on 26.04.2018.

### 2.1.2. cannabidiol - Orphan - EMEA/H/C/004675

GW Research Ltd; adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS)

Scope: possible oral explanation/ List of outstanding issues

**Action**: For adoption

List of Outstanding Issues adopted on 15.11.2018. List of Questions adopted on 31.05.2018.

See 3.2

### 2.1.3. pacritinib - Orphan - EMEA/H/C/004793

CTI Life Sciences Limited; treatment of disease-related splenomegaly and control of symptoms in patients with primary myelofibrosis (PMF), post-polycythemia vera myelofibrosis (PPV-MF), or post-essential thrombocythemia myelofibrosis (PET-MF) who have thrombocytopenia (platelet counts ≤100,000 /µL).

Scope: Oral explanation

**Action**: Oral explanation to be held on 29 January 2019 at time 11:00

List of Outstanding Issues adopted on 15.11.2018, 26.07.2018. List of Questions adopted on 09.11.2017.

Participation of patient representatives

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

treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC)

Scope: Oral explanation

Action: Oral explanation to be held on 29 January 2019 at time 09:00

List of Outstanding Issues adopted on 18.10.2018. List of Questions adopted on 31.05.2018.

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

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

Scope: Oral explanation

**Action**: Oral explanation to be held on 29 January 2019 at time 14:00

List of Outstanding Issues adopted on 15.11.2018. List of Questions adopted on 26.07.2018.

## 2.2. Re-examination procedure oral explanations

No items

## 2.3. Post-authorisation procedure oral explanations

### 2.3.1. Hemlibra - emicizumab - EMEA/H/C/004406/II/0002

Roche Registration GmbH

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

Scope: Oral explanation

**Action**: Oral explanation to be held on 28 January 2019 at time 16:00

Request for Supplementary Information adopted on 13.12.2018, 18.10.2018, 26.07.2018.

See 5.1

### 2.3.2. WS1344
### Edistride - dapagliflozin - EMEA/H/C/004161/WS1344/0025
### Forxiga - dapagliflozin - EMEA/H/C/002322/WS1344/0044

AstraZeneca AB

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

Annika Folin

Scope: Oral explanation

**Action**: Oral explanation to be held on 30 January 2019 at time 14:00

Request for Supplementary Information adopted on 13.12.2018, 18.10.2018, 31.05.2018.

See 5.1

## 2.4. Referral procedure oral explanations

No items

# 3. Initial applications

## 3.1. Initial applications; Opinions

### 3.1.1. fremanezumab - EMEA/H/C/004833

; prevention of episodic and chronic migraine

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 15.11.2018. List of Questions adopted on 31.05.2018.

### 3.1.2. atazanavir - EMEA/H/C/004859

; treatment of HIV-1 infection

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 15.11.2018. List of Questions adopted on 26.07.2018.

### 3.1.3. doxorubicin hydrochloride - EMEA/H/C/004110

; treatment of breast and ovarian cancer

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 14.09.2017.

### 3.1.4. febuxostat - EMEA/H/C/004773

; treatment of hyperuricaemia

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 13.12.2018. List of Questions adopted on 20.09.2018.

### 3.1.5. adalimumab - EMEA/H/C/004475

; treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 15.11.2018. List of Questions adopted on 22.03.2018.

### 3.1.6. adalimumab - EMEA/H/C/005158

; treatment of rheumatoid arthritis

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 15.11.2018.

### 3.1.7. paclitaxel - EMEA/H/C/004441

; treatment of metastatic breast cancer

Scope: Opinion

**Action**: For adoption

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

### 3.1.8. dacomitinib - EMEA/H/C/004779

; first-line treatment of adults with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR)-activating mutations.

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 15.11.2018. List of Questions adopted on 28.06.2018.

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

### 3.2.1. ambrisentan - EMEA/H/C/004955

; treatment of pulmonary arterial hypertension (PAH)

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 20.09.2018.

### 3.2.2. trientine dihydrochloride - Orphan - EMEA/H/C/004111

Univar BV; Treatment of Wilson's disease

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 28.06.2018.

### 3.2.3. cannabidiol - Orphan - EMEA/H/C/004675

GW Research Ltd; Adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS)

Scope: Possible oral explanation/ List of outstanding issues

**Action**: For adoption

List of Outstanding Issues adopted on 15.11.2018. List of Questions adopted on 31.05.2018.

See 2.1

### 3.2.4. cemiplimab - EMEA/H/C/004844

; as monotherapy, indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 26.07.2018.

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

; treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC)

Scope: List of outstanding Issues/Oral Explanation

**Action**: For adoption

List of Outstanding Issues adopted on 18.10.2018. List of Questions adopted on 31.05.2018.

See. 2.1

### 3.2.6. risankizumab - EMEA/H/C/004759

; treatment of psoriasis in adults

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 20.09.2018.

### 3.2.7. glutamine - Orphan - EMEA/H/C/004734

Emmaus Medical Europe Ltd; treatment of sickle cell disease

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 28.06.2018.

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

### 3.3.1. bortezomib - EMEA/H/C/005074

; treatment of multiple myeloma

Scope: List of questions

**Action**: For adoption

### 3.3.2. clopidogrel / acetylsalicylic acid - EMEA/H/C/004996

; indicated for the secondary prevention of atherothrombotic events

Scope: List of questions

**Action**: For adoption

### 3.3.3. dolutegravir / lamivudine - EMEA/H/C/004909

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

Scope: List of questions

**Action**: For adoption

### 3.3.4. fostamatinib - EMEA/H/C/005012

; indicated for the treatment of thrombocytopenia

Scope: List of questions

**Action**: For adoption

### 3.3.5. autologous CD34+ cell enriched population that contains hematopoietic stem cells transduced with LentiGlobin BB305 lentiviral vector encoding the beta-A-T87Q-globin gene - Orphan - ATMP - EMEA/H/C/003691

**Accelerated assessment**

bluebird bio GmbH; treatment of transfusion-dependent β-thalassaemia (TDT)

Scope: List of questions

**Action**: For information

### 3.3.6. clofarabine - EMEA/H/C/005039

; treatment of acute lymphoblastic leukaemia

Scope: List of questions

**Action**: For adoption

### 3.3.7. siponimod - EMEA/H/C/004712

; treatment of secondary progressive multiple sclerosis (SPMS)

Scope: List of questions

**Action**: For adoption

### 3.3.8. omadacycline tosilate - EMEA/H/C/004715

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

Scope: List of questions

**Action**: For adoption

### 3.3.9. netarsudil - EMEA/H/C/004583

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

Scope: List of questions

**Action**: For adoption

### 3.3.10. quizartinib - Orphan - EMEA/H/C/004468

**Accelerated assessment**

Daiichi Sankyo Europe GmbH; treatment of acute myeloid leukaemia

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

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 20.09.2018

**Action**: For adoption

List of Outstanding Issues adopted on 20.09.2018, 25.05.2018. List of Questions adopted on 08.09.2017.

### 3.4.2. - romosozumab - EMEA/H/C/004465

treatment of osteoporosis

Scope: List of experts to the Ad Hoc Expert meeting adopted via written procedure on 17.01.2019

**Action**: For information

List of Outstanding Issues adopted on 15.11.2018, 20.09.2018. List of Questions adopted on 26.04.2018.

### 3.4.3. - enasidenib - Orphan - EMEA/H/C/004324

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

Scope: Letter from the applicant dated 21 December 2018 requesting for an extension of clock-stop to respond to the list of questions adopted in October 2018.

**Action**: For adoption

List of Questions adopted on 18.10.2018.

### 3.4.4. rituximab - EMEA/H/C/004696

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

Scope: Letter from applicant dated 23 January 2019 requesting an extension of clock stop to respond to the list of questions adopted on 13 December 2018.

**Action**: For adoption

List of Questions adopted on 13.12.2018.

## 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

No items

## 3.7. Withdrawals of initial marketing authorisation application

### 3.7.1. avacopan - Orphan - EMEA/H/C/004487

ChemoCentryx Ltd; induction of response in adult patients with granulomatosis with polyangiitis (Wegener's) (GPA) or microscopic polyangiitis (MPA)

Scope: Withdrawal of initial marketing authorisation application

**Action**: For information

List of outstanding Issues adopted on 13.12.2018, List of Questions adopted on 26.04.2018.

### 3.7.2. - pegfilgrastim - EMEA/H/C/005008

; treatment of neutropenia

Scope: Withdrawal of initial marketing authorisation application

**Action**: For information

List of Questions adopted on 28.06.2018.

### 3.7.3. - pegfilgrastim - EMEA/H/C/004789

; treatment of neutropenia

Scope: Withdrawal of initial marketing authorisation application

**Action**: For information

List of Questions adopted on 28.06.2018.

# 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. Dupixent - dupilumab - EMEA/H/C/004390/X/0004/G

sanofi-aventis groupe

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension application to add a new strength of 200 mg solution for injection in pre-filled syringe with safety system (PFS-S) and pre-filled pen (PFP), grouped with a type II variation (C.I.6.a) to add the following indications:
- Add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older, who are inadequately controlled with medium-to-high dose inhaled corticosteroids (ICS) plus another medicinal product for maintenance treatment, including those with or without an eosinophilic phenotype;
- Maintenance therapy to improve lung function;
- Maintenance therapy to reduce oral steroid use and improve lung function in steroid-dependent asthma patients;
Based on the pivotal studies DRI12544, QUEST and VENTURE.
As a consequence, SmPC sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 have been updated and the Package Leaflet has been updated accordingly.
The RMP (version 2.0) is uppdated accordingly.
In addition, the MAH proposed to merge the SmPCs for the 200 mg and 300 mg strengths."

**Action**: For adoption

List of Outstanding Issues adopted on 15.11.2018. List of Questions adopted on 26.07.2018.

### 4.1.2. Orencia - abatacept - EMEA/H/C/000701/X/0117/G

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension application to add 2 new strengths of 50 mg and 87.5 mg for solution for injection in a pre-filled syringe with needle guard, for subcutaneous (SC) administration, grouped with a type II variation (C.I.6.a) to include paediatric use of polyarticular Juvenile Idiopathic Arthritis (2 years and above) for solution for injection (50 mg, 87.5 mg and 125 mg).
The above-described changes are grouped
The RMP (version 25.0) is updated in accordance.
In addition, the applicant took the opportunity to implement minor editorial changes in the product information."

**Action**: For adoption

List of Outstanding Issues adopted on 13.12.2018. List of Questions adopted on 26.07.2018.

### 4.1.3. Trisenox - arsenic trioxide - EMEA/H/C/000388/X/0068

Teva B.V.

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension application to add a new strength of 2 mg/ml. The RMP (version 2.0) is updated in accordance."

**Action**: For adoption

List of Questions adopted on 20.09.2018.

### 4.1.4. Zykadia - ceritinib - EMEA/H/C/003819/X/0025

Novartis Europharm Limited

Scope: "Extension application to introduce a new pharmaceutical form (film-coated tablets)."

**Action**: For adoption

List of Questions adopted on 20.09.2018.

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

### 4.2.1. Xeljanz - tofacitinib - EMEA/H/C/004214/X/0012

Pfizer Europe MA EEIG

Rapporteur: Robert James Hemmings, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Extension application to introduce a new pharmaceutical form (prolonged-release tablet) associated with a new strength (11 mg), and presented in pack sizes of 28, 30, 90 and 91 tablets.
The extension of indication includes a change in pharmacokinetics.
An updated RMP (version 4.0) has been provided."

**Action**: For adoption

List of Questions adopted on 26.07.2018.

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

### 4.3.1. Nucala - mepolizumab - EMEA/H/C/003860/X/0018

GlaxoSmithKline Trading Services Limited

Rapporteur: Peter Kiely, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension application to introduce a new pharmaceutical form, solution for injection (in pre-filled syringe or in pre-filled pen)."

**Action**: For adoption

### 4.3.2. Pemetrexed Fresenius Kabi - pemetrexed - EMEA/H/C/003895/X/0009

Fresenius Kabi Deutschland GmbH

Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension application to introduce a new pharmaceutical form (concentrate for solution for infusion) associated with new strength 25 mg/ml."

**Action**: For adoption

### 4.3.3. 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

Scope: "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)

**Action**: For adoption

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

No items

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

No items

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

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

### 5.1.1. Dupixent - dupilumab - EMEA/H/C/004390/II/0012

Sanofi-Aventis Groupe

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension of Indication to extend the adult atopic dermatitis indication to the

paediatric, 12 years to 17 years (adolescent) patients under Article 8 of the Paediatric Regulation (1901/2006). This study is submitted in accordance with the requirement of Article 46."

**Action**: For adoption

### 5.1.2. Hemlibra - emicizumab - EMEA/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).

Draft list of experts for the ad-hoc expert meeting scheduled on 25 January 2019 was adopted via written procedure on 24 January 2019

**Action**: For adoption

Request for Supplementary Information adopted on 13.12.2018, 18.10.2018, 26.07.2018.

See 2.3

### 5.1.3. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0060

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, in combination with carboplatin and either paclitaxel or nab-paclitaxel, for the first-line treatment of metastatic squamous NSCLC in adults for Keytruda.
As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is

updated in accordance. Additionally, editorial corrections to section 5.1 of the SmPC are introduced (concerning the procedure EMEA/H/C/003820/II/0052). The RMP version 20.1 has also been submitted."

**Action**: For adoption

Request for Supplementary Information adopted on 13.12.2018, 15.11.2018.

### 5.1.4. Lonsurf - trifluridine / tipiracil - EMEA/H/C/003897/II/0012

Les Laboratoires Servier

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Annika Folin

Scope: "Extension of Indication to include Lonsurf indicated for the treatment of adult patients with metastatic gastric cancer including adenocarcinoma of the gastroesophageal junction, who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, platinum-, and either a taxane- or irinotecan-based chemotherapy. 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.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. RMP version 6.1 has also been submitted and updated in accordance with Template Rev 2."

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

**Action**: For adoption

### 5.1.5. Lucentis - ranibizumab - EMEA/H/C/000715/II/0074/G

Novartis Europharm Limited

Rapporteur: Kristina Dunder, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of Indication to include new indication for Lucentis vial presentation: treatment of retinopathy of prematurity (ROP) in preterm infants; as a consequence, sections 2, 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance.
In addition, RMP version 18.0 is also submitted.
B.IV.1.a.1 – To introduce a low volume high accuracy syringe, as a stand-alone medical device for the administration of the Lucentis 0.2mg paediatric dose (corresponding to 0.02 ml of the Lucentis 10 mg/ml solution for injection in vial presentations)."

**Action**: For adoption

### 5.1.6. MabThera - rituximab - EMEA/H/C/000165/II/0150

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Doris Stenver

Scope: "Extension of indication to include the treatment of patients with moderate to severe

pemphigus vulgaris (PV) for MabThera; as a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package leaflet is updated accordingly."

**Action**: For adoption

Request for Supplementary Information adopted on 15.11.2018, 28.06.2018.

### 5.1.7. Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0012

AbbVie Deutschland GmbH & Co. KG

Rapporteur: Joseph Emmerich, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "Extension of indication to extend the Maviret indication to adolescents (from 12 to 18 years of age) with chronic hepatitis C infection, based on new clinical data from study M16-123, an open-label, multi-centre study to evaluate the pharmacokinetics, safety, and efficacy of glecaprevir/pibrentasvir in paediatric subjects with genotypes 1 - 6 chronic hepatitis C virus infection (DORA), using the adult co-formulated tablets in adolescents. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the marketing authorisation holder (MAH) submitted a revised RMP version 4, updated in accordance with the second revision of the RMP template."

**Action**: For adoption

Request for Supplementary Information adopted on 20.09.2018.

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

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

Request for Supplementary Information adopted on 18.10.2018.

### 5.1.9. SIRTURO - bedaquiline - Orphan - EMEA/H/C/002614/II/0033/G

Janssen-Cilag International NV

Rapporteur: Filip Josephson, Co-Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Grouping of an Extension of Indication to include patients 12 years of age and older for SIRTURO and a Type II variation to change the safety information in Section 4.9 of the SmPC.
The extension of indication is supported by the Week 24 analysis of Cohort 1 (adolescent

subjects aged ≥12 to <18 years) of Study TMC207-C211. Based on these data, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.
An updated version of the RMP (version 3.2) was included in the submission."

**Action**: For adoption

### 5.1.10. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0007/G

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of indication to include in combination with bevacizumab, paclitaxel and carboplatin the first-line treatment of adult patients with metastatic non-squamous non small cell lung cancer (NSCLC), based on the interim results of study GO29436 (IMpower 150). As a consequence sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated.
In addition update of section 4.8 of the SmPC in order to update the monotherapy safety data and reflect the largest pooled monotherapy population available (now including also data from IMvigor211 and PCD4989g studies).
The Package Leaflet and the RMP (version 4.0) are updated in accordance. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to make small corrections and formatting changes throughout the SmPC."

**Action**: For adoption

Request for Supplementary Information adopted on 20.09.2018, 31.05.2018.

### 5.1.11. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0018

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of indication to include Tecentriq, in combination with carboplatin and etoposide, for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC); as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. RMP version 8.0 has been submitted"

**Action**: For adoption

### 5.1.12. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0019

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of indication to include Tecentriq, in combination with nab-paclitaxel and carboplatin, for the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC) who do not have EGFR mutant or ALK-positive NSCLC; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. RMP version 9.0 has been submitted."

**Action**: For adoption

### 5.1.13. WS1344 Edistride - dapagliflozin - EMEA/H/C/004161/WS1344/0025 Forxiga - dapagliflozin - EMEA/H/C/002322/WS1344/0044

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 13.12.2018, 18.10.2018, 31.05.2018.

See 2.3

### 5.1.14. WS1501 Anoro Ellipta - umeclidinium / vilanterol - EMEA/H/C/002751/WS1501/0024 Laventair Ellipta - umeclidinium / vilanterol - EMEA/H/C/003754/WS1501/0027

GlaxoSmithKline (Ireland) Limited

Lead Rapporteur: Peter Kiely, Lead Co-Rapporteur: Ewa Balkowiec Iskra

Scope: "Update of sections 4.1. and 5.1 of the SmPC in order to update the efficacy information regarding the benefit on disease exacerbations of Umeclidinium and Umeclidinium/vilanterol from the CTT116855 study (InforMing the PAthway of COPD Treatment [IMPACT]) and the benefit on disease exacerbations of Vilanterol from the HZC113782 study (Study to Understand Mortality and Morbidity [SUMMIT]).
The Package Leaflet is updated in accordance."

**Action**: For adoption

### 5.1.15. WS1505 Incruse Ellipta - umeclidinium bromide - EMEA/H/C/002809/WS1505/0023 Rolufta Ellipta - umeclidinium - EMEA/H/C/004654/WS1505/0008

GlaxoSmithKline (Ireland) Limited

Lead Rapporteur: Concepcion Prieto Yerro, Lead Co-Rapporteur: Peter Kiely

Scope: "Update of sections 4.1. and 5.1 of the SmPC in order to update the efficacy information regarding the benefit of Umeclidinium and Umeclidinium/vilanterol from the CTT116855 study (InforMing the PAthway of COPD Treatment [IMPACT]).
The Package Leaflet is updated in accordance."

**Action**: For adoption

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

No items

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

No items

# 6. 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. - rVSVΔG-ZEBOV-GP - H0004554

Active immunization of at-risk individuals 18 years and older in reactive use situations to protect against Ebola Virus Disease (EVD) caused by Zaire Ebola virus

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

**Action:** For adoption

### 8.1.2. - GILTERITINIB - Orphan - H0004752

treatment in adults of FMS-like tyrosine kinase 3 (FLT3) mutation positive patients with relapsed or refractory acute myeloid leukemia (AML).

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

**Action:** For information

### 8.2.2. Recommendation for PRIME eligibility

**Action:** For adoption.

# 9. Post-authorisation issues

## 9.1. Post-authorisation issues

### 9.1.1. Arzerra - ofatumumab - EMEA/H/C/001131 - Orphan

Novartis Pharma AG

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Bjorg Bolstad

Scope: Withdrawal of marketing authorisation

**Action**: For information

### 9.1.2. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/LEG 037

Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Review of the potential benefit of Gilenya (fingolimod) use in pregnant women and women of child-bearing potential (WCBP) not using effective contraception, as well as up-to-date information on reproductive toxicity, as requested in the conclusions of PSUSA/00001393/201802 adopted in September 2018

PRAC List of questions to SAG Neurology

List of experts to SAG Neurology

**Action**: For adoption

### 9.1.3. Fotivda - tivozanib - EMEA/H/C/004131

EUSA PHARMA; treatment of adult patients with advanced renal cell carcinoma (RCC)

Rapporteur: Bruno Sepodes, Co-Rapporteur: Robert James Hemmings

Scope: Update on results from a phase 3 study, study AV-951-15-303 (TIVO-3) conducted in patients with advanced refractory RCC who have failed 2-3 prior systemic therapies.

**Action**: For discussion

### 9.1.4. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0047

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."

Discussion of EPAR following the positive opinion adopted on 18.10.2018

**Action:** For adoption

### 9.1.5. Kyprolis - carfilzomib - EMEA/H/C/003790, Orphan

Amgen Europe B.V.

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Alexandre Moreau

Scope: Update

**Action**: For discussion

### 9.1.6. PD1-PDL1 targeting agents

Scope: Report from SAG Oncology meeting on 10 January 2019

**Action**: For information

### 9.1.7. Pixuvri - pixantrone - EMEA/H/C/002055/R/0046

CTI Life Sciences Limited

Rapporteur: Tuomo Lapveteläinen, Co-Rapporteur: Filip Josephson

Scope: Request for Supplementary Information

**Action**: For adoption

### 9.1.8. STEGLATRO - Ertugliflozin – (PSUSA/00010682/201806), SEGLUROMET - Ertugliflozin, metformin – (PSUSA/00010680/201806), STEGLUJAN - Ertugliflozin, sitagliptin – (PSUSA/00010681/201806)

Merck Sharp & Dohme B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Agnes Gyurasics,
PRAC Rapporteur: Menno van der Elst

Scope: PRAC recommendation for variation to MA to update of section 4.4 of the SmPC to revise a warning on lower limb amputations

**Action**: For adoption

# 10. Referral procedures

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

### 10.1.1. Lartruvo – olaratumab – EMEA/H/A-20/1479/C/4216/015

Eli Lilly Nederland B.V.

Referral Rapporteur: TBC, Referral Co-Rapporteur: TBC

Scope: Start of procedure, List of Questions, Timetable, Appointment of Rapporteurs

**Action:** For adoption

Review of benefit-risk balance following preliminary results of the ANNOUNCE study (I5B-MC-JGDJ) which did not meet the primary endpoint of prolongation of overall survival in the study population.

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

### 10.2.1. Direct Oral Anticoagulants (DOAC) - EMEA/H/A-5(3)/1478

MAHs: various

Referral Rapporteur: TBC, Referral Co-Rapporteurs: TBC

Rapporteurs for involved CAPs:

Eliquis (APIXABAN):
Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Nithyanandan Nagercoil;

Pradaxa (DABIGATRAN ETEXILATE):
Rapporteur: Mark Ainsworth, Co-Rapporteur: Joseph Emmerich;

Xarelto (RIVAROXABAN):
Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise

Scope: Start of procedure, Timetable, Appointment of Rapporteurs

To assess the results of a non-interventional study regarding the risks of major bleeding in patients with non-valvular atrial fibrillation.

**Action**: For discussion

## 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

No items

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

No items

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

### 10.6.1. Angiotensin-II-receptor antagonists (sartans) containing a tetrazole group - EMEA/H/A-31/1471

MAHs: various

Overall Rapporteur: Martina Weise, Co-Rapporteurs: Candesartan: Kristina Dunder, Irbesartan: Concepcion Prieto Yerro, Losartan: Johann Lodewijk Hillege, Olmesartan: Milena Stain, Valsartan: Daniela Melchiorri

Scope: Opinion

**Action:** For discussion

Referral notification from European Commission regarding an API manufacturer (Zhejiang Huahai Pharmaceutical, China), who has detected the presence of a previously undetected impurity, N-nitrosodimethylamine (NDMA, also known as dimethylnitrosamine) in the valsartan API manufactured at its site in Chuannan. Zhejiang Huahai is one of the API manufacturers that are supplying valsartan for medicinal products authorised in the EU.

Furthermore it was agreed to extend the review to other sartans containing a tetrazole group (candesartan, irbesartan, losartan and olmesartan).

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

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

MAHs: various

Re-examination Rapporteur: TBC, Re-examination Co-Rapporteur: TBC

Scope: Re-examination, Appointment of Rapporteurs, Timetable

**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.

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

No items

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

No items

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

No items

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

No items

## 11. Pharmacovigilance issue

### 11.1. Early Notification System

January 2019 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

Scope: 2019 EMA Inspection Programme

**Action:** For adoption

GCP inspections

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

### 12.2. Pharmacovigilance inspections

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

### 12.3. 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

**Action**: For information

## 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

### 13.3.1. EC request for EMA opinion on the definitions of pharmacological, immunological, metabolic and medical diagnosis

Draft reports

**Action**: For information

## 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 CHMP Co-opted Member

Election of CHMP co-opted member in light of the expiry of the mandate of co-opted member Koenraad Norga on 24 January 2019.

**Action:** For adoption

Agreed areas of expertise:

1) Pharmacoepidemiology.

2) Statistics for clinical trials and observational studies.

### 14.1.2. Information in CHMP Assessment Reports

Information on scientific advice in CHMP assessment report

**Action**: For information

## 14.2. Coordination with EMA Scientific Committees

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

Summary of recommendations and advice of PRAC meeting held on 14-17 January 2019

**Action:** For information

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for January 2019

**Action:** For adoption

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

CAT draft minutes of meeting held on 23-25 January 2019
**Action**: For information

Regulatory consideration on medical products composed of, or produced using genome editing component

**Action:** For discussion

Follow up from January ORGAM

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

Report from the HMPC meeting held on 14-16 January 2019

**Action:** For information

### 14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at January 2019 PDCO

**Action:** For information

Report from the PDCO meeting held on 29 January 2019 – 01 February 2019

**Action:** For information

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

Report from the COMP meeting held on 22-24 January 2019
**Action:** For information

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

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 28-30 January 2019

**Action:** For information

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

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

Co-Vice-Chairs: Peter Mol/Kolbeinn Gudmundsson,

Report from the SAWP meeting held on 14-17 January 2019. 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.

### 14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held in January 2019.

**Action:** For adoption

### 14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse,

Scope: Reports from BWP January 2019 meeting to CHMP for adoption:

- 15 reports on products in scientific advice and protocol assistance
- 4 reports on products in pre-authorisation procedures
- 2 reports on products in post-authorisation procedures
- 4 reports on products in plasma master file

**Action:** For adoption

Scope: Review of seed sequencing data - annual influenza vaccines 2018-2019 BWP report
**Action**: For adoption

### 14.3.4. Antimicrobial Advice ad hoc Expert Group (AMEG)

Scope: Draft scientific advice by the Antimicrobial Advice Ad Hoc Expert Group (AMEG) on the categorisation of antimicrobials (EMA/682198/2017)

**Action:** For adoption

Background information: request from the European Commission for the update of the AMEG advice on the impact on public health and animal health of the use of antibiotics in animals.

## 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

## 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)*

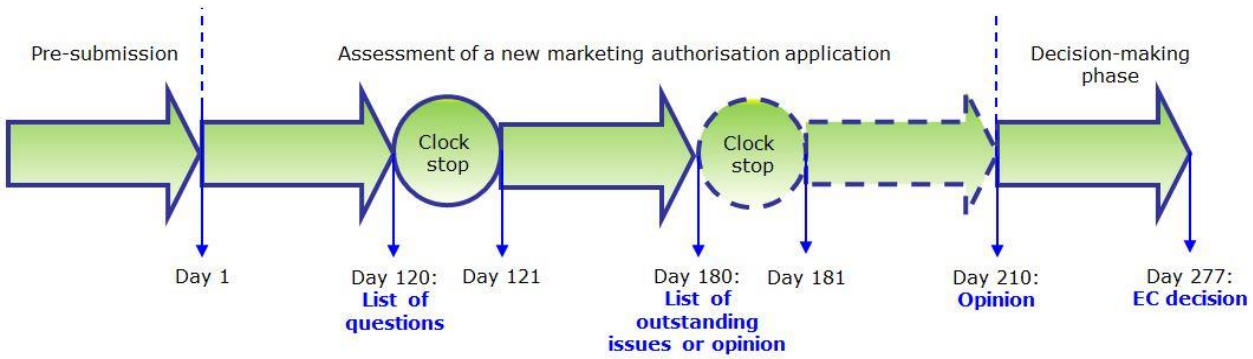
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures (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** *(section5.3)*

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 Pharmamacovigilance 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/

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# Annex to 28-31 January 2019 CHMP Agenda

Pre-submission and post-authorisations issues


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30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
**Telephone** +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
**Send a question via our website** www.ema.europa.eu/contact

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## A. PRE SUBMISSION ISSUES

### A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for January 2019: **For adoption**

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

Final Outcome of Rapporteurship allocation for January 2019: **For adoption**

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

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

## B. POST-AUTHORISATION PROCEDURES OUTCOMES

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

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

**Lojuxta - lomitapide -**
**EMEA/H/C/002578/S/0032**
Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 15.11.2018.

**Raxone - idebenone -**
**EMEA/H/C/003834/S/0012, Orphan**
Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli

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

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

**Gazyvaro - obinutuzumab -**
**EMEA/H/C/002799/R/0031, Orphan**
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ulla Wändel Liminga

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

**Afinitor - everolimus - EMEA/H/C/001038/R/0060**
Novartis Europharm Limited, Rapporteur: Janet Koenig, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber

**BiResp Spiromax - budesonide / formoterol - EMEA/H/C/003890/R/0027**
Teva Pharma B.V., Duplicate, Duplicate of DuoResp Spiromax, Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Anette Kirstine Stark

**DuoResp Spiromax - budesonide / formoterol - EMEA/H/C/002348/R/0027**
Teva Pharma B.V., Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Anette Kirstine Stark

**Envarsus - tacrolimus - EMEA/H/C/002655/R/0014**
Chiesi Farmaceutici S.p.A., Rapporteur: John Joseph Borg, PRAC Rapporteur: Ronan Grimes

**Instanyl - fentanyl - EMEA/H/C/000959/R/0049**
Takeda Pharma A/S, Rapporteur: Alexandre Moreau, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Ghania Chamouni

**Nuwiq - simoctocog alfa - EMEA/H/C/002813/R/0027**
Octapharma AB, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Ulla Wändel Liminga

**Plegridy - peginterferon beta-1a - EMEA/H/C/002827/R/0051**
Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Julie Williams

**Qutenza - capsaicin - EMEA/H/C/000909/R/0047**
Grunenthal GmbH, Rapporteur: Bruno Sepodes, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Ana Sofia Diniz Martins
Request for Supplementary Information adopted on 15.11.2018.

**SYLVANT - siltuximab - EMEA/H/C/003708/R/0029, Orphan**
Janssen-Cilag International NV, Rapporteur:

Concepcion Prieto Yerro, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Brigitte Keller-Stanislawski
Request for Supplementary Information adopted on 13.12.2018.

**Velphoro - mixture of polynuclear iron(III)-oxyhydroxide, sucrose and starches - EMEA/H/C/002705/R/0018**
Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Julie Williams

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

**Cometriq - cabozantinib - EMEA/H/C/002640/R/0029, Orphan**
Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 15.11.2018.

**Deltyba - delamanid - EMEA/H/C/002552/R/0033, Orphan**
Otsuka Novel Products GmbH, Rapporteur: Greg Markey, PRAC Rapporteur: Jean-Michel Dogné
Request for Supplementary Information adopted on 13.12.2018.

**Natpar - parathyroid hormone - EMEA/H/C/003861/R/0016, Orphan**
Shire Pharmaceuticals Ireland Limited, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Rhea Fitzgerald

**Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (H5N1) (live attenuated, nasal) - EMEA/H/C/003963/R/0019**
AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Daniela Philadelphy

**Pixuvri - pixantrone - EMEA/H/C/002055/R/0046**
CTI Life Sciences Limited, Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Kirsti Villikka

**Rubraca - rucaparib - EMEA/H/C/004272/R/0008, Orphan**

Clovis Oncology Ireland Limited, Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Annika Folin

## B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

**Signal detection**

PRAC recommendations on signals adopted at the PRAC meeting held on 14-17 January 2019 PRAC:

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its January 2019 meeting:

**EMEA/H/C/PSUSA/00000274/201805**
(azacitidine)
CAPS:
**Vidaza** (EMEA/H/C/000978) (azacitidine), Celgene Europe BV, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "19 May 2015 to 18 May 2018"

**EMEA/H/C/PSUSA/00000935/201806**
(dasatinib)
CAPS:
**Sprycel** (EMEA/H/C/000709) (dasatinib), Bristol-Myers Squibb Pharma EEIG, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "28 June 2017 – 27 June 2018"

**EMEA/H/C/PSUSA/00001725/201805**
(imatinib)
CAPS:
**Glivec** (EMEA/H/C/000406) (imatinib), Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia, "11-May-2015 to 10-May-2018"

**EMEA/H/C/PSUSA/00001937/201805**
(measles / mumps / rubella vaccines (live, attenuated))
CAPS:
**M-M-RVAXPRO** (EMEA/H/C/000604) (measles, mumps and rubella vaccine (live)), MSD Vaccins, Rapporteur: Jan Mueller-Berghaus
NAPS:
**NAPs** - MAH
, PRAC Rapporteur: Brigitte Keller-Stanislawski, "05/05/2015 - 04/05/2018"

**EMEA/H/C/PSUSA/00002665/201807**
(rotavirus vaccine monovalent (live, oral))
CAPS:

**Rotarix** (EMEA/H/C/000639) (human rotavirus, live attenuated), GlaxoSmithKline Biologicals S.A., Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Jean-Michel Dogné, "12 July 2017 - 11 July 2018"

**EMEA/H/C/PSUSA/00010031/201806**
(mirabegron)
CAPS:
**Betmiga** (EMEA/H/C/002388) (mirabegron), Astellas Pharma Europe B.V., Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, "1 July 2017 - 30 June 2018"

**EMEA/H/C/PSUSA/00010125/201806**
(pertuzumab)
CAPS:
**Perjeta** (EMEA/H/C/002547) (pertuzumab), Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "8th June 2017 to 7th June 2018"

**EMEA/H/C/PSUSA/00010379/201807**
(nivolumab)
CAPS:
**OPDIVO** (EMEA/H/C/003985) (nivolumab), Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, "04 January 2018 - 03 July 2018"

**EMEA/H/C/PSUSA/00010391/201806**
(lutetium (177Lu) chloride)
CAPS:
**EndolucinBeta** (EMEA/H/C/003999) (lutetium (177Lu) chloride), ITG Isotope Technologies Garching GmbH, Rapporteur: Peter Kiely
**LuMark** (EMEA/H/C/002749) (lutetium lu-177), I.D.B. Holland B.V., Rapporteur: Nithyanandan Nagercoil
NAPS:
**LUTAPOL** - NARODOWE CENTRUM BADAŃ JĄDROWYCH
, PRAC Rapporteur: Rhea Fitzgerald, "20.12.2017 - 19.06.2018"

**EMEA/H/C/PSUSA/00010595/201805**
(nusinersen)
CAPS:
**Spinraza** (EMEA/H/C/004312) (nusinersen), Biogen Netherlands B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ulla Wändel Liminga,

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| "01 December 2017 - 30 May 2018" |

**B.4. EPARs / WPARs**

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| **Besremi - ropeginterferon alfa-2b - EMEA/H/C/004128, Orphan**<br>AOP Orphan Pharmaceuticals AG, treatment of polycythemia vera, 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. |
| **pegfilgrastim - EMEA/H/C/005008**<br>STADA Arzneimittel AG, treatment of neutropenia<br>**WPAR** | For information only. Comments can be sent to the EPL in case necessary. |
| **pegfilgrastim - EMEA/H/C/004789**<br>Gedeon Richter Plc., treatment of neutropenia<br>**WPAR** | For information only. Comments can be sent to the EPL in case necessary. |
| **Lusutrombopag Shionogi - lusutrombopag - EMEA/H/C/004720**<br>Shionogi B.V., treatment of thrombocytopenia, 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. |
| **Miglustat Dipharma - miglustat - EMEA/H/C/004904**<br>Dipharma B.V., treatment of adult patients with mild to moderate type 1 Gaucher disease and only in the treatment of patients for whom enzyme replacement therapy is unsuitable, Generic, Generic of Zavesca, Generic application (Article 10(1) of Directive No 2001/83/EC) | For information only. Comments can be sent to the EPL in case necessary. |
| **Rizmoic - naldemedine - EMEA/H/C/004256**<br>Shionogi B.V., treatment of opioid-induced constipation (OIC) in adult patients., 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. |
| **Tobramycin PARI - tobramycin - EMEA/H/C/005086**<br>PARI Pharma GmbH, management of chronic pulmonary infection due to Pseudomonas aeruginosa in patients aged 6 years and older with cystic fibrosis (CF)., Hybrid application (Article 10(3) of Directive No 2001/83/EC) | For information only. Comments can be sent to the EPL in case necessary. |
| **Trecondi - treosulfan - EMEA/H/C/004751, Orphan**<br>medac Gesellschaft fur klinische Spezialpraparate mbH, conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT), Known active | For information only. Comments can be sent to the EPL in case necessary. |

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| substance (Article 8(3) of Directive No 2001/83/EC) | |
| **Zirabev - bevacizumab - EMEA/H/C/004697**<br>Pfizer Europe MA EEIG, Treatment of adult patients with metastatic carcinoma of the colon or rectum, metastatic breast cancer, unresectable advanced, metastatic or recurrent non-small cell lung cancer, advanced and/or metastatic renal cell cancer, persistent, recurrent, or metastatic carcinoma of the cervix, 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.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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| **Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0061, Orphan**<br>Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Aldurazyme - laronidase - EMEA/H/C/000477/II/0071/G**<br>Genzyme Europe BV, Rapporteur: Greg Markey<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Atriance - nelarabine - EMEA/H/C/000752/II/0045/G**<br>Novartis Europharm Limited, Rapporteur: Sinan B. Sarac | |
| **Bortezomib Accord - bortezomib - EMEA/H/C/003984/II/0014**<br>Accord Healthcare Limited, Generic, Generic of VELCADE, Rapporteur: Milena Stain<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 13.09.2018. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Braftovi - encorafenib - EMEA/H/C/004580/II/0002/G**<br>Pierre Fabre Medicament, Rapporteur: Janet Koenig | |
| **Cinryze - C1 esterase inhibitor (human) - EMEA/H/C/001207/II/0064**<br>Shire Services BVBA, Rapporteur: Jan | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP |

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| Mueller-Berghaus<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 25.10.2018. | recommendation. |
| **Darzalex - daratumumab - EMEA/H/C/004077/II/0018/G, Orphan**<br>Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac<br>Request for Supplementary Information adopted on 08.11.2018. | |
| **Dupixent - dupilumab - EMEA/H/C/004390/II/0009/G**<br>sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 13.09.2018. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Fasenra - benralizumab - EMEA/H/C/004433/II/0010**<br>AstraZeneca AB, Rapporteur: Bruno Sepodes | |
| **Firazyr - icatibant - EMEA/H/C/000899/II/0043/G, Orphan**<br>Shire Pharmaceuticals Ireland Limited, Rapporteur: Kristina Dunder | |
| **Flixabi - infliximab - EMEA/H/C/004020/II/0034**<br>Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| **Fulvestrant Mylan - fulvestrant - EMEA/H/C/004649/II/0005**<br>Mylan S.A.S, Generic, Generic of Faslodex, Rapporteur: Natalja Karpova<br>Request for Supplementary Information adopted on 06.12.2018. | |
| **HBVAXPRO - hepatitis B vaccine (rDNA) - EMEA/H/C/000373/II/0064**<br>MSD Vaccins, Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 11.10.2018. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Hulio - adalimumab - EMEA/H/C/004429/II/0001**<br>Mylan S.A.S, Rapporteur: Bart Van der Schueren<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| **Imfinzi - durvalumab - EMEA/H/C/004771/II/0003**<br>AstraZeneca AB, Rapporteur: Sinan B. Sarac<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| **Imfinzi - durvalumab - EMEA/H/C/004771/II/0004**<br>AstraZeneca AB, Rapporteur: Sinan B. Sarac | |
| **InductOs - dibotermin alfa - EMEA/H/C/000408/II/0093**<br>Medtronic BioPharma B.V., Rapporteur: Johann Lodewijk Hillege<br>Request for Supplementary Information adopted on 29.11.2018. | |
| **Inflectra - infliximab - EMEA/H/C/002778/II/0070/G**<br>Pfizer Europe MA EEIG, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey<br>Request for Supplementary Information adopted on 13.12.2018. | |
| **KANJINTI - trastuzumab - EMEA/H/C/004361/II/0006/G**<br>Amgen Europe B.V., BREDA, Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 06.12.2018. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Kevzara - sarilumab - EMEA/H/C/004254/II/0011/G**<br>sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus | |
| **Lucentis - ranibizumab - EMEA/H/C/000715/II/0075/G**<br>Novartis Europharm Limited, Rapporteur: Kristina Dunder | |
| **Menveo - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/001095/II/0078/G**<br>GSK Vaccines S.r.l, Rapporteur: Johann Lodewijk Hillege | |
| **Natpar - parathyroid hormone - EMEA/H/C/003861/II/0013/G, Orphan**<br>Shire Pharmaceuticals Ireland Limited, Rapporteur: Bart Van der Schueren | |
| **Natpar - parathyroid hormone - EMEA/H/C/003861/II/0015, Orphan** | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP |

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| Shire Pharmaceuticals Ireland Limited, Rapporteur: Bart Van der Schueren<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 13.12.2018. | Members were in agreement with the CHMP recommendation. |
| **Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0086/G**<br>Pfizer Europe MA EEIG, Rapporteur: Greg Markey<br>Request for Supplementary Information adopted on 06.12.2018. | |
| **Nulojix - belatacept - EMEA/H/C/002098/II/0051**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| **Nulojix - belatacept - EMEA/H/C/002098/II/0052/G**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| **Nulojix - belatacept - EMEA/H/C/002098/II/0053**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Nulojix - belatacept - EMEA/H/C/002098/II/0054/G**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Orencia - abatacept - EMEA/H/C/000701/II/0122/G**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola | |
| **Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0140**<br>CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 15.11.2018. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **RAVICTI - glycerol phenylbutyrate - EMEA/H/C/003822/II/0024, Orphan** | |

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| Horizon Pharma Ireland Limited, Rapporteur: Sinan B. Sarac | |
| **Remsima - infliximab - EMEA/H/C/002576/II/0060/G**<br>Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey<br>Request for Supplementary Information adopted on 13.12.2018. | |
| **Repatha - evolocumab - EMEA/H/C/003766/II/0026/G**<br>Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege<br>Request for Supplementary Information adopted on 17.01.2019, 19.07.2018. | Request for supplementary information adopted with a specific timetable. |
| **Sancuso - granisetron - EMEA/H/C/002296/II/0053/G**<br>Kyowa Kirin Holdings B.V., Rapporteur: Romaldas Mačiulaitis<br>Request for Supplementary Information adopted on 15.11.2018. | |
| **Semglee - insulin glargine - EMEA/H/C/004280/II/0009**<br>Mylan S.A.S, Rapporteur: Martina Weise<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| **Stocrin - efavirenz - EMEA/H/C/000250/II/0116/G**<br>Merck Sharp & Dohme B.V., Duplicate, Duplicate of Sustiva, Rapporteur: Bruno Sepodes<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Trazimera - trastuzumab - EMEA/H/C/004463/II/0002**<br>Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 08.11.2018. | |
| **Trazimera - trastuzumab - EMEA/H/C/004463/II/0005**<br>Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus | |
| **Ucedane - carglumic acid - EMEA/H/C/004019/II/0002/G**<br>Eurocept International B.V., Generic, Generic of Carbaglu, Rapporteur: Eleftheria Nikolaidi<br>Request for Supplementary Information adopted on 15.11.2018. | |

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| **Xofigo - radium-223 - EMEA/H/C/002653/II/0034**<br>Bayer AG, Rapporteur: Janet Koenig<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 18.10.2018. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1420**<br>**Ambirix-EMEA/H/C/000426/WS1420/0092**<br>**Twinrix Adult-EMEA/H/C/000112/WS1420/0126**<br>**Twinrix Paediatric-EMEA/H/C/000129/WS1420/0127**<br>GlaxoSmithkline Biologicals SA, Lead Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 08.11.2018. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1432**<br>**Ambirix-EMEA/H/C/000426/WS1432/0093**<br>**Twinrix Adult-EMEA/H/C/000112/WS1432/0127**<br>**Twinrix Paediatric-EMEA/H/C/000129/WS1432/0128**<br>GlaxoSmithkline Biologicals SA, Lead Rapporteur: Robert James Hemmings<br>Request for Supplementary Information adopted on 17.01.2019, 08.11.2018. | Request for supplementary information adopted with a specific timetable. |
| **WS1475**<br>**Infanrix hexa-EMEA/H/C/000296/WS1475/0249**<br>GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1479/G**<br>**Halimatoz-EMEA/H/C/004866/WS1479/0001/G**<br>**Hefiya-EMEA/H/C/004865/WS1479/0001/G**<br>**Hyrimoz-EMEA/H/C/004320/WS1479/0001/G**<br>Sandoz GmbH, Lead Rapporteur: Milena Stain, Lead PRAC Rapporteur: Ulla Wändel Liminga<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| on 22.11.2018. | |
| **WS1480**<br>**Rixathon-EMEA/H/C/003903/WS1480/0015**<br>**Riximyo-EMEA/H/C/004729/WS1480/0015**<br>Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 29.11.2018. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1500/G**<br>**HyQvia-EMEA/H/C/002491/WS1500/0045/G**<br>**Kiovig-EMEA/H/C/000628/WS1500/0086/G**<br>Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| **WS1546/G**<br>**Abseamed-EMEA/H/C/000727/WS1546/0081/G**<br>**Binocrit-EMEA/H/C/000725/WS1546/0081/G**<br>**Epoetin alfa**<br>**Hexal-EMEA/H/C/000726/WS1546/0080/G**<br>Hexal AG, Duplicate, Duplicate of Binocrit, Lead Rapporteur: Alexandre Moreau | |
| **WS1548**<br>**Abseamed-EMEA/H/C/000727/WS1548/0080**<br>**Binocrit-EMEA/H/C/000725/WS1548/0080**<br>**Epoetin alfa**<br>**Hexal-EMEA/H/C/000726/WS1548/0079**<br>Hexal AG, Duplicate, Duplicate of Binocrit, Lead Rapporteur: Alexandre Moreau | |
| **Hexacima-EMEA/H/C/002702/WS1496/0085/G**<br>**Hexaxim-EMEA/H/W/002495/WS1496/0090/G**<br>**Hexyon-EMEA/H/C/002796/WS1496/0089/G**<br>Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus | |

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

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| **ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0003**<br>Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, "Update to the section 5.1 of the SmPC to revise information on perioperative management including the number of surgical procedures, dosing and haemostatic efficacy based on the results from the final clinical study report for the surgery study 261204."<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0020**<br>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."<br>Request for Supplementary Information adopted on 17.01.2019, 22.11.2018. | Request for supplementary information adopted with a specific timetable. |
| **Biktarvy - bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449/II/0008/G**<br>Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, "Update of section 4.5 of the SmPC in order to remove the recommendation for caution when methadone is co-administered with Biktarvy based on final results from study AD-141-2321, an in vitro assessment of human Cytochrome P450 inhibition potential of GS-943389 (the sulfate metabolite, M20, of bictegravir). The Package Leaflet is updated accordingly.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to remove reference to boceprevir in sections 4.4 and 4.5 of the SmPC and in the Package Leaflet as it is no longer available in the EU; as well as to introduce some minor editorial corrections throughout the SmPC, Annex II and Package Leaflet.<br>Submission of the final report from study AD-141-2322, an in vitro assessment of the inhibition potential of GS-943389 against human P-gp and BCRP transporters." | |
| **Bronchitol - mannitol - EMEA/H/C/001252/II/0034, Orphan**<br>Pharmaxis Pharmaceuticals Limited, Rapporteur: | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP |

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| Nithyanandan Nagercoil, "Update of sections 4.8 and 5.1 of the SmPC in order to update the frequency of certain adverse events and to update the clinical safety and efficacy information based on the results of the clinical data from Study CF 303. This is a phase 3 safety and efficacy clinical trial in adult cystic fibrosis subjects. The package leaflet is updated accordingly.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in the product information and correct the Annex A."<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 08.11.2018. | recommendation. |
| **Dynastat - parecoxib - EMEA/H/C/000381/II/0075**<br>Pfizer Europe MA EEIG, Duplicate, Duplicate of Xapit (SRD), Rapporteur: Jayne Crowe, "Update section 4.4 of the SmPC in regard of the co-administration of NSAIDs and antiplatelet drugs as a class, and the association with an increased risk of gastrointestinal bleeding. The opportunity has been take for minor editorial amendments to be made in the SmPC, Labelling and Package Leaflet."<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| **Edurant - rilpivirine - EMEA/H/C/002264/II/0032**<br>Janssen-Cilag International NV, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.9 of the SmPC to remove the advice on the use of activated charcoal in the event of an overdose and to include advice to contact a poison control centre to obtain the latest recommendations for the management of an overdose." | |
| **ELOCTA - efmoroctocog alfa - EMEA/H/C/003964/II/0030**<br>Swedish Orphan Biovitrum AB (publ), Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2 and 4.8 of the SmPC in order to remove the class wording that no data are available in previously untreated patients and update the Frequency category for Blood and lymphatic system disorders in previously untreated patients following interim results from study 997HA306, this is an ongoing open-label, | |

single-arm, multicentre study evaluating the safety and efficacy of rFVIIIFc in paediatric previously untreated patients with severe haemophilia A when used according to local standard of care; the Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to delete the non-mandatory list of local representatives."

**Eylea - aflibercept - EMEA/H/C/002392/II/0050**

Bayer AG, Rapporteur: Alexandre Moreau, "Submission of the final report from study Study 16995, PLANET. This is a category 4 international randomized, double-masked, sham-controlled phase 4 study to evaluate the efficacy and safety of intravitreal aflibercept (IVT-AFL) monotherapy compared with IVTAFL with rescue PDT (photodynamic therapy) in patients with Polypoidal Choroidal Vasculopathy (PCV), subtype of neovascular age-related macular degeneration (wAMD)."

**Ferriprox - deferiprone - EMEA/H/C/000236/II/0126/G**

Apotex Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update safety information on the use of Ferriprox in patients with renal or hepatic impairment, based on the final results of two clinical studies LA39-0412 (An Open-Label Study to Compare the Pharmacokinetic Profiles of a Single Dose of Ferriprox in Subjects with Impaired Renal Function and Healthy Volunteers) and LA40-0412 (An Open-Label Study to Compare the Pharmacokinetic Profiles of a Single Dose of Ferriprox in Subjects with Impaired Hepatic Function and Healthy Volunteers). The studies are listed as category 3 study in the RMP. The Package leaflet and labelling are updated accordingly. The RMP version 13.1 has also been submitted to include consequential changes regarding these two clinical studies minor changes requested to be addressed at the next regulatory procedure, as well as the RMP format is updated to conform to GVP Module V Rev 2 template.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make some minor edits in the PI."

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| Request for Supplementary Information adopted on 15.11.2018. | |
| **Firdapse - amifampridine - EMEA/H/C/001032/II/0060, Orphan**<br>BioMarin International Limited, Rapporteur: Kristina Dunder, "Update section 5.1 of the SmPC to include results from study LMS-003: a double-blind, placebo-controlled, paralell group study to evaluate the efficacy and safety of amifampridine in patients with Lambert-Eaton Myasthenic Syndrome (LEMS)."<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| **Firdapse - amifampridine - EMEA/H/C/001032/II/0061, Orphan**<br>BioMarin International Limited, Rapporteur: Kristina Dunder, "Submission of the final reports from non-clinical studies (vpt 5604,vpt5336, vpt5401 and 100034669) on dependence and off-target effects as agreed during the last Annual Re-assessment."<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0084**<br>AstraZeneca AB, Rapporteur: Bart Van der Schueren, "Update of section 4.6 of the SmPC to include new information from a publication on breast-feeding. (Brady et al., 2018). The variation also includes recommendations from the Renewal procedure (EMEA/H/C/002617/0079) which included removal of the additional monitoring section, as well as updates from recommendations in the new EMA Guidelines for Vaccines. The Package Leaflet is updated accordingly.<br>In addition, the Marketing Authorisation Holder (MAH) took the opportunity to introduce minor editorial changes to the Product Information."<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 08.11.2018. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0028**<br>MSD Vaccins, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to consolidate the existing information following a | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| request of the CHMP (EMEA/H/C/003852/II/0024/G).<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."<br>Opinion adopted on 17.01.2019. | |
| **Halaven - eribulin - EMEA/H/C/002084/II/0047**<br>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."<br>Request for Supplementary Information adopted on 29.11.2018. | |
| **Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0102**<br>CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of section 2 of the SmPC in order to update the IgG subclass values according to performed analyses. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to make some editorial changes in the package leaflet."<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **IBRANCE - palbociclib - EMEA/H/C/003853/II/0016**<br>Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to update with information following submission of the final results from study the pivotal Study A5481023 "A double blind, Phase 3 trial of fulvestrant with or without palbociclib in pre- and postmenopausal women with hormone receptor positive, HER2-negative metastatic breast cancer that progressed on prior endocrine therapy" listed as a recommendation at the time of initial MA." | |
| **Instanyl - fentanyl - EMEA/H/C/000959/II/0047/G**<br>Takeda Pharma A/S, Rapporteur: Alexandre Moreau, "Update of section 4.4. to revise the risks of respiratory depression and the risks in patients with Chronic Obstructive Pulmonary Disease based on cumulative safety data respectively. Update of section 4.5 with regards | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

interactions with others CNS depressants and skeletal muscle relaxants based on literature data. Update of section 4.8 to add loss of consciousness. Update of section 4.3 and 4.5 to reflect the contraindication with sodium oxybate. The PL is updated accordingly. The MAH took this opportunity to update the labelling in line with QRD latest templates."
Opinion adopted on 17.01.2019.
Request for Supplementary Information adopted on 15.11.2018.

**Isentress - raltegravir - EMEA/H/C/000860/II/0078/G**

Merck Sharp & Dohme B.V., Rapporteur: Greg Markey, "Update of section 4.5 of the SmPC to reflect the data from 3 in vitro studies evaluating the inhibitory effect of raltegravir at higher concentrations on OATP1B3, OCT1, OCT2, MATE1 and MATE2-K transporters and CYP2B6, CYP2D6, UGT2B7 enzyme activities, and a final CSR undertaken to assess the drug-drug interaction (DDI) potential of raltegravir at a 1,200 mg once daily clinical dose."
Request for Supplementary Information adopted on 29.11.2018, 13.09.2018.

**Kuvan - sapropterin - EMEA/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 concomitanly based on pharmacokinetic study in healthy volunteers."
Request for Supplementary Information adopted on 18.10.2018.

**LUTATHERA - lutetium (177Lu) oxodotreotide - EMEA/H/C/004123/II/0005, Orphan**

Advanced Accelerator Applications, Rapporteur: Robert James Hemmings, "Update of the SmPC section 5.1 to include information on the quality of life based on analysis of Netter-I Quality of Life data."
Request for Supplementary Information adopted on 22.11.2018, 20.09.2018.

**Mycamine - micafungin - EMEA/H/C/000734/II/0039**

Astellas Pharma Europe B.V., Rapporteur: Janet

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| Koenig, "Update of section 4.4 of the SmPC in order to update the safety information, based on the Final Mortality Report and the 30-day Reanalysis Report from the MYCOS Study. The MYCOS Study is a post-authorisation commitment (MEA 013.7) to investigate the short and long-term safety of micafungin and other parenteral antifungal agents.<br>In addition, the MAH took the opportunity to implement a statement on a sodium excipient in the Package Leaflet, in accordance with the Annex of the updated Guideline on Excipient Labelling (EMA/CHMP/302620/2017)." | |
| **Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0008**<br>Roche Registration GmbH, Rapporteur: Mark Ainsworth, "Submission of the final report for Study 15-3109, an 8-week immunotoxicity study of ocrelizumab by intravenous injection in juvenile cynomolgus monkeys with a 9-month recovery period, to address a CHMP recommendation."<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Orfadin - nitisinone - EMEA/H/C/000555/II/0067**<br>Swedish Orphan Biovitrum International AB, Rapporteur: Daniela Melchiorri, "Update of sections 4.4 and 4.5 to add a warning on interaction with medicinal products with a narrow therapeutic window metabolized through CYP2C9 and information based on in vitro and in vivo drug drug interaction studies investigating effects of nitisinone on cytochromes CYP2C9, CYP1A2, CYP2B6, CYP3A4/5, P-gp, BCRP, OATP1B1, OATP1B3 or OCT2-mediated transport. This update is following PRAC conclusions on PSUSA (EMEA/H/CPSUSA/00002169/201802) adopted on 6 September 2018." | |
| **Orgalutran - ganirelix - EMEA/H/C/000274/II/0041**<br>Merck Sharp & Dohme B.V., Rapporteur: Outi Mäki-Ikola, "Update of section 4.3 of the SmPC to expand the existing contraindication regarding hypersensitivity to include also wording regarding dry natural rubber/latex and sections 4.4 and 6.5 of the SmPC to clarify that this product is in contact with dry natural rubber/latex. The labelling and Package Leaflet have been updated accordingly. In addition, the | |

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| MAH took the opportunity to update the contact details of the local representative in Belgium in the Package Leaflet."<br>Request for Supplementary Information adopted on 20.09.2018, 26.07.2018. | |
| **Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0114**<br>Boehringer Ingelheim International GmbH, Rapporteur: Mark Ainsworth, "Update of section 5.1 of the SmPC based on the final results of the Graham et al. study; this is a non-interventional Medicare study in US patients over 65 years of age comparing patients initiating dabigatran or warfarin for the treatment of non-valvular atrial fibrillation.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to make some corrections throughout the PI, update the contact details of the Austrian local representative in the package leaflet, to align section 2 of the package leaflet with section 4.3 of the SmPC and section 3 of the package leaflet with section 4.2 of the SmPC, and to make corrections to the Bulgarian and French translations." | |
| **PREVYMIS - letermovir - EMEA/H/C/004536/II/0009, Orphan**<br>Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to update the information on drug-drug interaction between letermovir and fluconazole based on the interim results from study MK-8228-037; this is an open-label, 3-period, fixed-sequence trial to evaluate the effect of single-dose administration of letermovir on the single-dose PK of fluconazole, and the effect of single dose administration of fluconazole on the single-dose PK of letermovir in healthy females. In addition, the Marketing authorisation holder (MAH) took the opportunity include minor editorial changes in the product information."<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| **Remicade - infliximab - EMEA/H/C/000240/II/0217**<br>Janssen Biologics B.V., Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to add the adverse drug reaction "acute generalised exanthematous pustulosis (AGEP)" with a frequency rare. The package leaflet is | |

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| updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet."<br>Request for Supplementary Information adopted on 15.11.2018. | |
| **Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0046**<br>Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, "Update of the PI to align with the company's Core Safety Data Sheet:<br>· Update of information related to liver function tests, thrombotic and thromboembolic complications, MDS in the section 4.4;<br>· Update of DDI and food interaction information in the sections 4.5 and 5.2;<br>· Update of the section 4.8 by: inclusion and removal of ADRs, changes in some ADRs frequencies following pooling of safety data;<br>· Reorganisation of the section 5.1 in relation to severe aplastic anaemia;<br>· Update of the section 5.3 with information related to Juvenile animal studies.<br>The MAH took the opportunity to make some editorial changes throughout the PI. The Package leaflet is updated accordingly."<br>Request for Supplementary Information adopted on 11.10.2018, 03.05.2018. | |
| **Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0053**<br>Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, "Update of section 4.4 and 4.8 of the SmPC in order to extend the warning on cytogenetic abnormalities to reflect the incidence of new genetic abnormalities following data from study ELT116826 (AUS18T) – An open-label, single center, non-randomized, Phase 2, dose modification study Pilot Study of a Thrombopoietin-Receptor Agonist (TPO-R Agonist), Eltrombopag, in Aplastic Anemia Patients With Immunosuppressive-Therapy Refractory Thrombocytopenia. listed as a category 3 study in the RMP"<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 15.11.2018. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Ryzodeg - insulin aspart / insulin degludec - EMEA/H/C/002499/II/0030/G**<br>Novo Nordisk A/S, Rapporteur: Kristina Dunder, "Update of sections 4.2 and section 5.1 of the | |

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| SmPC in order to update the information on dosing and administration interval of Ryzodeg (insulin aspart/insulin degludec) based on data from 2 trials:<br>• NN5401-4266, a 38 week trial comparing effect and safety of insulin degludec/insulin aspart vs. insulin glargine plus insulin aspart in subjects with type 2 diabetes treated with basal insulin with or without oral antidiabetic treatment in need of treatment intensification.<br>• NN5401-3996, a 26-week trial comparing efficacy and safety of insulin degludec/insulin aspart BID and insulin degludec OD plus insulin aspart in subjects with type 2 Diabetes Mellitus treated with basal insulin in need of treatment intensification with mealtime insulin.<br>In addition, the MAH took the opportunity to make editorial changes in the SmPC." | |
| **Skilarence - dimethyl fumarate - EMEA/H/C/002157/II/0008/G**<br>Almirall S.A, Rapporteur: Robert James Hemmings, "Submission of the final report from study AML/27. This is an in vitro study aimed to assess the potential of dimethyl fumarate to inhibit human hepatic cytochrome P450 (CYP) enzymes.<br>Submission of the final report from study AML/28. This is an in vitro study aimed to assess the potential interaction of dimethyl fumarate with p-glycoprotein (P-gp).<br>Submission of the final report from study Almirall-15-05May2017. This is an in vitro study aimed to assess the interaction of dimethyl fumarate with human BCRP efflux (ABC) transporters."<br>Request for Supplementary Information adopted on 17.01.2019, 13.09.2018. | Request for supplementary information adopted with a specific timetable. |
| **Symkevi - tezacaftor / ivacaftor - EMEA/H/C/004682/II/0002/G, Orphan**<br>Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.5 of the SmPC with the results of the following 4 non-clinical drug-drug interaction (DDI) studies :<br>Results from Study O092: Evaluation of VRT-1189001 as an Inducer of CYP1A2 and CYP2B6 using Primary Cryopreserved Human Hepatocytes<br>Results from O093: Evaluation of VRT-0996107 as an Inducer of CYP2B6 using Primary | Request for supplementary information adopted with a specific timetable. |

Cryopreserved Human Hepatocytes
Results from OPT-2018-041: Assessment of VRT-0893661, VRT-0996107, VRT-1189001 and VRT-1074233 as inhibitors of human OCT1, MATE1, MATE2-K, and BSEP mediated transport
Results fOPT-2018-040: Assessment of VRT-0813077, VRT-0837018 and VRT-0842917 as substrates of human BCRP mediated transport.
The MAH took the oportunity to introduce some additional minor updates in the Product information."
Request for Supplementary Information adopted on 17.01.2019.

**Telzir - fosamprenavir - EMEA/H/C/000534/II/0094/G**

ViiV Healthcare B.V., Rapporteur: Joseph Emmerich, "Update of sections 4.3 and 4.5 of the SmPC in order to implement information on a drug-drug interaction between fosamprenavir (with or without ritonavir) and the antipsychotic lurasidone and update of sections 4.4 and 4.5 of the SmPC in order to implement information on a drug-drug interaction between fosamprenavir (with or without ritonavir) and various antineoplastic agents (including dasatinib, nilotinib, ibrutinib, vinblastine, everolimus), based on an assessment of recent safety data. The Package Leaflets are updated accordingly."

**Translarna - ataluren - EMEA/H/C/002720/II/0049, Orphan**

PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "Submission of the final CSR for study PTC124-GD-030-DMD (Study 030) listed as a category 3 study in the RMP. This is a phase 2 Study of the safety, pharmacokinetics, and pharmacodynamics of ataluren in patients aged ≥2 to <5 years with nonsense mutation dystrophinopathy (nmDMD). This submission is also made in accordance with the requirements of the Article 46 of the Paediatric Regulation."

**Trulicity - dulaglutide - EMEA/H/C/002825/II/0032**

Eli Lilly Nederland B.V., Rapporteur: Greg Markey, "Update of section 4.4 of the SmPC, following a cumulative review of Acute Kidney Injury events undertaken upon request by PRAC (EPITT No 19204), to add information regarding

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| the potential for dulaglutide to possibly contribute to the volume depletion event, which could indirectly contribute to the occurrence of AKI. The Package Leaflet has been updated accordingly."<br>Request for Supplementary Information adopted on 15.11.2018. | |
| **Veltassa - patiromer - EMEA/H/C/004180/II/0007**<br>Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Jayne Crowe, "Update of section 4.2, 4.5 and 5.1 of the SmPC to reflect the results of study RLY5016-401;an Open-Label, Randomized, Parallel Group Phase 4 Study of the Efficacy and Safety of Patiromer for Oral Suspension With or Without Food for the Treatment of Hyperkalemia (TOURMALINE). The PL has been updated accordingly."<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| **Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0196**<br>Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, "Submission of the final abbreviated clinical study report from the post-authorisation safety study (PASS) GS-EU-174-1403, a pharmacoepidemiology study to define the long-term safety profile of tenofovir disoproxil fumarate (TDF) and describe the management of TDF-associated renal and bone toxicity in Chronic Hepatitis B (CHB)-infected adolescents aged 12 to <18 years in Europe, listed in the Viread RMP as a category 3 study. This submission fulfils this additional pharmacovigilance activity and fulfils the post-authorisation measures MEA 255.1, MEA 255.2 and MEA 265.8."<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0005, Orphan**<br>Ipsen Pharma, Rapporteur: Janet Koenig, "Update of section 5.2 of the SmPC in order to add information from an in vivo drug interaction study (study identifier: LX1606.1-110-NRM) to evaluate the effect of multiple doses of concomitant gastric acid reducers such as PPIs on the PK of telotristat ethyl, LP-778902."<br>Request for Supplementary Information adopted on 15.11.2018. | |

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| **Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/II/0067**<br>Bial - Portela & Cª, S.A., Rapporteur: Martina Weise, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect the long-term safety and efficacy data obtained from the open-label extensions (parts II to V) of the phase III study BIA-2093-305. The study was assessed in procedure EMA/H/C/988/P46 025."<br>Request for Supplementary Information adopted on 15.11.2018. | |
| **Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0038**<br>Pfizer Ireland Pharmaceuticals, Rapporteur: Greg Markey, "Update of section 4.2 of the SmPC to amend the recommended duration of ceftaroline fosamil intravenous (IV) infusion for standard dose regimens in adults and paediatrics to a range of 5 to 60 minutes from the currently recommended infusion duration of 1 hour. The PIL is updated accordingly. In addition the MAH has also taken the opportunity to reformat section 4.2 of the SmPC Posology and method of administration and to incorporate minor editorial updates to sections 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC."<br>Request for Supplementary Information adopted on 20.09.2018. | |
| **Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0042**<br>Pfizer Ireland Pharmaceuticals, Rapporteur: Alar Irs, "Update of section 4.8 of the SmPC to include revised frequency of the adverse drug reaction (ADR) eosinophilia from not known to rare. The Package leaflet is updated accordingly." | |
| **WS1422**<br>**CONTROLOC**<br>**Control-EMEA/H/C/001097/WS1422/0030**<br>**PANTOLOC**<br>**Control-EMEA/H/C/001100/WS1422/0034**<br>**PANTOZOL**<br>**Control-EMEA/H/C/001013/WS1422/0032**<br>**SOMAC**<br>**Control-EMEA/H/C/001098/WS1422/0031**<br>Takeda GmbH, Lead Rapporteur: Greg Markey, "Update of section 5.3 of the SmPC in order to update the safety information based on the final results of study 14GR325 "A pre- and postnatal developmental toxicity study of pantoprazole | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

sodium (PF-05208751) by oral gavage in rats focused on postnatal evaluation of bone development" as required by the PRAC Recommendation of EMEA/H/C/PSUSA/00002285/201708."
Opinion adopted on 17.01.2019.
Request for Supplementary Information adopted on 20.09.2018.

**WS1451**
**Keppra-EMEA/H/C/000277/WS1451/0173**
UCB Pharma S.A., Lead Rapporteur: Koenraad Norga, "Update of section 4.8 of the SmPC in order to add delirium (with frequency unknown) as adverse drug reaction based on results of category 4 .
In addition, the Worksharing applicant (WSA) took the opportunity to correct a typological error in section 4.2: addition of equals sign in creatinine clearance values equal to or above 80 ml/min/1.73 m2.
The Labelling is updated in accordance."

**WS1504**
**Bexsero-EMEA/H/C/002333/WS1504/0071**
**Menveo-EMEA/H/C/001095/WS1504/0079**
GSK Vaccines S.r.l, Lead Rapporteur: Kristina Dunder, "Update of Section 4.4 of the SmPC for the four GSK's meningococcal vaccines (i.e. Bexsero, Menveo, Menjugate and Menitorix) to add a warning relative to individuals receiving treatment that inhibits terminal complement activation (for example eculizumab). The proposed change is based on results from clinical study V72-28, performed on Bexsero.
The Package Leaflets (PL) are updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to amend the list of local representatives in the PL of Bexsero and Menveo. Minor editorial updates in the SmPC of Bexsero and Menveo are also carried out."

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

**Avastin - bevacizumab -**
**EMEA/H/C/000582/II/0106/G**
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "1) Type

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| 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.<br>2) Type IB Variation (C.I.11.z): Change in the deadline for the fulfilment of ANX 086 from Q4 2018 to Q2 2019.<br>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)."<br>Request for Supplementary Information adopted on 18.10.2018. | |
| **Daklinza - daclatasvir - EMEA/H/C/003768/II/0031**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of section 5.1 of the SmPC in order to add information on long-term efficacy and drug resistance based on final results from study AI444046, listed as a category 3 study in the RMP. This is a phase 3 non-randomized, open-label, long-term follow-up and observational study of durability of efficacy, resistance and characterization of progression of liver disease in subjects with chronic hepatitis C previously treated with daclatasvir and/or asunaprevir.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to postpone the due date of the safety study AI444427 evaluating recurrence of hepatocellular carcinoma. Annex II is updated in accordance.<br>The RMP version 6.0 has also been submitted."<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| **Darzalex - daratumumab - EMEA/H/C/004077/II/0020, Orphan**<br>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 smoldering multiple myeloma, including data evaluating the relationship between daratumumab concentration and QTc prolongation; consequently, onsequently, the RMP is updated (version 4.0) in order to remove QTc prolongation as an Important Potential Risk from the RMP." | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 29.11.2018. | |
| **Esmya - ulipristal acetate - EMEA/H/C/002041/II/0045/G**<br>Gedeon Richter Plc., Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Submission of the final study reports from the 5 mechanistic in vitro studies following Esmya Article 20 referral procedure (EMEA/H/A-20/1460/C/2041/0043). These are 3083-N03-050 (PAM MEA 020), 3083-N04-050 (PAM MEA 021), 3083-N05-050 (PAM MEA 022), 3083-N01-050 (PAM REC) and 3083-N02-050 (PAM REC). In addition, the MAH submitted updated RMP version 16.1, as part of this application."<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| **Hepsera - adefovir dipivoxil - EMEA/H/C/000485/II/0081**<br>Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Adrien Inoubli, "Update of RMP to version 2.1 in order to bring it to the new revision 2 template. As a result, the safety concerns are being updated."<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Hulio - adalimumab - EMEA/H/C/004429/II/0004**<br>Mylan S.A.S, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from study (FKB327-003) listed as a category 3 study in the RMP. This is an open-label extension study to compare the long term efficacy, safety, immunogenicity and pharmacokinetics of Hulio and Humira in patients with rheumatoid arthritis on concomitant methotrexate (ARABESC-OLE). The RMP version 2.0 is updated accordingly. In addition, the MAH took the opportunity to remove the product information texts from Annex 6 of the RMP and would like to only keep the text for patient alert card in the RMP as additional risk minimisation measures."<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| **IMVANEX - modified vaccinia ankara virus - EMEA/H/C/002596/II/0035**<br>Bavarian Nordic A/S, Rapporteur: Greg Markey, | Request for supplementary information adopted with a specific timetable. |

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| 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."<br>Request for Supplementary Information adopted on 17.01.2019, 04.10.2018. | |
| **Kisqali - ribociclib - EMEA/H/C/004213/II/0003/G**<br>Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver, "C.I.4: Update of section 5.2 of the SmPC in order to reflect on results from study CLEE011A2109: A Phase I, open label, multi-centre, parallel cohort, single dose study to evaluate the pharmacokinetics of LEE011 in healthy subjects with normal hepatic function and subjects with impaired hepatic function; C.I.4: Update of section 4.2 and 5.2 of the SmPC in order to reflect on results from study CLEE011A2116-Part I: A phase I, open label, multicentre, parallel-group, single dose two-staged study to evaluate the pharmacokinetics and safety of a single 400 mg oral dose of LEE011 in subjects with varying degrees of impaired renal function compared to matched healthy volunteers with normal renal function.<br>The RMP version 2.0 has also been submitted."<br>Request for Supplementary Information adopted on 17.01.2019, 06.09.2018. | Request for supplementary information adopted with a specific timetable. |
| **MabThera - rituximab - EMEA/H/C/000165/II/0157**<br>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."
Request for Supplementary Information adopted on 29.11.2018.

**MabThera - rituximab - EMEA/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 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

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| to include the changes on the concluded commitment such as the prolonged B-cell depletion and immunogenicity associated with the subcutaneous formulation."<br>Request for Supplementary Information adopted on 29.11.2018. | |
| **Mircera - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/II/0068**<br>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."<br>Request for Supplementary Information adopted on 17.01.2019, 04.10.2018. | Request for supplementary information adopted with a specific timetable. |
| **NovoMix - insulin aspart - EMEA/H/C/000308/II/0095**<br>Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of sections 4.2, 4.5 and 5.1 of the SmPC to include data on the use of NovoMix® 30 combination use with GLP-1 receptor agonists. The PIL is updated accordingly. The RMP is laso updated (version 3)"<br>Request for Supplementary Information adopted on 15.11.2018, 20.09.2018. | |
| **TAGRISSO - osimertinib - EMEA/H/C/004124/II/0026**<br>AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst, "C.I.11: Submission of an updated RMP version 12.0 following the completion of study D6030C00001 (BLOOM) (A Phase I, Open-label, Multicentre Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Anti-Tumour Activity of AZD9291 in Patients with EGFR Mutation Positive Advanced Stage Non-Small Cell Lung Cancer [NSCLC]; BLOOM in order to remove the following safety concerns | |

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| included as missing information: Use in patients with ECOG performance status≥2" and "Use in patients with symptomatic brain metastases."<br>Request for Supplementary Information adopted on 15.11.2018. | |
| **Toujeo - insulin glargine - EMEA/H/C/000309/II/0105/G**<br>Sanofi-Aventis Deutschland GmbH, Duplicate, Duplicate of Lantus, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst<br>Request for Supplementary Information adopted on 13.12.2018, 20.09.2018. | |
| **Yervoy - ipilimumab - EMEA/H/C/002213/II/0063**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4 and 4.8 of the SmPC and of annex II in order to add safety information regarding Graft Versus Host Disease (GVHD) in allogeneic hematopoietic stem cell transplant (HSCT) recipients after treatment with ipilimumab. The update is based on a review of post-marketing data. The Package Leaflet and the RMP (version 25.0) is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some editorial changes in the PI and RMP and to include some changes in the RMP due to previous procedures."<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| **Zykadia - ceritinib - EMEA/H/C/003819/II/0026**<br>Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Annika Folin, "Update of section 4.2, 4.5 and 5.2 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."<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| Request for Supplementary Information adopted on 29.11.2018. | |

**B.5.4. PRAC assessed procedures**

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| PRAC Led<br>**Abraxane - paclitaxel - EMEA/H/C/000778/II/0092**<br>Celgene Europe BV, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of the RMP to version 17.1 in order to reclassify known safety concerns in accordance with the new Guideline on Good Pharmacovigilance Practices (GVP) Module V, version 2."<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 31.10.2018. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**Betmiga - mirabegron - EMEA/H/C/002388/II/0030**<br>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."<br>Request for Supplementary Information adopted on 17.01.2019, 04.10.2018. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**Bydureon - exenatide - EMEA/H/C/002020/II/0054**<br>AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final study report, upon request by PRAC following the assessment of MEA 11.5, from study H8O-MC-B015 extension/ D5550R00003; 'Incidence of Pancreatic Malignancy and Thyroid Neoplasm in Type 2 Diabetes Mellitus Patients who Initiate Exenatide Compared to Other Antihyperglycemic Drugs', as well as the feasibility study 'Incidence of pancreatic cancer and thyroid neoplasm among type 2 diabetes patients who initiated Bydureon (exenatide) as compared with those who initiated other glucose | Request for supplementary information adopted with a specific timetable. |

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| lowering drugs'. An updated RMP (version 32) was provided as part of the application."<br>Request for Supplementary Information adopted on 17.01.2019. | |
| PRAC Led<br>**Cayston - aztreonam - EMEA/H/C/000996/II/0075, Orphan**<br>Gilead Sciences Ireland UC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP (version 7.1) for Cayston in order to comply with Revision 2 of the EU-RMP template, in accordance with the revised guidance in the Guideline on good pharmacovigilance practices (GVP) Module V (EMA/838713/2011; Revision 2)."<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0072**<br>UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP (version 14.1) in order to revise it in line with the new RMP template (GVP Module V rev.2) including the update of the important identified risks, important potential risks and missing information, to stop the distribution of prescriber guide, to update the protocol of UP0038 study and to rename patient alert card by patient reminder card. The SmPC, Annex II and package leaflet are updated accordingly. In addition, the MAH took the opportunity to make some administrative changes in the RMP."<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 31.10.2018. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0074/G**<br>UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from studies (RA0021 and RA005) listed as a category 3 studies in the RMP. Study RA0021 (ARTIS registry) is to provide short- and long-term safety | Request for supplementary information adopted with a specific timetable. |

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| data from the use of certolizumab pegol (CZP) in Sweden for rheumatoid arthritis (RA) patients. Study RA005 (NBD registry) is to obtain safety and outcome data on RA patients receiving CZP and other RA treatments. In addition, the MAH submitted interim results for two ongoing registries studies (RA0020/RABBIT and RA0022/BSRBR). Study RA0020/RABBIT is a German long-term observation of biologics/ DMARD in RA. Study RA0022/BSRBR is a longitudinal observational study of patients with RA treated with biologic agents, and prospective surveillance study for adverse events."<br>Request for Supplementary Information adopted on 17.01.2019. | |
| PRAC Led<br>**Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0043**<br>Merck Sharp & Dohme B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "C.I.11.b (type II): Submission of an updated RMP version 8.1 in order to implement revision 2 of the RMP template and to include data following completion of study P017, a phase III follow-up trial to collect outcome and safety of frozen-thawed embryo transfer (FTET) cycles performed with the embryos cryopreserved in studies P016 and P031, as requested as part of the assessment of PSUSA/00000875/201407 and to delete the important potential risks 'hypersensitivity' and 'lack of effect due to immunogenicity' from the list of safety concerns as requested as part of PSUSA/00000875/201707. In addition the MAH has taken the opportunity to include some data from the ongoing study P043, a multi-centre, open label, single-group trial to investigate the efficacy and safety of corifollitropin alfa in combination with hCG for initiation or restoration of puberty assessed by increased testicular volume in adolescent males 14 to < 18 years old with HH."<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**Eviplera - emtricitabine / rilpivirine / tenofovir disoproxil - EMEA/H/C/002312/II/0098**<br>Gilead Sciences Ireland UC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 14.0 in order to 1) implement Revision 2 of the EU-RMP template, 2) remove certain safety concerns in line with the new RMP guidance and based on exposure data from clinical studies and post-marketing use and 3) change the Marketing Authorisation Holder name from Gilead Sciences International Ltd., Cambridge, UK (GSIL) to Gilead Sciences Ireland UC, Cork, Ireland (GSIUC)."<br>Opinion adopted on 17.01.2019. | |
| PRAC Led<br>**Humira - adalimumab - EMEA/H/C/000481/II/0185**<br>AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from The Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT) registry, an ongoing long-term observational cohort study initiated in Germany in 2001 by The German Society of Rheumatology to investigate the long-term safety, effectiveness, and costs of biologic therapies for rheumatoid arthritis, listed as a category 3 study in the RMP."<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**Invokana - canagliflozin - EMEA/H/C/002649/II/0040**<br>Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Provision of the final CSR for Study RRA-21651; a retrospective, observational, new-user cohort study using 4 administrative claims databases in the US, undertaken to investigate the incidence of diabetic ketoacidosis among patients with type 2 diabetes mellitus treated with SGLT2 inhibitors or other antihyperglycemic agents."<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**JETREA - ocriplasmin - EMEA/H/C/002381/II/0042/G**<br>Oxurion NV, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "C.I.13z: Submission of the final | Request for supplementary information adopted with a specific timetable. |

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| 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.<br>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).<br>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.<br>In addition, RMP V7.2 has been updated accordingly and the second revision of the RMP template has been implemented as well."<br>Request for Supplementary Information adopted on 17.01.2019, 29.11.2018. | |
| PRAC Led<br>**Mycamine - micafungin - EMEA/H/C/000734/II/0038**<br>Astellas Pharma Europe B.V., Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of an updated RMP version 20.0 in order to streamline and improve the educational programme and communication to physicians prescribing Mycamine as requested in variation II/0035." | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 31.10.2018, 06.09.2018. | |
| PRAC Led<br>**Perjeta - pertuzumab - EMEA/H/C/002547/II/0041**<br>Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final report from the pregnancy registry (H4621g/GE28099; MotHER; listed as a category 3 study in the RMP). This is a an observational study of pregnancy and pregnancy outcomes in women with breast cancer treated with Herceptin (trastuzumab), Perjeta (pertuzumab) in combination with Herceptin, or Kadcyla (ado-trastuzumab emtansine) during pregnancy or within 7 months prior to conception. In addition, the MAH submitted updated RMP version 11, as part of this application"<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**Prolia - denosumab - EMEA/H/C/001120/II/0078/G**<br>Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 25 in order to align with the revised guideline GVP module 5 and addition of two category 3 studies:<br>• Addition of a new category 3 study (20170534), which is an open-label extension of the currently ongoing Study 20130173, a RMP category 3, involving pediatric subjects with osteogenesis imperfecta. This is based on the MAH commitment arising from Prolia approved Pediatric Investigation Plan (EMEA-000145-PIP02-12); open-label, prospective, extension study<br>• Addition of a new category 3 study to further characterize potential increased risk of cerebrovascular events (stroke) and other serious cardiovascular events in subjects with osteoporosis as per Pharmacovigilance Risk Assessment Committee (PRAC) recommendation during Prolia procedure EMEA/H/C/PSUSA/000954/201709. PRAC recommendation was to include the study in the RMP as a category 3 at the next regulatory opportunity; retrospective cohort database | Request for supplementary information adopted with a specific timetable. |

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| study."<br>Request for Supplementary Information adopted on 17.01.2019. | |
| PRAC Led<br>**Remicade - infliximab - EMEA/H/C/000240/II/0218**<br>Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder,<br>"Submission of the final study report on Remicade for the RABBIT Cohort 2 portion of the registry.<br>Rheumatoide Arthritis - Beobachtung der Biologika-Therapie (RABBIT) is a German RA registry established as a prospective observational cohort study on the long-term safety and effectiveness of biologic disease-modifying anti-rheumatic drugs in patients with RA.<br>RMP (v19) was updated with the conclusion of the study. The MAH also revised the list of safety concerns in the RMP as requested in the assessment of LEG 156."<br>Request for Supplementary Information adopted on 17.01.2019. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**RoActemra - tocilizumab - EMEA/H/C/000955/II/0082**<br>Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final study report: "Safety Report On Hypersensitivity In Patients Who Switched Between Tocilizumab Intravenous And Subcutaneous Routes Of Administration" based on safety data from UK BSRBR rheumatoid arthritis registry, WA22479 and ML22928 studies; listed as a category 3 study in the RMP."<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**Simponi - golimumab - EMEA/H/C/000992/II/0085**<br>Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder,<br>"Submission of the final report from study (CNTO148ART4002) listed as a category 3 study in the RMP. This is an observational phase 4 study | Request for supplementary information adopted with a specific timetable. |

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| using the Optum Research Database (ORD) to estimate the long-term safety profile in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) who are initiating Simponi treatment and/or other types of biologic and non-biologic treatments. In addition, the RMP (version 19.0) is updated to reflect the final study report from study CNTO148ART4002 and to revise the list of safety concerns in accordance with the GVP Module V guideline (rev. 2)."<br>Request for Supplementary Information adopted on 17.01.2019. | |
| PRAC Led<br>**Sutent - sunitinib - EMEA/H/C/000687/II/0073**<br>Pfizer Europe MA EEIG, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, "C.I.11: Submission of an updated RMP version 17 in order to review the list of safety concerns to make it more risk proportionate based on any available safety data. The updates are in line with the new GVP Module V (Rev 2) guidelines and new RMP template." | |
| PRAC Led<br>**Vokanamet - canagliflozin / metformin - EMEA/H/C/002656/II/0041**<br>Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Provision of the final CSR for Study RRA-21651; a retrospective, observational, new-user cohort study using 4 administrative claims databases in the US, undertaken to investigate the incidence of diabetic ketoacidosis among patients with type 2 diabetes mellitus treated with SGLT2 inhibitors or other antihyperglycemic agents."<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**WS1270 Enbrel-EMEA/H/C/000262/WS1270/0216 LIFMIOR-EMEA/H/C/004167/WS1270/0013**<br>Pfizer Europe MA EEIG, Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Robert James Hemmings, "Update of section 4.6 of the SmPC in | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| order to update the current safety information on pregnancy based on the final results from study B1801396, a non-interventional PASS listed as a category 3 study in the RMP. This is a non-interventional, population-based, multi-country, observational cohort register study to evaluate the risk of adverse pregnancy outcomes in patients with rheumatoid arthritis and related inflammatory diseases, who were treated with etanercept compared to patients with the same diseases of interest who were treated with non-biologic systemic drugs, but without etanercept or other biologics during pregnancy, using merged data from Sweden, Denmark and Finland. The Package Leaflet is updated accordingly."<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 06.09.2018, 17.05.2018. | |
| PRAC Led<br>**WS1509**<br>**Atripla-EMEA/H/C/000797/WS1509/0138**<br>**Truvada-EMEA/H/C/000594/WS1509/0158**<br>Gilead Sciences Ireland UC, Lead Rapporteur: Janet Koenig, Lead PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of updated RMPs version 17.1 for Atripla and version 15.5 for Truvada, in order to 1) implement Revision 2 of the EU-RMP template and amend the safety concerns accordingly, 2) remove the additional risk minimisation measures for tenofovir disoproxil fumarate in the form of education materials regarding renal toxicity and bone events, with the resulting amendment of Annex II of the product information, 3) add clinical data from study GS-US-104-0352 (A Phase III, Randomized, Open-Label Study Comparing the Safety and Efficacy of Switching Stavudine or Zidovudine to Tenofovir Disoproxil Fumarate Versus Continuing Stavudine or Zidovudine in Virologically Suppressed HIV-Infected Children Taking Highly Active Antiretroviral Therapy), 4) revise the due dates for two category 3 studies, GS-US-276-0103 (A Prospective, Observational Study of Individuals Who Seroconvert While Taking Truvada for Pre Exposure Prophylaxis (PrEP)) and GS-EU-276-4027 (A Cross-Sectional Post Authorization Safety Study to Assess | Request for supplementary information adopted with a specific timetable. |

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| Healthcare Provider's Level of Awareness of Risk Minimisation Materials for Truvada for Pre Exposure Prophylaxis in the European Union) and 5) implement already approved administrative changes."<br>Request for Supplementary Information adopted on 17.01.2019. | |

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

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| **Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - EMEA/H/C/003854/II/0016, Orphan, ATMP**<br>Orchard Therapeutics (Netherlands) BV, Rapporteur: Christiane Niederlaender, CHMP Coordinator: Robert James Hemmings | |
| **YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0003, Orphan, ATMP**<br>Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, Coordinator: Jan Mueller-Berghaus , "Update of the sections 4.8, 5.1 of the SmPC to add information based on Phase 1/2 Multicenter Study Evaluating the Safety and Efficacy of KTE-C19 in Subjects with Refractory Aggressive Non-Hodgkin Lymphoma (ZUMA-1), an addendum presenting 24-month analysis. The Package Leaflet has been updated accordingly.<br>Furthermore, editorial changes have been introduced throughout the PI." | |

### 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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| **WS1469**<br>**Glyxambi-EMEA/H/C/003833/WS1469/0016**<br>**Jentadueto-EMEA/H/C/002279/WS1469/0046**<br>**Trajenta-EMEA/H/C/002110/WS1469/0034**<br>Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 15.11.2018. | |
| **WS1489/G**<br>**Suboxone-EMEA/H/C/000697/WS1489/0039/G**<br>Indivior Europe Limited, Lead Rapporteur: Janet Koenig | |
| **WS1493/G**<br>**Rivastigmine 1A Pharma-EMEA/H/C/001181/WS1493/0025/G**<br>**Rivastigmine Hexal-EMEA/H/C/001182/WS1493/0026/G**<br>**Rivastigmine Sandoz-EMEA/H/C/001183/WS1493/0027/G**<br>Hexal AG, Informed Consent of Exelon, Lead Rapporteur: Alexandre Moreau, | |
| **WS1494**<br>**HyQvia-EMEA/H/C/002491/WS1494/0046**<br>**Kiovig-EMEA/H/C/000628/WS1494/0087**<br>Baxalta Innovations GmbH, Lead Rapporteur: Jan Mueller-Berghaus | |
| **WS1512**<br>**M-M-RVAXPRO-EMEA/H/C/000604/WS1512/0092**<br>**ProQuad-EMEA/H/C/000622/WS1512/0129**<br>**Zostavax-EMEA/H/C/000674/WS1512/0123**<br>MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 17.01.2019. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1513**<br>**Eucreas-EMEA/H/C/000807/WS1513/0072**<br>**Galvus-EMEA/H/C/000771/WS1513/0062**<br>**Icandra-EMEA/H/C/001050/WS1513/0074**<br>**Jalra-EMEA/H/C/001048/WS1513/0063**<br>**Xiliarx-EMEA/H/C/001051/WS1513/0061**<br>**Zomarist-EMEA/H/C/001049/WS1513/0074**<br>Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| Opinion adopted on 17.01.2019. | |
| **WS1516/G**<br>**Blitzima-EMEA/H/C/004723/WS1516/0018/G**<br>**Ritemvia-EMEA/H/C/004725/WS1516/0018/G**<br>**Rituzena-EMEA/H/C/004724/WS1516/0019/G**<br>**Truxima-EMEA/H/C/004112/WS1516/0020/G**<br>Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz | |
| **WS1528**<br>**Rixathon-EMEA/H/C/003903/WS1528/0017**<br>**Riximyo-EMEA/H/C/004729/WS1528/0017**<br>Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus | |
| **WS1537/G**<br>**Humalog-EMEA/H/C/000088/WS1537/0167/G**<br>**Liprolog-EMEA/H/C/000393/WS1537/0128/G**<br>Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder | |
| **WS1549**<br>**Iblias-EMEA/H/C/004147/WS1549/0013**<br>**Kovaltry-EMEA/H/C/003825/WS1549/0021**<br>Bayer AG, Lead Rapporteur: Kristina Dunder | |
| **Hexacima-EMEA/H/C/002702/WS1455/0084/G**<br>**Hexaxim-EMEA/H/W/002495/WS1455/0089/G**<br>**Hexyon-EMEA/H/C/002796/WS1455/0088/G**<br>Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 17.01.2019.<br>Request for Supplementary Information adopted on 08.11.2018. | Positive Opinion adopted by consensus on 17.01.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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

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

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

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

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| **arsenic trioxide - EMEA/H/C/005175**<br>, treatment of relapsed acute promyelocytic leukaemia (APL) |
| **budesonide / glycopyrronium / formoterol fumarate dihydrate - EMEA/H/C/004983**<br>, as a maintenance treatment in adult patients with moderate to very severe chronic obstructive pulmonary disease (COPD) |
| **dexmedetomidine - EMEA/H/C/005152**<br>, light to moderate sedation, Generic, Generic of Dexdor |
| **lifitegrast - EMEA/H/C/004653**<br>, treatment of moderate to severe dry eye disease in adults for whom prior artificial tears has not been sufficient |

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

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| **Humalog - insulin lispro - EMEA/H/C/000088/X/0169**<br>Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin |
| **Kalydeco - ivacaftor - EMEA/H/C/002494/X/0075/G, Orphan**<br>Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, "Extension application to add a new strength of 25 mg granules in sachet in the treatment of cystic fibrosis in children aged 6 to less than 12 months old.<br>C.I.4 - To update sections 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC, and sections 2 and 3 of the PL for the 150 mg film-coated tablet presentations to bring it in line with the new dosage form (25 mg granules), which supports the extension of indication for children aged 6 to 12 months old. The RMP (version 8.3) is updated in accordance. In addition, the MAH took the opportunity to implement minor updates in the Product Information." |
| **Liprolog - insulin lispro -** |

**EMEA/H/C/000393/X/0130**
Eli Lilly Nederland B.V., Informed Consent of Humalog, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

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

**Aimovig - erenumab - EMEA/H/C/004447/X/0001**
Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Kirsti Villikka, "Extension application to add a new strength of 140 mg."
List of Questions adopted on 13.12.2018.

**ambrisentan - EMEA/H/C/004985**
, treatment of pulmonary arterial hypertension (PAH)
List of Questions adopted on 20.09.2018.

**cabazitaxel - EMEA/H/C/004951**
, treatment of prostate cancer
List of Questions adopted on 20.09.2018.

**avatrombopag - EMEA/H/C/004722**
, treatment of thrombocytopenia
List of Questions adopted on 20.09.2018.

**posaconazole - EMEA/H/C/005005**
, treatment of fungal infections, Generic, Generic of Noxafil
List of Questions adopted on 20.09.2018.

**edaravone - EMEA/H/C/004938, Orphan**
Mitsubishi Tanabe Pharma Europe Ltd, treatment of amyotrophic lateral sclerosis (ALS)
List of Questions adopted on 20.09.2018.

**crisaborole - EMEA/H/C/004863**
, treatment of mild to moderate atopic dermatitis
List of Questions adopted on 20.09.2018.

**ioflupane (123i) - EMEA/H/C/004745**
, indicated for detecting loss of functional dopaminergic neuron terminals in the striatum
List of Questions adopted on 20.09.2018.

**talazoparib - EMEA/H/C/004674**
, for the treatment of adult patients with germline breast cancer susceptibility gene (BRCA) mutated human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer.

List of Questions adopted on 20.09.2018.

**ravulizumab - EMEA/H/C/004954, Orphan**
Alexion Europe SAS, treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH).
List of Questions adopted on 15.11.2018.

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

**defibrotide - EMEA/H/C/002393/S/0038, Orphan**
Gentium S.r.l.

**cholic acid - EMEA/H/C/002081/S/0029, Orphan**
Retrophin Europe Ltd

**tafamidis - EMEA/H/C/002294/S/0047, Orphan**
Pfizer Europe MA EEIG

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

**Abasaglar - insulin glargine - EMEA/H/C/002835/R/0023**
Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Amelia Cupelli

**Adjupanrix - pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - EMEA/H/C/001206/R/0062**
GlaxoSmithkline Biologicals SA, Informed Consent of Pandemrix (EXP), Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst

**ILARIS - canakinumab - EMEA/H/C/001109/R/0062**
Novartis Europharm Limited, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Brigitte Keller-Stanislawski

**Imbruvica - ibrutinib - EMEA/H/C/003791/R/0049, Orphan**
Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce

**VIZAMYL - flutemetamol (18F) - EMEA/H/C/002557/R/0017**
GE Healthcare AS, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber

**Xultophy - insulin degludec / liraglutide - EMEA/H/C/002647/R/0028**
Novo Nordisk A/S, Rapporteur: Kristina Dunder, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Menno van der Elst

### 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

**Axumin - fluciclovine (18F) - EMEA/H/C/004197/II/0011**
Blue Earth Diagnostics Ltd, Rapporteur: Janet Koenig, PRAC Rapporteur: Jolanta Gulbinovic, "Extension of Indication to include Diagnosis and continuing assessment of Glioma in adult patients as a new indication for Axumin; as a consequence, sections 4.1, 4.2, 4.4, 4.6, 5.1, 5.2 and 11 of the SmPC and the Annex II are updated. The Package Leaflet is updated in accordance."
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

**Keytruda - pembrolizumab - EMEA/H/C/003820/II/0065**
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "Extension of Indication to include, as monotherapy or in combination with platinum and 5-fluorouracil (5-FU) Chemotherapy, first-line treatment of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) in adults for Keytruda; based on the results from KEYNOTE-048, a randomized, multi-center, open-label phase 3 study investigating pembrolizumab, or pembrolizumab plus platinum plus 5-FU chemotherapy versus platinum plus 5-FU plus cetuximab in subjects with first-line recurrent or metastatic HNSCC. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is

updated in accordance. An updated version of the RMP (Version 22.1) is also being submitted."

**Stelara - ustekinumab - EMEA/H/C/000958/II/0071**

Janssen-Cilag International NV, Rapporteur: Jayne Crowe, Co-Rapporteur: Mark Ainsworth, PRAC Rapporteur: Rhea Fitzgerald, "Extension of Indication for Stelara to include treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic or have medical contraindications to such therapies. As a consequence, the SmPC, Package Leaflet and RMP have been updated."

**Victoza - liraglutide - EMEA/H/C/001026/II/0049**

Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Menno van der Elst, "Extension of Indication to include treatment of children and adolescents (age 10-17 years) with T2D based on Study NN2211-1800; a Phase 1 clinical pharmacology, multi-centre, randomised, double-blind placebo controlled trial, and Study NN2211-3659; a Phase 3a efficacy and safety, multi-centre, randomised, parallel group, placebo controlled trial with a 26-week double blind period followed by a 26-week open label period (main part). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, and 5.2 of the SmPC are being updated and the Package Leaflet is updated accordingly.
Additionally, in accordance with the guideline from 2017 about excipients, the MAH took the opportunity to include sodium in SmPC section 4.4 and the Package Leaflet.
An updated RMP version 30 was provided as part of the application."

**Zerbaxa - ceftolozane / tazobactam - EMEA/H/C/003772/II/0020**

Merck Sharp & Dohme B.V., Rapporteur: Svein Rune Andersen, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Adam Przybylkowski, "Extension of Indication to include treatment of Nosocomial pneumonia, including ventilator associated pneumonia for Zerbaxa, based on results from the randomised, double-blind, multicentre clinical trial CXA-NP-11-04 (PN008).

As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance (sections 1, 2, 3, 4 and 6).
The applicant also took the opportunity to implement editorial changes in sections in sections 5.2 of the SmPC and to bring Section 4.4 of the SmPC and section 2 of the PL in line with the latest Annex to the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'.
Version 2.1 of the RMP was also submitted."

**WS1542**
**Bretaris Genuair-EMEA/H/C/002706/WS1542/0040**
**Eklira Genuair-EMEA/H/C/002211/WS1542/0040**

AstraZeneca AB, Lead Rapporteur: Ewa Balkowiec Iskra, Lead Co-Rapporteur: Ewa Balkowiec Iskra, "Extension of Indication to include reduction of COPD exarcerbations for Eklira Genuair and Bretaris Genuair; as a consequence, sections 4.1, 4.4, 4.8 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet for Bretaris Genuair and to implement minor editorial changes in section 4.4, 4.6, 5.3 of the SmPC and section 2 of the PL for both Eklira Genuair and Bretaris Genuair."

**WS1554**
**Riarify-EMEA/H/C/004836/WS1554/0002**
**Trydonis-EMEA/H/C/004702/WS1554/0002**

Chiesi Farmaceutici S.p.A., Informed Consent of Trimbow, Lead Rapporteur: Janet Koenig, Lead PRAC Rapporteur: Jan Neuhauser, "Extension of indication, based on results from two Phase III studies: Triple 7 (CCD-05993AA1-07) and Triple 8 (CCD-05993AA1-08), to include maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who are not adequately treated by combination of a long-acting beta2-agonist and a long-acting muscarinic antagonist. Sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated

accordingly to reflect the studies' results. The package leaflet and the risk management plan (version 6.0) are updated accordingly."

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

**BeneFIX - nonacog alfa -**
**EMEA/H/C/000139/II/0156/G**
Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus

**Dupixent - dupilumab -**
**EMEA/H/C/004390/II/0013/G**
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus

**Entyvio - vedolizumab -**
**EMEA/H/C/002782/II/0038/G**
Takeda Pharma A/S, Rapporteur: Daniela Melchiorri

**Firazyr - icatibant -**
**EMEA/H/C/000899/II/0046, Orphan**
Shire Pharmaceuticals Ireland Limited, Rapporteur: Kristina Dunder

**Flixabi - infliximab -**
**EMEA/H/C/004020/II/0038**
Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus

**Imraldi - adalimumab -**
**EMEA/H/C/004279/II/0021**
Samsung Bioepis NL B.V., Rapporteur: Outi Mäki-Ikola

**Keytruda - pembrolizumab -**
**EMEA/H/C/003820/II/0066/G**
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri

**Keytruda - pembrolizumab -**
**EMEA/H/C/003820/II/0067/G**
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri

**Matever - levetiracetam -**
**EMEA/H/C/002024/II/0032**
Pharmathen S.A., Generic, Generic of Keppra, Rapporteur: Ondřej Slanař

**Myozyme - alglucosidase alfa -**
**EMEA/H/C/000636/II/0072**
Genzyme Europe BV, Rapporteur: Alexandre

Moreau

**Ontruzant - trastuzumab - EMEA/H/C/004323/II/0015/G**
Samsung Bioepis NL B.V., Rapporteur: Koenraad Norga

**OPDIVO - nivolumab - EMEA/H/C/003985/II/0061/G**
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez

**Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (H5N1) (live attenuated, nasal) - EMEA/H/C/003963/II/0020/G**
AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus

**Praxbind - idarucizumab - EMEA/H/C/003986/II/0014/G**
Boehringer Ingelheim International GmbH, Rapporteur: Jan Mueller-Berghaus

**Rixubis - nonacog gamma - EMEA/H/C/003771/II/0028**
Baxalta Innovations GmbH, Rapporteur: Andrea Laslop

**Simponi - golimumab - EMEA/H/C/000992/II/0087/G**
Janssen Biologics B.V., Rapporteur: Kristina Dunder

**Soliris - eculizumab - EMEA/H/C/000791/II/0104/G, Orphan**
Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez

**Synagis - palivizumab - EMEA/H/C/000257/II/0118**
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Mark Ainsworth

**Taltz - ixekizumab - EMEA/H/C/003943/II/0025/G**
Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder

**Tremfya - guselkumab - EMEA/H/C/004271/II/0009/G**
Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics

**Trumenba - meningococcal group B vaccine (recombinant, adsorbed) -**

**EMEA/H/C/004051/II/0016/G**
Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege

**Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0054/G**
Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez

**WS1464/G**
**Revatio-EMEA/H/C/000638/WS1464/0084/G**
**Viagra-EMEA/H/C/000202/WS1464/0100/G**
Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege

**WS1519/G**
**HyQvia-EMEA/H/C/002491/WS1519/0047/G**
**Kiovig-EMEA/H/C/000628/WS1519/0089/G**
Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus

**WS1524**
**HyQvia-EMEA/H/C/002491/WS1524/0048**
**Kiovig-EMEA/H/C/000628/WS1524/0090**
Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus

**WS1532**
**Bexsero-EMEA/H/C/002333/WS1532/0075**
**Menveo-EMEA/H/C/001095/WS1532/0082**
GSK Vaccines S.r.l, Lead Rapporteur: Kristina Dunder

**WS1534**
**Infanrix hexa-EMEA/H/C/000296/WS1534/0254**
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

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

**Adempas - riociguat - EMEA/H/C/002737/II/0028, Orphan**
Bayer AG, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4 and 4.5 of the SmPC to include information for recommended starting dose for riociguat for patients who are on stable

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| doses of strong multi pathway cytochrome P450 proteins (CYP) and P-gp/BCRP inhibitors based on date from Study 17957 which investigated the potential pharmacokinetic (PK) interaction of human immunodeficiency virus (HIV) antiretroviral agents as fixed-dose combination and riociguat in HIV patients, data from a statistical drug-drug interaction (DDI) which was evaluated in study 18634, in which PK data from study 17957 was compared to the historical PK data and data from a nonclinical study to elucidate the DDI potential of the different components included in the HIV combination products in vitro.<br>The package leaflet is updated accordingly." | |
| **Apealea - paclitaxel - EMEA/H/C/004154/II/0001**<br>Oasmia Pharmaceutical AB, Rapporteur: Bart Van der Schueren, "Update of section 5.1 of the SmPC in order to present post-hoc analyses of efficacy results for patients with first relapse in accordance with the approved indication. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct minor typographical errors in the SmPC." | |
| **Axumin - fluciclovine (18F) - EMEA/H/C/004197/II/0010**<br>Blue Earth Diagnostics Ltd, Rapporteur: Janet Koenig, PRAC Rapporteur: Jolanta Gulbinovic, "Submission of an updated RMP version 2.0 in order to update to GVP Module V Rev.2 and any new information required as part of the updated template format; update to include new exposure details to Axumin from the current approved version of the Axumin 1.3 dated 14 March 2017 from both clinical trials and worldwide commercial exposure from US and EU countries and to correct the effectiveness measurement of the image interpretation training from a review of self-assessments scores to normal pharmacovigilance activities." | |
| **Bexsero - meningococcal group B vaccine (recombinant, component, adsorbed) - EMEA/H/C/002333/II/0073**<br>GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, "Update of sections 4.2 and 5.1 of the SmPC to add data on antibody persistence and response to a 3rd dose in children, adolescents and adults, based on clinical studies V72_28E1 and V72_75. | |

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| Study V72_28E1 was a phase 3b, open label, multicentre extension study that evaluated the antibody persistence in children 4 through 12 years of age at 24 through 36 months after the last dose in follow-on subjects from the parent study V72_28. Study V72_75 was a phase 3b, open label, controlled, multicentre study that assessed the long-term antibody persistence of bactericidal activity at 4 to 7.5 years after 2-dose primary series of vaccination and the booster response to a third dose in adolescents and young adults 15 through 24 years of age who previously participated in studies V72P10 and V72_41.<br>The Package Leaflet is updated accordingly." | |
| **Bexsero - meningococcal group B vaccine (recombinant, component, adsorbed) - EMEA/H/C/002333/II/0074**<br>GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, "Update of section 4.5 of the SmPC in order to include the possibility of concomitant administration with the MenACWY vaccines based on final results from study V72_56. This was a phase 3b study assessing the safety and immunogenicity of Bexsero administered concomitantly with MenACWY vaccine as compared to their individual administration in healthy infants at approximately 3, 5, 7 and 13 months of age.<br>The Package Leaflet is updated accordingly.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes throughout the Product Information and Annex A." | |
| **Biktarvy - bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449/II/0011**<br>Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, "Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information based on the pooling of 96-week data from two randomized, double-blind, active controlled studies GS-US-380-1489 and GS-US-380-1490 in HIV-1 infected, antiretroviral treatment-naïve adults receiving Biktarvy compared with each of the comparator treatment groups (i.e. pooled Biktarvy (BVY) vs abacavir /dolutegravir /lamivudine and pooled BVY vs dolutegravir + emtricitabine/tenofovir alafenamide). | |

In addition the Marketing authorisation holder (MAH) took the opportunity to introduce some minor linguistic amendments in the SmPC and the Package Leaflet”

**Bosulif - bosutinib - EMEA/H/C/002373/II/0036**

Pfizer Europe MA EEIG, Rapporteur: Janet Koenig, “Submission of the analysis of the pop PK data as recommended by the CHMP.”

**Brinavess - vernakalant - EMEA/H/C/001215/II/0034**

Correvio, Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.8 and 5.1 of the SmPC based on the final results from the non-interventional PASS SPECTRUM study, listed as a category 3 study in the RMP, in order to fulfil MEA 026.5; SPRECTRUM (6621-019) study is a prospective observational registry study to characterise normal conditions of use, dosing and safety following administration of vernakalant IV sterile concentrate.”

**Bydureon - exenatide - EMEA/H/C/002020/II/0057**

AstraZeneca AB, Rapporteur: Kristina Dunder, “Update of sections 4.8 and 5.1 of the SmPC in order to implement minor changes in line with the revised study report for the DURATION 7 study (previously assessed as part of variation II/45) following the exclusion of a site . In addition, the MAH took the opportunity to implement editorial changes for increased clarity in the SmPC section 6.6 and the Package Leaflet of the pre-filled pen.”

**Cerdelga - eliglustat - EMEA/H/C/003724/II/0020, Orphan**

Genzyme Europe BV, PRAC Rapporteur: Eva A. Segovia, “Submission of the final report from study ELIGLC06912 listed as a category 3 study in the RMP (MEA006). This is a Drug Utilization Study of Eliglustat in the United States (US) Population Using MarketScan Database and the International Collaborative Gaucher Group Registry. Consequently, submission of an updated RMP version 6 in order to reflect the submission of the final data for study ELIGLC06912. In addition, RMP version 6.0 has been aligned with the Guideline on GVP - Module V, revision 2 and the related new EU RMP template has been implemented.”

**Cerdelga - eliglustat - EMEA/H/C/003724/II/0021, Orphan**

Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, "Submission of the final report from study PKM14281 , A Randomized, Three-Period Crossover Study of Single and Repeated Doses for Three Different Strengths of Eliglustat in Healthy Adult, CYP2D6 Extensive and Poor Metabolizers, to characterize dose proportionality of 21, 42 and 84 mg eliglustat dosage strengths, in line with CHMP recommendation."

**Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0099**

GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of section 4.5 of the SmPC in order to update the safety information for the concomitant administration of Cervarix with meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine (Nimenrix), based on results from study MENACWY-TT-054. This is a phase III, open, randomised, controlled, multicentre study aimed to assess the immunogenicity and reactogenicity of Nimenrix administered alone as compared to Nimenrix co-administered with HPV vaccine Cervarix or co-administered with Cervarix and tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine adsorbed (Boostrix) in female adolescents and adults at 9 to 25 years of age; as requested in the CHMP conclusion of procedure P46/093. The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity update the package leaflet to correct inconsistencies related to the indication in males."

**Cyramza - ramucirumab - EMEA/H/C/002829/II/0029**

Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik, "Submission of results of post-authorisation efficacy study (PAES): In order to investigate the potential correlation between biomarker measures (VEGF-C. VEGF-D, sVEGFR1, sVEGFR2 and sVEGFR3 from plasma, VEGFR2 IHC, additional KRAS, NRAS and BRAF mutations) and efficacy outcome (PFS, OS), the MAH should submit the results of a biomarker assay from the RAISE translational research

population. Data presented corresponds with VEGF-C and VEGF-D biomarkers to complete the already submitted data for sVEGFR1, sVEGFR2 and sVEGFR3 from plasma, VEGFR2 IHC, KRAS, NRAS and BRAF mutations. As a result, Annex II of the product information is updated to remove this condition."

**Defitelio - defibrotide - EMEA/H/C/002393/II/0039, Orphan**

Gentium S.r.l., Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC to amend the mechanism of action with new data on non-clinical studies identified from published literature."

**Delstrigo - doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746/II/0001**

Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information based on the results from the clinical study report P024: ' Phase III Multicenter, Open-Label, Randomized Study to Evaluate a Switch to MK-1439A in HIV-1-Infected Subjects Virologically Suppressed on a Regimen of a Ritonavir-boosted Protease Inhibitor and Two Nucleoside Reverse Transcriptase Inhibitors (NRTIs)'. The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity implement editorial changes in the SmPC and patient leaflet."

**Eliquis - apixaban - EMEA/H/C/002148/II/0059**

Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.3, 4.4 and 4.5 of the SmPC based on the current European Society of Cardiology (ESC) guideline for direct oral anti-coagulants (DOACs) and the literature including the AXAFA-AFNET 5 study, a major investigator's sponsored trial with apixaban, in order to include an exception to the contraindicated concomitant treatment with any other anticoagulant agent for heparin co-administration during catheter ablation for atrial fibrillation. In addition, the Marketing authorisation holder (MAH) took the opportunity to clarify the wording in section 4.2 of the SmPC to include a reference to transesophageal

echocardiogram (TEE) guided cardioversion."

**EXJADE - deferasirox - EMEA/H/C/000670/II/0064**

Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "To update the Risk Management Plan (RMP) version 16.0 for Exjade® (deferasirox, EMEA/H/C/000670), covering all formulations (dispersible tablets, film-coated tablets and granules).
With this update, the MAH introduces the alignment with requirements of the new RMP template (as per the revised Good Pharmacovigilance Practices (GVP) Module V Rev.2) and consequential removal of the food interaction and drug-drug interactions (DDI) from the list of important identified risks. In addition, "drug reaction with eosinophilia and systemic symptoms" (DRESS) has been reclassified from important potential risk to important identified risk. The reclassification of DRESS was agreed with the PRAC during a previous procedure (EMEA/H/C/PSUSA/00000939/201710).
Additional minor changes are have been also implemented in the RMP.
With this variation, the Health Care Professional (HCP) guide is also updated."

**Fasenra - benralizumab - EMEA/H/C/004433/II/0012**

AstraZeneca AB, Rapporteur: Fátima Ventura, "Update of sections 4.5 and 5.2 of the SmPC to include a statement relating to the humoral antibody responses induced by the seasonal influenza virus vaccination, the observed responses were similar between placebo and benralizumab."

**Fasenra - benralizumab - EMEA/H/C/004433/II/0013**

AstraZeneca AB, Rapporteur: Fátima Ventura, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect the final results from study D3250C00021 (BORA) listed as a category 3 in the RMP; this is a randomised phase 3 study to evaluate the safety and tolerability of benralizumab in asthmatic adults and adolescents on inhaled corticosteroid plus long-acting β2 agnostic. In addition, section 4.2 of the SmPC is updated to reflect the extended

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| PIP waiver age group" | |
| **Humira - adalimumab - EMEA/H/C/000481/II/0187**<br>AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, "Submission of the final report from study M11-327: A Multicenter Open-Label Study of the Long-term Safety and Efficacy of the Human Anti-TNF Monoclonal Antibody Adalimumab in Subjects with Non-infectious Intermediate Uveitis, Posterior Uveitis, or Panuveitis; listed as a category 3 study in the RMP." | |
| **Imbruvica - ibrutinib - EMEA/H/C/003791/II/0048, Orphan**<br>Janssen-Cilag International NV, Rapporteur: Filip Josephson, "Update of section 4.4 of the SmPC Special warnings and precautions for use in order to add a warning under "bleeding-related events' based on the final clinical study reports results to evaluate the risks of major hemorrhage with the administration of IMBRUVICA® (ibrutinib)). The study is listed in section III.2 additional Pharmacovigilance Activities A non-interventional PASS clinical study report (CSR) for serious haemorrhage in the RMP.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to include a minor edit in the list of local representatives in the Package Leaflet." | |
| **Inflectra - infliximab - EMEA/H/C/002778/II/0072**<br>Pfizer Europe MA EEIG, Duplicate, Duplicate of Remsima, Rapporteur: Outi Mäki-Ikola, "Submission of the final study report of study CT-P13 4.1- An Open-label, Single-arm, Phase IV Study to Evaluate Safety and Efficacy of infliximab in Korean Patients with Inflammatory Bowel Disease." | |
| **INTELENCE - etravirine - EMEA/H/C/000900/II/0055**<br>Janssen-Cilag International NV, Rapporteur: Joseph Emmerich, "Update of sections 4.4 and 4.8 of the SmPC to include the information that a higher incidence of Stevens-Johnson Syndrome (SJS) has been observed in children compared to the incidence reported in adult clinical trials, as assessed in the TMC125-EPPICC study submitted according to Art. 46 procedure (no. EMA/H/C/000900/P46/052). The Package | |

Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make an amendment in section 4.2 of the SmPC by replacing the word "tablet" with "dose" in the missed dose information. The Package Leaflet is updated accordingly."

**Jivi - damoctocog alfa pegol - EMEA/H/C/004054/II/0001, Orphan**
Bayer AG, Rapporteur: Sinan B. Sarac, "Submission of the final report from study (T103483-9, a 13- and 26-Week Intravenous Toxicity Study of BAY 94-9027 in the Nude Rat (Rowett nude rats, Crl:NIHFoxn1rnu) followed by a 26-Week Recovery Period) in fulfilment of recommendation adopted at the time of initial marketing authorisation opinion."

**Kalydeco - ivacaftor - EMEA/H/C/002494/II/0076, Orphan**
Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Concepcion Prieto Yerro, "Update of sections 4.4, and 5.1 of the SmPC to clarify the classification of the G970R CFTR mutation as a splicing mutation, based on data from the Study 770-112 G970R substudy (reviously submitted in procedure II/54) and an additional mRNA analysis (report N052)."

**Kanuma - sebelipase alfa - EMEA/H/C/004004/II/0019, Orphan**
Alexion Europe SAS, Rapporteur: Bart Van der Schueren, "Submission of the final report from study LAL-CL04, in order to fulfil this recommendation (REC). This is an open label multicentre extension study to evaluate the long-term safety, tolerability and efficacy of sebelipase alfa in adult subjects with liver dysfunction due to lysosomal acid lipase deficiency who previously received treatment in study LAL-CL01."

**Kolbam - cholic acid - EMEA/H/C/002081/II/0028, Orphan**
Retrophin Europe Ltd, Rapporteur: Constantinos Markopoulos, "Submission of the final report from study CAC-002-01, listed as a category 3 study in the RMP. This is a Phase 3, open-label, single arm, non-randomized study investigating cholic acid in the treatment of subjects with inborn errors of bile acid metabolism.
The study was a continuation study that included

eligible subjects who had previously received cholic acid in studies CAC-91-10-10 or CAC-001-01 as well as newly diagnosed subjects."

**Luminity - perflutren - EMEA/H/C/000654/II/0026**

Lantheus MI UK Ltd., Rapporteur: Peter Kiely, "Submission of the final report from study Luminity 422, a category 3 study in the RMP, in order to fulfil MEA 004.4. This is a phase IV, multi-centre, parallel-group, randomised, cross-over trial to compare the efficacy of Luminity and SonoVue in the evaluation of left ventricular border definition."

**Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0021**

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Joseph Emmerich, "Submission of the final report from study M16-127 (EXPEDITION-5), a multicentre, open-label study to evaluate the efficacy and safety of glecaprevir/pibrentasvir in renally-impaired adults with chronic hepatitis C virus genotype 1-6 infection."

**Mekinist - trametinib - EMEA/H/C/002643/II/0033**

Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.6 of the SmPC in order to update information on Fertility, pregnancy and lactation after routine review of the company core data sheet, taking into consideration the original source documentation from GSK (former MAH), current scientific knowledge, published literature, as well as health authority and working group guidelines. The Package leaflet is being updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some editorial changes in section 4.4 and 4.8 of the SmPC."

**Pifeltro - doravirine - EMEA/H/C/004747/II/0001**

Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information based on the results from the clinical study report P024: ` Phase III Multicenter, Open-Label, Randomized Study to Evaluate a Switch to MK-1439A in HIV-1-Infected Subjects

Virologically Suppressed on a regimen of a ritonavir-boosted protease Inhibitor and two Nucleoside Reverse Transcriptase Inhibitors (NRTIs)'. The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity implement editorial changes in the SmPC and patient leaflet."

**Remsima - infliximab - EMEA/H/C/002576/II/0063**
Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola, "Submission of the final study report of study CT-P13 4.1- An Open-label, Single-arm, Phase IV Study to Evaluate Safety and Efficacy of infliximab in Korean Patients with Inflammatory Bowel Disease."

**Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0012**
GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of section 4.8 of the SmPC in order to add "hypersensitivity reactions including rash, urticaria and angioedema" as an adverse drug reaction with frequency "rare". This update is based on data from clinical trials, literature and post-marketing surveillance reports.
The Package Leaflet is updated accordingly."

**Strensiq - asfotase alfa - EMEA/H/C/003794/II/0035/G, Orphan**
Alexion Europe SAS, Rapporteur: Daniela Melchiorri, "Update of sections 4.4, 4.6, 4.8 and 5.2 of the SmPC with the results of the integrated safety analysis of pooled asfotase alfa clinical studies, and section 5.1 of the SmPC with the final results of study ENB-002-08/ENB-003-08 (an open-label, non-randomised, non-controlled study) and study ENB-010-10 (a controlled, open label study to evaluate the efficacy, safety, and PK of asfotase alfa in infants and children ≤ 5 years of age with hypophosphatasia (HPP)). The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the SmPC and Package Leaflet."

**Tafinlar - dabrafenib - EMEA/H/C/002604/II/0038**
Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC in

order to update information on Fertility, pregnancy and lactation after routine review of the company core data sheet, taking into consideration the original source documentation from GSK (former MAH), current scientific knowledge, published literature, as well as health authority and working group guidelines. The Package leaflet is being updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some editorial changes in section 4.4 and 4.8 of the SmPC and in section 4 of the package leaflet."

**Tremfya - guselkumab - EMEA/H/C/004271/II/0010**
Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, "Update of sections 4.8 and 5.1 of the SmPC to add the long term 3-year clinical data from the two ongoing clinical studies CNTO1959PSO3001 (VOYAGE 1) and CNTO1959PSO3002 (VOYAGE 2) in subjects with plaque psoriasis."

**Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0009, Orphan**
Ipsen Pharma, Rapporteur: Janet Koenig, "Update of sections 4.2 and 5.2 of the SmPC in order to add PK information in subjects with mild, moderate and severe renal impairment based on study D-FR-01017-002 (A Phase I, open-label study to compare the pharmacokinetics of telotristat ethyl and its metabolite in subjects with impaired renal function to healthy subjects with normal renal function after a single dose of telotristat etiprate) (MEA005). The Package Leaflet is updated accordingly."

**Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0010, Orphan**
Ipsen Pharma, Rapporteur: Janet Koenig, "Update of section 5.3 of the SmPC in order to add information on carcinogenicity based on final results from study 8273113 (104-Week Oral Gavage Carcinogenicity and Toxicokinetic Study with LX1606 in Rats). The MAH took also the occasion to introduce some editorial changes in section 5.3 of the SmPC in alignment with the QRD wording."

**Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/II/0069**
Bial - Portela & Cª, S.A., Rapporteur: Martina Weise, "Update of section 4.2 of the SmPC in

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| order to update information related to the switch of tablet and suspension formulation based on the final results from study IA-2093-132, a pharmacokinetic study conducted to address the post-approval commitment: to compare the pharmacokinetic profile of the oral suspension versus the tablets." | |
| **Zydelig - idelalisib - EMEA/H/C/003843/II/0044**<br>Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, "Submission of the final clinical study report from study 101-99, A phase 1/2 extension study to investigate the safety and durability of clinical activity of CAL-101 in patients with hematologic malignancies, listed as category 1 commitment in the Risk Management Plan of Idelalisib and a post-authorisation measure listed within Annex IID of the product information (ANX 002).<br>The product information annex IID has been updated." | |
| **Zydelig - idelalisib - EMEA/H/C/003843/II/0045**<br>Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, "Submission of the final clinical study report for Phase 3 extension study GS US 312 0117, to evaluate the efficacy and safety of idelalisib (GS 1101) in combination with rituximab for previously treated CLL for patients with or without 17p deletion/TP53 mutation.<br>This is a category 1 imposed pharmacovigilance activity, listed on the Risk Management Plan and is a post-authorisation measure listed within Annex IID of the product information (ANX 001).<br>The product information annex IID has been updated." | |
| **WS1511/G Advagraf-EMEA/H/C/000712/WS1511/0052/G Modigraf-EMEA/H/C/000954/WS1511/0031/G**<br>Astellas Pharma Europe B.V., Lead Rapporteur: Jayne Crowe, "Update of sections 4.5 and 4.8 of the SmPC to add the drug-drug interaction with letemovir and to add the febrile neutropenia with frequency unknown, based on the cumulative review of the MAH safety database.<br>Update of section 4.6 of the SmPC to add the information on pregnancy and lactation following | |

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| the cumulative review of the cases reported in the MAH global safety database, published literature and the transplantation pregnancy exposure registry.<br>The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor editorial changes throughout the PI and to implement the wording from the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'." | |
| **WS1523**<br>**Epclusa-EMEA/H/C/004210/WS1523/0031**<br>**Harvoni-EMEA/H/C/003850/WS1523/0072**<br>**Sovaldi-EMEA/H/C/002798/WS1523/0054**<br>**Vosevi-EMEA/H/C/004350/WS1523/0022**<br>Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, "Update of sections 4.3, 4.4 and 4.5 of the SmPC in order implement additional guidance on the use of sofosbuvir-based therapy with concomitant drugs, based on final results from study GS-US-334-2130. This was a phase I study to evaluate the effects of cytochrome P450 and drug transporter inducers on sofosbuvir and probe drug pharmacokinetics in healthy subjects. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor editorial changes throughout the Product Information." | |
| **WS1540**<br>**Docetaxel**<br>**Zentiva-EMEA/H/C/000808/WS1540/0057**<br>**Taxotere-EMEA/H/C/000073/WS1540/0130**<br>Aventis Pharma S.A., Lead Rapporteur: Alexandre Moreau, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information following review of a safety signal of secondary malignancies for docetaxel requested in the response to PRAC PSUR (EMEA/H/C/PSUSA/00001152/201611); the Package Leaflet is updated accordingly." | |
| **Aluvia-EMEA/H/W/000764/WS1555/0107**<br>**Kaletra-EMEA/H/C/000368/WS1555/0175**<br>**Norvir-EMEA/H/C/000127/WS1555/0152**<br>AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Joseph Emmerich, "Update of | |

sections 4.3 and 4.5 of the SmPC in order to add information on the contraindication and interaction between ritonavir and lomitapide based on a cumulative safety review of the SmPCs of protease inhibitors currently approved for the treatment of HIV in the EU in combination with the pharmacokinetic enhancer (ritonavir), during the period from 1st August 2017 to 31st July 2018. This is in fulfilment of LEG 33.9. The Package Leaflets are updated accordingly.
In addition, the Worksharing applicant (WSA) took the opportunity to correct a minor typographical error in the Norvir and Kaletra product information."

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

**Avonex - interferon beta-1a - EMEA/H/C/000102/II/0182/G**

Biogen Netherlands B.V., Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, "2x type II (C.I.4):
1) Update of section 4.3, and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054).
2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles.
The Package leaflet has been updated accordingly.
This submission fulfils MEA 87.2 and 84."

**Betaferon - interferon beta-1b - EMEA/H/C/000081/II/0124/G**

Bayer AG, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "2x type II (C.I.4):
1) Update of section 4.3 and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054).
2) Update of section 4.6 of the SmPC in order to

update the statement regarding breast-feeding following a review of studies, case reports and literature articles.
The Package leaflet has been updated accordingly.
This submission fulfils MEA 024.2 and 21.
An updated RMP version 4.1 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes' and an update of the EU-RMP template (rev.2)."

**Extavia - interferon beta-1b - EMEA/H/C/000933/II/0096/G**

Novartis Europharm Limited, Informed Consent of Betaferon, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "2x type II (C.I.4):
1) Update of section 4.3 and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054).
2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles.
The Package leaflet has been updated accordingly.
This submission fulfils MEA 022.2 and 019.
An updated RMP version 4.1 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes' and an update of the EU-RMP template (rev. 2)."

**Fasenra - benralizumab - EMEA/H/C/004433/II/0014/G**

AstraZeneca AB, Rapporteur: Fátima Ventura, PRAC Rapporteur: David Olsen
C.I.4 – Update of sections 4.2, 6.4, 6.5, 6.6 of the SmPC in order to update the information for self-administration for Fasenra 30 mg solution for injection in pre-filled syringe. The labelling and the package leaflet are updated accordingly.
In addition, the RMP (version 2.0) is updated to reflect the information about the new presentation, to include additional information about completed studies (ALIZE, GREGALE, AMES, GRECO), to add updated exposure data post MAA approval, and to reflect additional details on the post-authorisation safety studies

(Pregnancy registry (D3250R00026) and Malignancy Post Authorization Safety Study (D3250R00042)). Furthermore, the RMP is revised in line with the RMP template (GVP Module V rev.2)."

**Gardasil - human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) - EMEA/H/C/000703/II/0080**

MSD Vaccins, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.4 and 5.1 of the SmPC in order to update the information related to the effectiveness and immunogenicity of the immune response of Gardasil, based on the final results from the long-term follow-up of study V501-P015-21 listed as a category 3 study in the RMP; this study was designed to evaluate the effectiveness, immunogenicity and safety of the quadrivalent human papillomavirus (qHPV) vaccine for at least 10 years; the Package Leaflet is updated accordingly. The RMP version 12.1 has also been submitted following revision 2.
The MAH is taking the opportunity to implement minor editorial changes in the product information (SmPC, labelling and package leaflet)."

**IBRANCE - palbociclib - EMEA/H/C/003853/II/0017/G**

Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver, "Update of section 5.3 of the SmPC in order to include information from two completed non-clinical studies: a 6-month carcinogenicity study in mice (20084764), and a 2-year carcinogenicity study in rats (20066483). Furthermore, the MAH submitted the final report from the non-clinical study 20084675, a Pre- and Postnatal Developmental Toxicity Study in rats. The MAH took the opportunity to introduce minor editorial changes in SmPC and PL."

**Intuniv - guanfacine - EMEA/H/C/003759/II/0015**

Shire Pharmaceuticals Ireland Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Maria del Pilar Rayon, "Update of section 4.5 of the SmPC in order to remove the statement on potential drug interactions with drugs that inhibit OCT1 based on final results from study V8953M-SPD503; this is a non-clinical

study (Transporter Interaction - OCT1 inhibition);
The RMP version 3.0 has also been submitted."

**Kineret - anakinra - EMEA/H/C/000363/II/0064/G**

Swedish Orphan Biovitrum AB (publ), Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, "Update of section 4.4 of the SmPC in order to add a warning on pulmonary events based on post-marketing data. The package leaflet is updated accordingly. Consequently, the important potential risks and the list of target medical events in the RMP (version 4.6) are updated to include pulmonary events and a specific follow-up questionnaire is created.
The RMP is also revised in line with the GVP Module V RMP template (revision 2).
In addition, the due date for submission of the final study report for the post-authorisation study (Sobi ANAKIN-302) is proposed to be extended.
Furthermore, the MAH took the opportunity to move the text about macrophage activation syndrome (MAS) and malignancies from section 4.8 to 4.4 of the SmPC."

**NINLARO - ixazomib - EMEA/H/C/003844/II/0014/G, Orphan**

Takeda Pharma A/S, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Annika Folin, "Group of variations onsisting of a type 2 variation to include submission of final report of progression free survival (PFS) in fulfilment of SOB004 and a type IB variation to request and extension of the due date of SOB003. Annex II is amended accordingly. Consequently the RMP is updated (version 4.0)."

**Nucala - mepolizumab - EMEA/H/C/003860/II/0021**

GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information based on final results from Study 200363 Part B and two open label extension (OLE) studies (201312 and MEA115666) listed as category 3 studies in the RMP. These are interventional post-authorisation safety studies conducted to assess the long-term (52 weeks) safety and tolerability of

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| mepolizumab when administered subcutaneously to patients aged 6 to 11 years old with severe eosinophilic asthma (study 200363 Part B), to describe the long-term safety profile of mepolizumab (MEA115666), and to provide extended treatment to subjects from study MEA115661 and further describe long-term safety in these subjects (study 201312).<br>The RMP (version 5.0) has also been submitted to reflect the completion of the studies and to be aligned with GVP Module V, rev.2 template.” | |
| **Ontruzant - trastuzumab - EMEA/H/C/004323/II/0016**<br>Samsung Bioepis NL B.V., Rapporteur: Koenraad Norga, PRAC Rapporteur: Brigitte Keller-Stanislawski | |
| **OPDIVO - nivolumab - EMEA/H/C/003985/II/0060/G**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to include information from studies CA209171 (A Phase 2, single-arm, open-label, multicentre clinical trial with nivolumab monotherapy in subjects with advanced or metastatic squamous (Sq) cell non-small cell lung cancer (NSCLC) who have received at least one prior systemic regimen for the treatment of Stage IIIb/IV Sq NSCLC) and CA209172 (A Phase 2, single-arm, open-label, multicentre clinical trial with nivolumab monotherapy in subjects with histologically confirmed Stage III (unresectable) or Stage IV melanoma progressing after prior treatment containing an anti-CTLA-4 monoclonal antibody). In addition the MAH take the occasion to update annex II to reflect already fulfilled requirement regarding biomarkers data (ANX 005.3, ANX 006, ANX 023, ANX 024, ANX 026 and ANX 027). The RMP has been updated accordingly (submitted version 13.4).” | |
| **Plegridy - peginterferon beta-1a - EMEA/H/C/002827/II/0052/G**<br>Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ulla Wändel Liminga, “2x type II (C.I.4):<br>1) Update of section 4.3, and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding | |

breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054).
2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles.
The Package leaflet has been updated accordingly.
This submission fulfils MEA 8.2 and 002.
An updated RMP version 4.1 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes' and an update of the EU-RMP template (rev. 2)."

**Rebif - interferon beta-1a - EMEA/H/C/000136/II/0137/G**

Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "2x type II (C.I.4):
1) Update of section 4.3, 4.6 and 5.3 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054).
2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles.
The Package leaflet has been updated accordingly.
This submission fulfils MEA 43.2 and 39.
An updated RMP version 10.0 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes' and an update of the EU-RMP template (rev.2)."

**Uptravi - selexipag - EMEA/H/C/003774/II/0022**

Janssen-Cilag International N.V., Rapporteur: Martina Weise, PRAC Rapporteur: Adrien Inoubli, "Update of Sections 4.2, 4.4 and 4.5 of the SmPC in order to update the safety information based on the final results from study AC-065-117 a listed category 3 study in the RMP which is a clinical pharmacology drug-drug interaction (DDI) study, evaluating the effect of clopidogrel a

moderate inhibitor of CYP2C8, on the pharmacokinetics of selexipag and its active metabolite ACT-333679. The package leaflet is updated accordingly.
The RMP version 6.1 has also been submitted.
In addition, the Marketing authorisation holder (MAH) took the opportunity to correct minor discrepancies in the SmPC."

**Venclyxto - venetoclax - EMEA/H/C/004106/II/0020, Orphan**
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, PRAC Rapporteur: Eva Jirsová, "Update of sections 4.2 and 5.2 of the SmPC in order to include that no dose adjustment is recommended in patients with mild or moderate hepatic impairment; a 50% dose reduction of ventoclax is recommended. based on final results from study M15-342 (A Study to Evaluate the Safety and Pharmacokinetics of a Single Dose of Ventoclax in Female Subjects with Mild, Moderate, or Severe Hepatic Impairment) listed as a category 3 study in the RMP; the Package Leaflet is updated accordingly. The RMP version 3.4 has also been submitted."

**Wakix - pitolisant - EMEA/H/C/002616/II/0017, Orphan**
BIOPROJET PHARMA, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.4, 4.5, 4.6 of the SmPC in order to reflect available information of co-administration of pitolisant with CYP3A4 substrats based on the results from studies R-B478-2.649, R.BF2.649-SK-005, R-B472-1.11413.
The MAH took the opportunity to update the section 5.2 of SMPC to more accurately reflect information previously assessed during procedure EMEA/H/C/2616/II/0004/G (CD 13/10/2017).
The RMP version 6.0 has also been submitted.
In addition, the Marketing authorisation holder (MAH) took the opportunity to clarify the details about finished product manufacturers in the Package Leaflet."

**Xiapex - collagenase clostridium histolyticum - EMEA/H/C/002048/II/0107**
Swedish Orphan Biovitrum AB (publ), Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, "Update of sections 4.4 and 5.1 of

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| the SmPC to update the efficacy and safety information following the final results from study AUX-CC-810: Long-term Safety, Curvature Deformity, Characterization, and Immunogenicity over time in Subjects Previously Treated with AA4500 for Peyronie's Disease in Studies AUX-CC-802, AUX-CC-803, AUC-X-CC-804, and AUX-CC-806; listed as a category 3 study in the RMP.<br>The RMP version 14.1 has also been submitted. In addition, the Marketing authorisation holder took the opportunity to introduce minor editorial changes to SmPC and Package Leaflet." | |
| **Yervoy - ipilimumab - EMEA/H/C/002213/II/0064**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of section 4.8 of the SmPC in order to update the safety information following final results from study CA184143 (A Multi-National, Prospective, Observational Study in Patients with Unresectable or Metastatic Melanoma) listed as a category 3 study in the RMP (MEA017.11); The RMP has been updated accordingly (submitted version 26.0). In addition, the Marketing authorisation holder (MAH) took the opportunity to update the RMP in regards to already assessed MEA 036.1 concerning protocol synopsis on the extension of the Dutch Melanoma Treatment Registry (DMTR) to paediatric melanoma patients treated with ipilimumab. Furthermore the MAH took the opportunity to request a 6-month shift in the dates associated to the next implementation steps of the DMTR extension (Registration of paediatric patients in the DMTR register and final CSR submission). Editorial changes have also been included in section 5.1 of the SmPC to provide more clarity on whether studies relate to melanoma or RCC and to monotherapy or combination therapy with nivolumab." | |
| **WS1490**<br>**IKERVIS-EMEA/H/C/002066/WS1490/0014**<br>**Verkazia-EMEA/H/C/004411/WS1490/0001**<br>Santen Oy, Lead Rapporteur: Peter Kiely, Lead PRAC Rapporteur: Jan Neuhauser, "Submission of an updated RMP version 7.0 in order to implement RMP revision 2 template, as a | |

consequence safety concerns have been updated: all safety concerns were moved from important safety concerns to the new section of Risks not considered important for inclusion in the list of safety concerns in the RMP. The milestones for VERKAZIA PASS have also been updated.
In addition, the MAH is proposing to align IKERVIS SmPC section 4.4 on concomitant therapy and effects on immune system with VERKAZIA SmPC in order to harmonize the routine risk minimization measures for both products. The MAH took this opportunity to implement the latest QRD template and the safety features for IKERVIS."

**WS1557**
**Exelon-EMEA/H/C/000169/WS1557/0120**
**Prometax-EMEA/H/C/000255/WS1557/0121**
Novartis Europharm Limited, Lead Rapporteur: Alexandre Moreau, Lead PRAC Rapporteur: Ghania Chamouni, "Submission of the final report of the Drug Utilization Study (CENA713D2409) aimed to assess the extent of inappropriate use of Exelon and Prometax. The DUS final report is fulfilling the post-authorisation measures Exelon MEA 034 and Prometax MEA 035."

### B.6.11. PRAC assessed procedures

PRAC Led
**Forsteo - teriparatide - EMEA/H/C/000425/II/0050/G**
Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final study reports of the European Union (EU) components of two post-authorisation safety studies (PASS); Study B3DMC-GHBX(2.2) and Study B3D-MC-GHBX(2.3b) both US population-based comparative cohort studies undertaken to evaluate a potential association between teriparatide and adult Osteosarcoma. An updated RMP version 7.0 was submitted as part of the application."

PRAC Led
**Gardasil - human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant,**

**adsorbed) - EMEA/H/C/000703/II/0081**
MSD Vaccins, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 13.1 in order to update the list of safety concerns by removing all remaining important identified and potential risks and missing information."

PRAC Led
**Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0029**
MSD Vaccins, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Bart Van der Schueren, "Submission of an updated RMP version 3.1 in order to bring it to the new revision 2 template. As a result, the safety concerns are being updated."

PRAC Led
**Hemangiol - propranolol - EMEA/H/C/002621/II/0019**
PIERRE FABRE DERMATOLOGIE, Rapporteur: Joseph Emmerich, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Concepcion Prieto Yerro, "Update of Package Leaflet in order to strengthen the warning on Hypoglycemia and Bronchospasm following completion of Drug Utilisation Study (DUS) performed in Germany and France to evaluate off-label use and effectiveness of RMM in a real-life clinical setting (MEA 002). In additions editorial changes has been introduced in section 4.4 of the SmPC as well as changes in the PL in accordance with QRD template 10.0. RMP version 3.1 has been submitted in order to updates the additional RMMs as a consequence of the results of the DUS."

PRAC Led
**Keytruda - pembrolizumab - EMEA/H/C/003820/II/0068**
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "C.I.11: Submission of an updated RMP version 23.1 in order to discuss the effectiveness of the educational materials put in place for Keytruda at the time of the initial marketing authorization and to provide a proposal to update these materials as well as to revise the safety specification as

requested by PRAC during PSUSA/00010403/2018 procedure."

PRAC Led

**Orencia - abatacept - EMEA/H/C/000701/II/0124/G**

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of the final reports from studies IM101125, IM101127, IM101211, IM101213 and the interim report from study IM101121 listed as category 3 studies in the RMP. These are biologic registries and pharmacoepidemiology studies to assess the risk associated with the use of abatacept during post-marketing in geographically diverse populations and subgroups.
Submission of the final study report from study IM101488 as supporting study but not listed in the RMP. This is a retrospective cohort study assessing the long-term safety of abatacept.
The deadline for submission of the final study report from study IM101121 (pregnancy registry) is proposed to be extended.
The RMP (version 26) is updated to reflect the completion of the studies IM101125, IM101127, IM101211, and IM101213, to update the information from studies IM101211 with the proposed extended deadline for submission of the final study report and to add two additional epidemiological studies IM101803 and IM101W52 as category 3 studies in the RMP. In addition, the MAH proposes to remove the following missing information items: combination therapy, including biologic therapy, and elderly patients."

PRAC Led

**Ozempic - semaglutide - EMEA/H/C/004174/II/0006**

Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 3.0 in order to reflect that the first milestones (Final protocol submission) for 2 of the additional pharmacovigilance activities have been fulfilled (for trials NN9535-4447 and NN9535-4352). Further the RMP is updated in line with the new template in accordance with Guideline on GVP

Module V – Risk management systems (Rev 2)."

PRAC Led

**RoActemra - tocilizumab - EMEA/H/C/000955/II/0082**

Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final study report: "Safety Report On Hypersensitivity In Patients Who Switched Between Tocilizumab Intravenous And Subcutaneous Routes Of Administration" based on safety data from UK BSRBR rheumatoid arthritis registry, WA22479 and ML22928 studies; listed as a category 3 study in the RMP."
Opinion adopted on 17.01.2019.

PRAC Led

**Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0011**

GlaxoSmithkline Biologicals SA, PRAC Rapporteur: Jan Neuhauser, PRAC-CHMP liaison: Andrea Laslop, "Submission of an updated RMP version 2 in order to extend the due dates of four category 3 studies (ZOSTER-002, ZOSTER-039, ZOSTER-041, ZOSTER-028) listed as required additional pharmacovigilance activities and to change the study design and due dates of a category 3 (EPI-ZOSTER-030 VS) listed as a required additional pharmacovigilance activity. In addition, the MAH took the opportunity to implement the new RMP template (Rev.2)."

PRAC Led

**Somavert - pegvisomant - EMEA/H/C/000409/II/0089**

Pfizer Europe MA EEIG, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Joseph Emmerich, "Submission of the final report from ACROSTUDY (Study A6291010), an open-label, global, non-interventional post-authorisation safety study (PASS) performed to monitor the long-term safety and outcomes of pegvisomant treatment in clinical practice. This final CSR relates to the Post Approval Measure MEA 059, listed as a category 3 study in the RMP."

PRAC Led

**Truvada - emtricitabine / tenofovir disoproxil - EMEA/H/C/000594/II/0159**

Gilead Sciences Ireland UC, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "Submission of the final study report for the non-interventional study GS-EU-276-4027, a Cross-Sectional Post-authorisation Safety Study to Assess Healthcare Providers' Level of Awareness of Risk Minimisation Materials for Truvada for Pre-Exposure Prophylaxis (PrEP) in the European Union, listed as a Category 3 study in the EU Risk Management Plan. This submission fulfils the post-authorisation measure MEA 045.7."

PRAC Led

**Xiapex - collagenase clostridium histolyticum - EMEA/H/C/002048/II/0106**

Swedish Orphan Biovitrum AB (publ), Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of the final report from a non-interventional post-authorisation safety study: Effectiveness of Xiapex educational material for healthcare professionals in the treatment of Peyronie's disease; listed as a category 3 study in the RMP."

PRAC Led

**Zaltrap - aflibercept - EMEA/H/C/002532/II/0051**

sanofi-aventis groupe, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Filip Josephson, "Submission of the final report from study OBS13597 / OZONE listed as a category 3 study in the RMP. This is a Prospective international observational cohort non-comparative study describing the safety and effectiveness of ZALTRAP® administered in combination with FOLFIRI for the treatment of patients with metastatic colorectal cancer in current clinical practice: A Post-Authorisation Safety Study (PASS). The RMP is updated accordingly and also transposed to revision 2 including revision of the List of Safety Concerns according to GVP module V Rev 2."

PRAC Led

**Zydelig - idelalisib - EMEA/H/C/003843/II/0046**

Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Greg Markey, "Submission of

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| the clinical study report for study GS-EU-313-4226, A Cross-Sectional Post-Authorization Safety Study to Assess Healthcare Provider Awareness of Risks Associated with Zydelig® in the European Union. This is a category 3 PASS study to assess the effectiveness of additional risk minimization measures by determining the level of knowledge of haematologists and oncologists (who manage patients with CLL or FL) about the infection risks associated with Zydelig treatment and the corresponding recommendation to minimize these risks as outlined in the SmPC and communicated in the direct healthcare professional communication (DHPC). This is to fulfill RMP post-authorisation measure MEA 016." | |
| PRAC Led<br>**WS1510**<br>**Mirapexin-EMEA/H/C/000134/WS1510/0089**<br>**Sifrol-EMEA/H/C/000133/WS1510/0080**<br>Boehringer Ingelheim International GmbH, Lead Rapporteur: Mark Ainsworth, Lead PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "RMP update to implement changes requested by PRAC in the context of the PSUSA procedure or in connection with a PRAC signal assessment procedure. The RMP update covers additionally the conversion into the new RMP template as per GVP Module V Revision 2 (EMA/838713/2011 Rev 2). Lastly the applicant takes the opportunity to adapt the medical search strategies and data retrieval approach without any impact on the overall safety conclusion." | |
| PRAC Led<br>**WS1521**<br>**Kivexa-EMEA/H/C/000581/WS1521/0079**<br>**Trizivir-EMEA/H/C/000338/WS1521/0112**<br>**Ziagen-EMEA/H/C/000252/WS1521/0105**<br>ViiV Healthcare B.V., Lead PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Joseph Emmerich, "Submission of an RMP version 1.0 combining the RMPs for Ziagen, Kivexa and Trizivir into one Abacavir active-substance RMP" | |
| PRAC Led<br>**WS1526**<br>**Enbrel-EMEA/H/C/000262/WS1526/0223**<br>**LIFMIOR-EMEA/H/C/004167/WS1526/00** | |

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Pfizer Europe MA EEIG, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Concepcion Prieto Yerro, "Submission of the final report from study (RABBIT register Cohort 2) listed as a category 3 study in the RMP. This is a prospective, non-interventional, observational, long-term cohort Germanic biologics register to evaluate the long-term effectiveness, safety, and costs associated with tumour necrosis factor (TNF)-inhibitor therapies in the treatment of rheumatoid arthritis (RA) in comparison to cohorts of RA patients treated with conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) and biologic (b)DMARDs."

PRAC Led

**WS1536**

**Levitra-EMEA/H/C/000475/WS1536/0064**

**Vivanza-EMEA/H/C/000488/WS1536/0060**

Bayer AG, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Concepcion Prieto Yerro, "Submission of the final clinical study report of a non-interventional PASS (category 3 study) to investigate the NAION risk associated with PDE5 inhibitors together with a consequential update of the RMP."

PRAC Led

**WS1543**

**Ultibro Breezhaler-EMEA/H/C/002679/WS1543/0029**

**Ulunar Breezhaler-EMEA/H/C/003875/WS1543/0029**

**Xoterna Breezhaler-EMEA/H/C/003755/WS1543/0033**

Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth, Lead PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final study report of the Category I Post-Authorisation Safety Study (PASS) CQVA149A2402 (Multinational database cohort study in Europe in COPD patients, to assess the incidence rates and hazard ratios of various safety outcomes in new users of indacaterol/glycopyrronium compared to new

users of comparator drugs (at the drug-class level).
The PI has been updated by the removal of the black triangle and amendments in Annex II.D (Conditions or restrictions with regard to the safe and effective use of the medicinal product). RMP version 5.0 has been submitted accordingly."

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

### B.6.13. CHMP-PRAC-CAT assessed procedures

**Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0029, ATMP**
Amgen Europe B.V., Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 5.2 of the SmPC in order to update the pharmacokinetic properties information based on the final results from study 20120324, a phase 2, multicenter, single-arm trial to evaluate the biodistribution and shedding of talimogene laherparepvec in subjects with unresected, stage IIIB to IVM1c melanoma. This submission fulfils MEA 006.1. In addition, the Marketing authorisation holder (MAH) took the opportunity to update Annex II as per the already assessed EMEA/H/C/002771/ANX/001 procedure."

### B.6.14. PRAC assessed ATMP procedures

### B.6.15. Unclassified procedures and worksharing procedures of type I variations

**WS1497/G**
**Infanrix hexa-EMEA/H/C/000296/WS1497/0251/G**
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

**WS1515**
**Infanrix hexa-EMEA/H/C/000296/WS1515/0253**
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

**WS1525**
**Hexacima-EMEA/H/C/002702/WS1525/0086**
**Hexaxim-EMEA/H/W/002495/WS1525/0091**
**Hexyon-EMEA/H/C/002796/WS1525/009**

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Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus

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**WS1529**
**Ambirix-EMEA/H/C/000426/WS1529/0094**
**Cervarix-EMEA/H/C/000721/WS1529/0100**
**Infanrix hexa-EMEA/H/C/000296/WS1529/0255**
**Rotarix-EMEA/H/C/000639/WS1529/0111**
**Twinrix Adult-EMEA/H/C/000112/WS1529/0129**
**Twinrix Paediatric-EMEA/H/C/000129/WS1529/0130**
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

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**WS1529**
**Ambirix-EMEA/H/C/000426/WS1529/0094**
**Cervarix-EMEA/H/C/000721/WS1529/0100**
**Infanrix hexa-EMEA/H/C/000296/WS1529/0255**
**Rotarix-EMEA/H/C/000639/WS1529/0111**
**Twinrix Adult-EMEA/H/C/000112/WS1529/0129**
**Twinrix Paediatric-EMEA/H/C/000129/WS1529/0130**
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

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**WS1531**
**Herceptin-EMEA/H/C/000278/WS1531/0150**
**Kadcyla-EMEA/H/C/002389/WS1531/0043**
Roche Registration GmbH, Lead Rapporteur: Jan Mueller-Berghaus

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**WS1533**
**Fluenz Tetra-EMEA/H/C/002617/WS1533/0088**
**Pandemic influenza vaccine H5N1 AstraZeneca-EMEA/H/C/003963/WS1533/0022**
AstraZeneca AB, Lead Rapporteur: Jan

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Mueller-Berghaus

**WS1545**
**Kivexa-EMEA/H/C/000581/WS1545/0080**
**Trizivir-EMEA/H/C/000338/WS1545/0113**
**Ziagen-EMEA/H/C/000252/WS1545/0106**
ViiV Healthcare B.V., Lead Rapporteur: Joseph Emmerich

**WS1551**
**Filgrastim**
**Hexal-EMEA/H/C/000918/WS1551/0047**
**Zarzio-EMEA/H/C/000917/WS1551/0048**
Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege

**WS1552**
**Fluenz**
**Tetra-EMEA/H/C/002617/WS1552/0087**
**Pandemic influenza vaccine H5N1**
**AstraZeneca-EMEA/H/C/003963/WS1552/0021**
AstraZeneca AB, Lead Rapporteur: Jan Mueller-Berghaus

**WS1560**
**Renvela-EMEA/H/C/000993/WS1560/0048**
**Sevelamer carbonate**
**Winthrop-EMEA/H/C/003971/WS1560/0019**
Genzyme Europe BV, Lead Rapporteur: Bart Van der Schueren

**WS1561**
**Enurev**
**Breezhaler-EMEA/H/C/002691/WS1561/0029**
**Seebri**
**Breezhaler-EMEA/H/C/002430/WS1561/0029**
**Tovanor**
**Breezhaler-EMEA/H/C/002690/WS1561/0033**
Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth

**B.7. DOCUMENTS TABLED IN MMD AFTER THE CHMP PLENARY**

**B.7.1. Yearly Line listing for Type I and II variations**

**B.7.2. Monthly Line listing for Type I variations**

**B.7.3. Opinion on Marketing Authorisation transfer (MMD only)**

**B.7.4. Notifications in accordance with Article 61(3) of Council Directive 2001/83/EC (MMD only)**

**B.7.5. Request for supplementary information relating to Notification of Type I variation (MMD only)**

**B.7.6. Notifications of Type I Variations (MMD only)**

**C. Annex C - Post-Authorisation Measures (PAMs), (Line listing of Post authorisation measures with a description of the PAM. Procedures starting in that given month with assessment timetabled)**

**D. Annex D - Post-Authorisation Measures (PAMs), (Details on PAMs including description and conclusion, for adoption by CHMP in that given month, or finalised ones with PRAC recommendation and no adoption by CHMP needed)**

**E. Annex E - 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:**

**E.2. Time Tables – starting & ongoing procedures: For information**

| | |
|---|---|
| PMF timetables starting and ongoing procedures | Tabled in MMD and sent by post mail (folder E). |

**F. ANNEX F - Decision of the Granting of a Fee Reduction/Fee Waiver**

**F.1. Parallel Distribution - Pursuant to Article 9 of Council Regulation (EC) No. 2743/98 of 14 December 1998, as amended**

**F.2. Request for scientific opinion on justification of exceptional circumstance and for imperative grounds of public health**

**G. ANNEX G**

**G.1. Final Scientific Advice (Reports and Scientific Advice letters):**

Information related to Scientific Advice cannot be released at the present time as these contain commercially confidential information.

**HTA:**

### G.2. Ongoing procedures

### G.3. PRIME

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

#### G.3.1. List of procedures concluding at 28-31 January 2019 CHMP plenary:

#### G.3.2. List of procedures starting in January 2019 for February 2019 CHMP adoption of outcomes

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