25 June 2018
EMA/CHMP/424087/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

# Committee for medicinal products for human use (CHMP)

## Draft agenda for the meeting on 25-28 June 2018

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

25 June 2018, 13:00 – 19:30, room 2A

26 June 2018, 08:30 – 19:30, room 2A

27 June 2018, 08:30 – 19:30, room 2A

28 June 2018, 08:30 – 16:00, room 2A

**Health and safety information**

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

**Disclaimers**

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

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

**Note on access to documents**

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

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# 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 25-28 June 2018. See June 2018 CHMP minutes (to be published post July 2018 CHMP meeting).

## 1.2. Adoption of agenda

CHMP agenda for 25-28 June 2018

## 1.3. Adoption of the minutes

CHMP minutes for 28-31 May 2018.

# 2. Oral Explanations

## 2.1. Pre-authorisation procedure oral explanations

### 2.1.1. vestronidase alfa - Orphan - EMEA/H/C/004438

Ultragenyx Germany GmbH; treatment of Mucopolysaccharidosis VII (MPS VII; Sly syndrome) for patients of all ages

Scope: Possible oral explanation, Report from the ad-hoc expert group meeting held on 19 June 2018, Opinion

Action: Possible oral explanation to be held on 26 June 2018 at time 16:00

List of Outstanding Issues adopted on 26.04.2018, 22.02.2018. List of Questions adopted on 14.09.2017.

Note: The final list of experts for the ad-hoc expert group meeting held on 19 June 2018 was adopted via written procedure on 18.06.2018

See 3.1

### 2.1.2. volanesorsen - Orphan - EMEA/H/C/004538

Akcea Therapeutics UK Ltd.; as an adjunct to diet for the treatment of patients with familial chylomicronemia syndrome (FCS)

Scope: Oral explanation, Report from the ad-hoc expert group meeting on 19 June 2018.

**Action**: Oral explanation to be held on 26 June 2018 at time 11:00

List of Outstanding Issues adopted on 26.04.2018. List of Questions adopted on 14.12.2017.

### 2.1.3. tezacaftor / ivacaftor - Orphan - EMEA/H/C/004682

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

Scope: Oral explanation

**Action**: Oral explanation to be held on 28 June 2018 at time 09:00

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

### 2.1.4. abemaciclib - EMEA/H/C/004302

treatment of hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer

Scope: Oral explanation

**Action**: Oral explanation to be held on 25 June 2018 at time 16:00

List of Outstanding Issues adopted on 26.04.2018. List of Questions adopted on 14.12.2017.

## 2.2. Re-examination procedure oral explanations

### 2.2.1. Nerlynx - neratinib - EMEA/H/C/004030

Puma Biotechnology Limited; extended adjuvant treatment of adult patients with early-stage HER2-overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab based therapy

Scope: Oral explanation

**Action**: Oral explanation to be held on 26 June 2018 at time 09:00

Opinion adopted on 22.02.2018.

See 3.5

## 2.3. Post-authorisation procedure oral explanations

### 2.3.1. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/II/0063/G

Vertex Pharmaceuticals (Europe) Ltd.

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Melinda Sobor, PRAC Rapporteur: Dolores Montero Corominas

Scope: Oral explanation

**Action**: Oral explanation to be held on 28 June 2018 at time 09:00

**Action**: For adoption

Request for Supplementary Information adopted on 31.05.2018, 22.03.2018, 14.12.2017.

### 2.3.2. Opdivo - nivolumab - EMEA/H/C/003985/II/0039

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Oral explanation

**Action**: Oral explanation to be held on 27 June 2018 at time 14:00

Request for Supplementary Information adopted on 26.04.2018, 14.12.2017.

See 5.1

### 2.3.3. Opdivo - nivolumab - EMEA/H/C/003985/II/0041

Bristol-Myers Squibb Pharma EEIG

Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Oral explanation, Report from the SAG-Oncology meeting scheduled 18 June.

**Action**: Oral explanation to be held on 27 June 2018 at time 11:00

Request for Supplementary Information adopted on 26.04.2018, 25.01.2018.

Note: The list of experts for the SAG-Oncology meeting held on 18 June was adopted via written procedure on 15 June 2018

See 5.1

## 2.4. Referral procedure oral explanations

# 3. Initial applications

## 3.1. Initial applications; Opinions

### 3.1.1. caplacizumab - Orphan - EMEA/H/C/004426

Ablynx NV; treatment of acquired thrombotic thrombocytopenic purpura (aTTP)

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 31.05.2018, 25.01.2018. List of Questions adopted on 22.06.2017.

### 3.1.2. lesinurad / allopurinol - EMEA/H/C/004412

gout

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 26.04.2018. List of Questions adopted on 09.11.2017.

### 3.1.3. vigabatrin - PUMA - EMEA/H/C/004534

Treatment in monotherapy of infantile spasms (West's syndrome) and resistant partial epilepsy in infants and children

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 26.04.2018. List of Questions adopted on 14.12.2017.

### 3.1.4. tisagenlecleucel - Orphan - ATMP - EMEA/H/C/004090

Novartis Europharm Limited; treatment of B cell acute lymphoblastic leukaemia (ALL) and diffuse large B cell lymphoma (DLBCL)

Scope: Opinion, Report from the SAG-Oncology meeting held 18 June 2018

**Action**: For adoption

List of Outstanding Issues adopted on 25.05.2018. List of Questions adopted on 16.03.2018.

### 3.1.5. vestronidase alfa - Orphan - EMEA/H/C/004438

Ultragenyx Germany GmbH; treatment of Mucopolysaccharidosis VII (MPS VII; Sly syndrome) for patients of all ages

Scope: possible oral explanation, Report from the ad-hoc expert group meeting, Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 26.04.2018, 22.02.2018. List of Questions adopted on 14.09.2017.

Note: The final list of experts for the ad-hoc expert group meeting held on 19 June 2018 was adopted via written procedure on 18.06.2018

### 3.1.6. ulipristal acetate - EMEA/H/C/005017

treatment of uterine fibroids

Scope: Opinion

**Action**: For adoption

### 3.1.7. vonicog alfa - Orphan - EMEA/H/C/004454

Baxalta Innovations GmbH; Treatment of von Willebrand Disease (VWD)

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 31.05.2018, 22.03.2018. List of Questions adopted on 12.10.2017.

### 3.1.8. daunorubicin / cytarabine - Orphan - EMEA/H/C/004282

Jazz Pharmaceuticals Ireland Limited; treatment of adults with high-risk acute myeloid leukaemia (AML)

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 31.05.2018, 24.04.2018. List of Questions adopted on 20.02.2018.

### 3.1.9. axicabtagene ciloleucel - Orphan - ATMP - EMEA/H/C/004480

Kite Pharma EU B.V.; treatment of diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL) and transformed follicular lymphoma (TFL)

Scope: Opinion

**Action**: For adoption

List of Outstanding Issues adopted on 20.04.2018. List of Questions adopted on 08.12.2017.

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

### 3.2.1. doravirine - EMEA/H/C/004747

treatment of adults infected with HIV-1 without past or present evidence of viral resistance to doravirine

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 22.03.2018.

### 3.2.2. doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746

treatment of adults infected with HIV-1 without past or present evidence of viral resistance to doravirine, lamivudine, or tenofovir

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 22.03.2018.

### 3.2.3. fexinidazole - Article 58 - EMEA/H/W/002320

Accelerated assessment

treatment of human African trypanosomiasis (HAT)

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 24.04.2018.

### 3.2.4. damoctocog alfa pegol - Orphan - EMEA/H/C/004054

Bayer AG; Treatment and prophylaxis of haemophilia A

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 25.01.2018.

### 3.2.5. patisiran - Orphan - EMEA/H/C/004699

Accelerated assessment

Alnylam Netherlands B.V.; treatment of hereditary transthyretin-mediated amyloidosis

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 24.04.2018.

### 3.2.6. pegfilgrastim - EMEA/H/C/004700

treatment of neutropenia

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 25.01.2018.

### 3.2.7. pegfilgrastim - EMEA/H/C/004413

treatment of neutropenia

Scope: List of outstanding issues

**Action**: For adoption

List of Outstanding Issues adopted on 14.12.2017. List of Questions adopted on 23.03.2017.

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

### 3.3.1. bevacizumab - EMEA/H/C/004697

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

Scope: List of questions

**Action**: For adoption

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

treatment of neutropenia

Scope: List of questions

**Action**: For adoption

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

Univar BV; Treatment of Wilson's disease

Scope: List of questions

**Action**: For adoption

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

treatment of neutropenia

Scope: List of questions

**Action**: For adoption

### 3.3.5. apalutamide - EMEA/H/C/004452

treatment of non-metastatic castration resistant prostate cancer (NM CRPC)

Scope: List of questions

**Action**: For adoption

### 3.3.6. hydroxycarbamide - EMEA/H/C/004837

prevention of complications of Sickle Cell disease

Scope: List of questions

**Action**: For adoption

### 3.3.7. silodosin - EMEA/H/C/004964

treatment of prostatic hyperplasia (BPH)

Scope: List of questions

**Action**: For adoption

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

Accelerated assessment

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

Scope: List of questions

**Action**: For adoption

### 3.3.9. 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: List of questions

**Action**: For adoption

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

Emmaus Medical Europe Ltd; treatment of sickle cell disease

Scope: List of questions

**Action**: For adoption

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

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

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

Scope: Request for an extension to the clock stop to respond to the list of outstanding issues adopted on 31.05.2018

**Action:** For adoption

List of Outstanding Issues adopted on 31.05.2018, 23.03.2017. List of Questions adopted on 21.07.2016.

### 3.4.2. pegfilgrastim - EMEA/H/C/004556

reduction in the duration of neutropenia and the incidence of febrile neutropenia

Scope: Request by the applicant for an extension to the clock stop to respond to the list of question adopted on 22.03.2018

**Action**: For adoption

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

### 3.5.1. Nerlynx - neratinib - EMEA/H/C/004030

Puma Biotechnology Limited; extended adjuvant treatment of adult patients with early-stage HER2-overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab based therapy

Scope: Re-examination of Opinion

**Action**: For adoption

Opinion adopted on 22.02.2018.

See 2.2

### 3.5.2. Exondys - eteplirsen - Orphan - EMEA/H/C/004355

AVI Biopharma International Ltd; treatment of Duchenne muscular dystrophy

Scope: Appointment of re-examination Rapporteurs

**Action**: For adoption

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

Opinion adopted on 31.05.2018. List of Outstanding Issues adopted on 14.12.2017. List of Questions adopted on 21.04.2017.

### 3.5.3. Eladynos - abaloparatide - EMEA/H/C/004157

Radius International Ltd; treatment of osteoporosis

Scope: Final list of questions and draft list of experts to the ad-hoc expert group meeting

**Action:** For adoption

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

Opinion adopted on 22.03.2018.

### 3.5.4. Dexxience - betrixaban - EMEA/H/C/004309

Portola Pharma UK Limited; treatment of prophylaxis of venous thromboembolism (VTE)

Scope: List of questions to the SAG

**Action:** For adoption

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

Opinion adopted on 22.03.2018.

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

No items

## 3.7. Withdrawals of initial marketing authorisation application

No items

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

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

### 4.1.1. Bydureon - exenatide - EMEA/H/C/002020/X/0048/G

AstraZeneca AB; treatment of type 2 diabetes mellitus

Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue

Scope: "Extension application to introduce new pharmaceutical form (prolonged-release suspension for injection) grouped with type II variation to align the PI for the approved Bydureon products (powder and solvent for prolonged-release suspension for injection, and powder and solvent for prolonged-release suspension for injection in pre-filled pen) with the PI proposed for the Bydureon new pharmaceutical form (prolonged-release suspension for injection in autoinjector). In addition, the MAH took the opportunity to make minor editorial changes through SmPC. Moreover, RMP version 28 has been submitted as part of this application."

**Action**: For adoption

List of Outstanding Issues adopted on 26.04.2018. List of Questions adopted on 25.01.2018.

## 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. Inhixa - enoxaparin sodium - EMEA/H/C/004264/X/0018

Techdow Europe AB

Rapporteur: Andrea Laslop, PRAC Rapporteur: Menno van der Elst

Scope: "Extension application to add two new strengths of 12,000 IU (120 mg)/0.8 mL and 15,000 IU (150 mg)/1 mL for enoxaparin sodium solution for injection in pre-filled syringe, for subcutaneous, extracorporeal and intravenous administration."

**Action**: For adoption

List of outstanding issues adopted on 31.05.2018. List of Questions adopted on 14.12.2017.

### 4.2.2. Inhixa - enoxaparin sodium - EMEA/H/C/004264/X/0026

Techdow Europe AB

Rapporteur: Andrea Laslop, PRAC Rapporteur: Menno van der Elst

Scope: “Extension application to add two new strengths of 30,000 IU (300 mg)/3 mL and 50,000 IU (500 mg)/5 mL for enoxaparin sodium solution for injection in vial, for subcutaneous, extracorporeal and intravenous administration.”

**Action**: For adoption

List of Questions adopted on 22.03.2018.

## 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. Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/X/0034/G

Vertex Pharmaceuticals (Europe) Ltd

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Almath Spooner

Scope: “1. Extension application to introduce a new pharmaceutical form (granules) in 2 strengths (100/125 mg and 150/188 mg) for paediatric use (2 to 5 years). An updated RMP (v 4.0) has been submitted.
2. Type II (C.I.4): Update of sections 4.1, 4.2, 4.5, 4.8 and 5.3 of the SmPC of the tablets formulation to bring it in line with the proposed paediatric 2-5 years old extension application.”

**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. Blincyto - blinatumomab - Orphan - EMEA/H/C/003731/II/0018

Amgen Europe B.V.

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Eva Jirsová

Scope: “Extension of Indication to include the children 1 month and older to the authorised population for the treatment of adults with Philadelphia chromosome-negative relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL) for BLINCYTO;
as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated in order to include the new population, update the posology and update the safety information. The Package Leaflet is updated in accordance.
RMP version 6.0 has been submitted”

**Action**: For adoption

Request for Supplementary Information adopted on 22.03.2018, 12.10.2017.

### 5.1.2. Cabometyx - cabozantinib - EMEA/H/C/004163/II/0005

Ipsen Pharma

Rapporteur: Robert James Hemmings, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Sabine Straus

Scope: “Extension of indication to include the treatment of advanced hepatocellular carcinoma in adults following prior systemic therapy for Cabometyx; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC are updated with safety and efficacy information. The package leaflet and the risk management plan (version 4.0) are also updated accordingly.”

**Action**: For adoption

### 5.1.3. Dexdor - dexmedetomidine - EMEA/H/C/002268/II/0026

Orion Corporation

Rapporteur: Greg Markey, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Julie Williams

Scope: “Extension of Indication to include "For sedation of non-intubated adult patients prior to and/or during diagnostic or surgical procedures requiring sedation, i.e. procedural/awake sedation" for Dexdor; as a consequence, section 4.1, 4.2, 4.4, 4.6, 4.7, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.

RMP version 7 has been submitted"

**Action**: For adoption

Request for Supplementary Information adopted on 26.04.2018.

### 5.1.4. Inovelon - rufinamide - Orphan - EMEA/H/C/000660/II/0045

Eisai Ltd

Rapporteur: Alexandre Moreau, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension of indication to include the treatment of seizures associated with Lennox Gastaut syndrome in patients 1 year of age and older as adjunctive therapy. As a consequence sections 4.1, 4.2, 4.5, 5.1 and 5.2 are updated. The Package Leaflet and the RMP (version 10.0) are updated accordingly. In addition the Marketing Authorisation Holder (MAH) took the opportunity to make small corrections in the Product Information and to update the name and contact details of the local representative in Belgium and Luxembourg. Furthermore, the Product Information is brought in line with the latest QRD template version 10."

**Action**: For adoption

Request for Supplementary Information adopted on 31.05.2018, 14.12.2017.

### 5.1.5. Jinarc - tolvaptan - EMEA/H/C/002788/II/0009

Otsuka Pharmaceutical Europe Ltd

Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Julie Williams

Scope: "Extension of Indications based on the results of a completed Post Authorisation Efficacy Study (PAES, Trial 156-13-210) as mandated by Annex II of the Product Information with tolvaptan (ANX 006). Trial 156-13-210 is a Phase 3b, Multi-centre, Randomized-withdrawal, Placebo-controlled, Double-blind, Parallel-group Trial to Compare the Efficacy and Safety of Tolvaptan (45 to 120 mg/day, Split-dose) in Subjects with Chronic Kidney Disease between Late Stage 2 to Early Stage 4 Due to Autosomal Dominant Polycystic Kidney Disease.

Updates to SmPC Sections 4.1, 4.8 (to add 'abdominal pain' to the table of adverse events and present the data in line with QRD recommendations) and 5.1 are being proposed. The Package Leaflet is updated in accordance. Minor additional editorial changes to the PI were also carried out.

Version 13.2 of the RMP was submitted, updated to reflect the study results."

**Action**: For adoption

Request for Supplementary Information adopted on 26.04.2018.

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

Vertex Pharmaceuticals (Europe) Ltd.

Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Extension of Indication to include treatment of cystic fibrosis in children age 12 to less than 24 months who have one of the currently approved gating mutations in the CFTR gene for Kalydeco 50 mg & 75 mg Granules; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. Relevant consequential changes are made to the Kalydeco 150 mg film-coated tablet Product Information. The Package Leaflet is updated in accordance.
The RMP version 7.2 has also been submitted."

**Action**: For adoption

### 5.1.7. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0042

Merck Sharp & Dohme B.V.

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include treatment as monotherapy of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) on or after platinum-containing chemotherapy based on the results from KEYNOTE-040 (KN040) with supportive data from two additional single arm studies (KEYNOTE-012/ KEYNOTE-055). KN040 is a randomized, multi-center, pivotal phase III study investigating KEYTRUDA as a monotherapy versus standard treatment (methotrexate, docetaxel or cetuximab) in 495 patients with recurrent or metastatic HNSCC who have previously progressed on prior platinum. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to include in SmPC section 5.2 the description of pembrolizumab PK results on time-dependent change in clearance using a time-dependent pharmacokinetic (TDPK) model structure rather than the static PK model structure.
An updated RMP version 15.1 was provided as part of the application."

**Action**: For adoption

Request for Supplementary Information adopted on 26.04.2018.

### 5.1.8. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0043

Merck Sharp & Dohme B.V.

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include 1st line treatment of non-squamous non-small cell lung cancer (NSCLC) in combination with pemetrexed and platinum chemotherapy based on the efficacy and safety data from pivotal study KEYNOTE-189, supported by data from KEYNOTE-021 cohorts C and G.
KEYNOTE-189 is a phase 3, randomized, placebo-controlled study undertaken to evaluate the efficacy and safety of pembrolizumab +pemetrexed + carboplatin or cisplatin (pembro

combo) versus saline placebo + pemetrexed + carboplatin or cisplatin (control) in previously untreated subjects with advanced/metastatic nonsquamous NSCLC with no EGFR or ALK genomic tumor aberrations.
As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated and the Package Leaflet is updated in accordance.
An updated RMP version 16.2 was provided as part of the application."

**Action**: For adoption

### 5.1.9. Lenvima - lenvatinib - Orphan - EMEA/H/C/003727/II/0011/G

Eisai Europe Ltd.

Rapporteur: Bart Van der Schueren, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include treatment of hepatocellular carcinoma (HCC) based on pivotal Study 304. Consequently, sections 4.1, 4.2, 4.4, 4.8, 5.1, and 5.2 of the SmPC are being updated and the package leaflet is updated accordingly. In addition, section 4.2 of the SmPC is being updated to add that the product can be administered as a suspension in water or apple juice. In addition, the labelling is updated to include the unique identifier. An updated RMP version 10 was provided as part of the application."

**Action**: For adoption

Request for Supplementary Information adopted on 31.05.2018, 22.02.2018, 09.11.2017.

### 5.1.10. Lynparza - olaparib - EMEA/H/C/003726/II/0020

AstraZeneca AB

Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to include the use of Lynparza tablets as a montherapy for the treatment of adult patients with BRCA1/2-mutated HER2 negative metastatic breast cancer who have previously been treated with chemotherapy. These patients could have received chemotherapy in the neoadjuvant, adjuvant or metastatic setting.

As a consequence, section 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC for Lynparza tablets have been updated. Section 4.8 of Lynparza capsules and relevant sections of the package leaflet have been updated accordingly. Furthermore, RMP version 16 has also been provided."

**Action**: For adoption

### 5.1.11. MabThera - rituximab - EMEA/H/C/000165/II/0149

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver

Scope: "Extension of indication to include the maintenance of remission of polyangiitis (Wegener's) (GPA) and microscopic polyangiitis (MPA) for MabThera; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package leaflet is updated

accordingly. In addition, the MAH took the opportunity to implement a terminology change in Annex II."

**Action**: For adoption

### 5.1.12. 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

### 5.1.13. Opdivo - nivolumab - EMEA/H/C/003985/II/0039

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include treatment of adult patients with advanced or recurrent gastric or gastroesophageal junction (GEJ) cancer after two or more prior systemic therapies, based on data from study ONO-4538-12. As a consequence, sections 4.1, 4.4, 4.8, and 5.1 of the SmPC are updated. The Annex II and Package Leaflet are updated in accordance. The RMP version version 11.0 has also been submitted."

**Action**: For adoption

Request for Supplementary Information adopted on 26.04.2018, 14.12.2017.

### 5.1.14. Opdivo - nivolumab - EMEA/H/C/003985/II/0041

Bristol-Myers Squibb Pharma EEIG

Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include adjuvant treatment of adults and adolescents 12 years of age and older with completely resected Stage III and IV melanoma for OPDIVO; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add efficacy and safety information from the pivotal Study CA209238. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to the PI.
The RMP version 12.0 has also been submitted. The MAH also took the opportunity to revise the due dates for two Category 4 studies (CA209172 and CA209171) to a later date."

Report from the SAG-Oncology meeting held on 18 June 2018

**Action**: For adoption

Request for Supplementary Information adopted on 26.04.2018, 25.01.2018.

### 5.1.15. Rapamune - sirolimus - EMEA/H/C/000273/II/0164

Pfizer Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include the treatment of patients with lymphangioleiomyomatosis. As a consequence section 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 6.0) are updated in accordance. In addition the MAH took the opportunity to make very minor formatting changes in the Labelling."

**Action**: For adoption

Request for Supplementary Information adopted on 26.04.2018, 25.01.2018, 20.07.2017.

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

GE Healthcare AS

Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty

Scope: "Extension of Indication to include use in the measurement of fractional flow reserve (FFR) during invasive coronary angiography (ICA) in patients presenting a coronary artery stenosis for Rapiscan based on study 060912001: Comparison of Regadenoson (RAPISCAN) and Central Intravenous Adenosine for Measurement of Fractional Flow Reserve and data from published literature. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. An updated RMP version 10.0 was provided as part of this extension of indication."

**Action**: For adoption

### 5.1.17. RoActemra - tocilizumab - EMEA/H/C/000955/II/0076

Roche Registration GmbH

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "To add the paediatric indication 'treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 1 year of age and older, who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids' to the RoActemra 162 mg solution for injection in pre-filled syringe formulation, based on data from the Phase Ib pharmacokinetic/pharmacodynamic bridging study WA28118 (JIGSAW 118), designed to confirm the RoActemra subcutaneous dosing regimens in patients aged 1 to 17 years old with sJIA, as well as assess the safety of the RoActemra subcutaneous formulation. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet is updated accordingly.
In addition, sections 4.2, 4.8 and 5.2 of the SmPC of the RoActemra 20 mg/mL concentrate for solution for infusion formulation are updated to reflect data from the pivotal RoActemra intravenous study WA18221 (TENDER), a randomised, placebo-controlled study to evaluate the effect of tocilizumab on disease response in patients with active sJIA."

**Action**: For adoption

### 5.1.18. RoActemra - tocilizumab - EMEA/H/C/000955/II/0078

Roche Registration GmbH

Rapporteur: Jan Mueller-Berghaus

Scope: "Extension of indication to include the indication 'treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS) in adults and paediatric patients 2 years of age and older' for the RoActemra 20mg/ml concentrate for solution for infusion. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 6.6 the SmPC are updated. The Package Leaflet is updated in accordance."

**Action:** For adoption

### 5.1.19. Trimbow - beclometasone dipropionate / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004257/II/0002

Chiesi Farmaceutici S.p.A.

Rapporteur: Harald Enzmann, PRAC Rapporteur: Jan Neuhauser

Scope: "Extension of Indication for Trimbow to all adult patients with moderate or severe chronic obstructive pulmonary disease (COPD).

As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated in order to add the results of two Phase III studies (Triple 7 and Triple 8);

Triple 7 (CCD-05993AA1-07) is a multinational, multicentre, randomised, open-label, active-controlled, 26-week, 2-arm, parallel group study to evaluate the non-inferiority of fixed combination of beclomethasone dipropionate plus formoterol fumarate plus glycopyrronium bromide administered via pressurised metered dose inhaler (pMDI) (CHF 5993) versus (vs.) fixed combination of fluticasone furoate plus vilanterol administered via dry powder inhaler (DPI) (Relvar®) plus tiotropium bromide (Spiriva®) for the treatment of patients with Chronic Obstructive Pulmonary Disease (COPD).

Triple 8 (CCD-05993AA1-08) is a 52-week, double blind, double dummy, randomized, multinational, multicentre, 2-arm parallel group, active controlled clinical trial of fixed combination of beclomethasone dipropionate plus formoterol fumarate plus glycopyrronium bromide administered via pMDI (CHF 5993) versus indacaterol/glycopyrronium (Ultibro®) via DPI in patients with Chronic Obstructive Pulmonary Disease (TRIBUTE)

The Package Leaflet and the Risk Management Plan are updated in accordance."

**Action**: For adoption

### 5.1.20. Tyverb - lapatinib - EMEA/H/C/000795/II/0051

Novartis Europharm Limited

Rapporteur: Filip Josephson, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Update of sections 4.1 and 5.1 of the SmPC based on results from study EGF114299/LAP016A2307 listed as a condition (ANX027.4) in the Annex II; a Phase III trial

to compare the safety and efficacy of
lapatinib plus trastuzumab plus an aromatase inhibitor (AI) versus trastuzumab plus an AI versus lapatinib plus an AI as first- or second-line therapy in postmenopausal subjects with hormone receptor positive, HER2-positive metastatic breast cancer (MBC) who have received prior trastuzumab and endocrine therapies. Annex II has been updated accordingly. A revised RMP version 34.0 has also been submitted as part of the application."

**Action**: For adoption

Request for Supplementary Information adopted on 22.03.2018.

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

No items

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

### 5.3.1. Sutent - sunitinib - EMEA/H/C/000687/II/0065

Pfizer Limited

Scope: "Extension of Indication to include adjuvant treatment of patients at high risk of recurrent renal cell carcinoma (RCC) following nephrectomy for Sutent; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated based on the study A6181109 ("a randomized double-blind phase 3 study of adjuvant sunitinib vs. placebo in subjects at high risk of recurrent RCC"). The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to the SmPC and Package Leaflet and in addition, to fulfil PAM (FU2 22.5). Furthermore, the PI is brought in line with the latest QRD template version 10. Moreover, updated RMP version 16 has been submitted."

Report from the SAG-Oncology meeting held on 19 June 2018

**Action**: For adoption

Opinion adopted on 22 February 2018.

Note: The list of experts for the SAG-Oncology meeting held on 19 June was adopted via written procedure on 15 June 2018

# 6. Ancillary medicinal substances in medical devices

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

No items

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

No items

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

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

No items

# 8. Pre-submission issues

## 8.1. Pre-submission issue

### 8.1.1. esketamine hydrochloride - H0004535

For the treatment of moderate to severe treatment resistant depression (Major Depressive Disorder in adults who have not responded sufficiently to at least two different antidepressants to treat the current depressive episode). Must be co-administered with a newly initiated oral antidepressant therapy

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

No items

# 10. Referral procedures

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

No items

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

No items

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

No items

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

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

MAHs: various

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Harald Enzmann

Scope: List of outstanding issues

**Action:** For adoption

Second wave of repeat use of MRP procedure

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

### 10.5.1. Septanest/Septanest Forte and associated names – Articaine (hydrochloride)/ Adrenaline (tartrate) - EMEA/H/A-30/1461

Septodont group of companies and associated companies

Rapporteur: TBC, Co-rapporteur: TBC

Scope: Start of procedure, timetable, appointment of Rapporteurs

**Action:** For adoption

Harmonisation exercise for Septanest and associated names. Summary of Product Characteristics and Module 3 harmonisation was triggered by the MAH.

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

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

MAHs: various

Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise

Scope: List of outstanding issues

**Action:** For adoption

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

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

MAH various

Rapporteur: TBC, Co-rapporteur: TBC,

Scope: Start of procedure, appointment of Rapporteurs, list of questions

**Action:** For adoption

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

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

No items

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

No items

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

No items

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

No items

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

No items

## 11. Pharmacovigilance issue

### 11.1. Early Notification System

June 2018 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

**Action**: For information

## 12. Inspections

### 12.1. GMP inspections

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

### 12.2. GCP inspections

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

### 12.3. Pharmacovigilance inspections

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

## 12.4. GLP inspections

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

# 13. Innovation Task Force

## 13.1. Minutes of Innovation Task Force

No items

## 13.2. Innovation Task Force briefing meetings

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

ITF Briefing Meeting - Meeting date: 28th June 2018

**Action:** For adoption

ITF Briefing Meeting Meeting date: 19th July 2018

**Action:** For adoption

ITF Briefing Meeting - Meeting date: 27th June or 2nd July 2018

**Action:** For adoption

ITF Briefing Meeting - Meeting date: 25th June 2018

**Action:** For adoption

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

No items

## 13.4. Nanomedicines activities

No items

# 14. Organisational, regulatory and methodological matters

## 14.1. Mandate and organisation of the CHMP

### 14.1.1. Seating plan for CHMP under Austrian EU Presidency, 1 July – 31 December 2018

CHMP Seating Plan 1 July – 31 December 2018, under Austrian EU presidency

**Action:** For information

### 14.1.2. Anti-PD-1/PD-L1 – Trend for initial worse efficacy performance

CHMP: Daniela Melchiorri

Scope: Follow up discussion from May 2018 Plenary meeting, strategy

**Action:** For discussion

## 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 11-14 June 2018

**Action:** For information

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

**Action:** For adoption

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

CAT draft minutes of meeting held on 20-22 June 2018
**Action**: For information

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

Report from the HMPC meeting held on 4-5 June 2018

**Action:** For information

### 14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at June 2018 PDCO

**Action:** For information

Report from the PDCO meeting held on 26-29 June 2018

**Action:** For information

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

Report from the COMP meeting held on 19-21 June 2018
**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 25-27 June 2018

**Action:** For information

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

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

Report from the SAWP meeting held on 11-14 June 2018. Table of conclusions

**Action:** For information

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

Call for interest for nomination of a replacement SAWP member and his/her alternate following resignation of Jan Sjoberg.

The required area of expertise is Virology and Oncology / Onco-Haematology

The letters of candidacy together with the CV of both member and alternate, as per the SAWP Mandate requirements, should be sent directly to the SAWP Secretariat by **20 July 2018**

**Action:** For information

### 14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 28-29 May 2018.

**Action:** For adoption

### 14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP June 2018 meeting to CHMP for adoption:

- 16 reports on products in scientific advice and protocol assistance
- 8 reports on products in pre-authorisation procedures
- 1 reports on products in post-authorisation procedures
- 2 reports on products in plasma master file

**Action:** For adoption

### 14.3.4. Safety Working Party (SWP)

Chair: Jan Willem Van der Laan

SWP report on anaesthetics and sedatives in young children and pregnant women (EMA/CHMP/SWP/172599/2018)

**Action**: For adoption

### 14.3.5. Blood Products Working Party (BPWP)

Chair: Jacqueline Kerr

Guideline on the clinical investigation of human normal immunoglobulin for intravenous administration (IVIg) and related core SmPC

**Action:** For adoption

### 14.3.6. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus

Appointment of a new core member to RIWP

One new member is envisaged, for the development of a “Concept paper on development strategies for allergen products intended for allergies with low prevalence” experts with regulatory and/or clinical expertise for this topic are sought.

Please send the nominations to the Agency **by 22 June 2018**.

**Action:** For adoption

## 14.4. Cooperation within the EU regulatory network

No items

## 14.5. Cooperation with International Regulators

No items

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

No items

## 14.7. CHMP work plan

No items

## 14.8. Planning and reporting

### 14.8.1. New marketing authorisation applications for 2018 with and without appointed rapporteurs

**Action:** For information

## 14.9. Others

No items

# 15. Any other business

## 15.1. AOB topic

No items

## 16. Explanatory notes

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

**Oral explanations** *(section 2)*

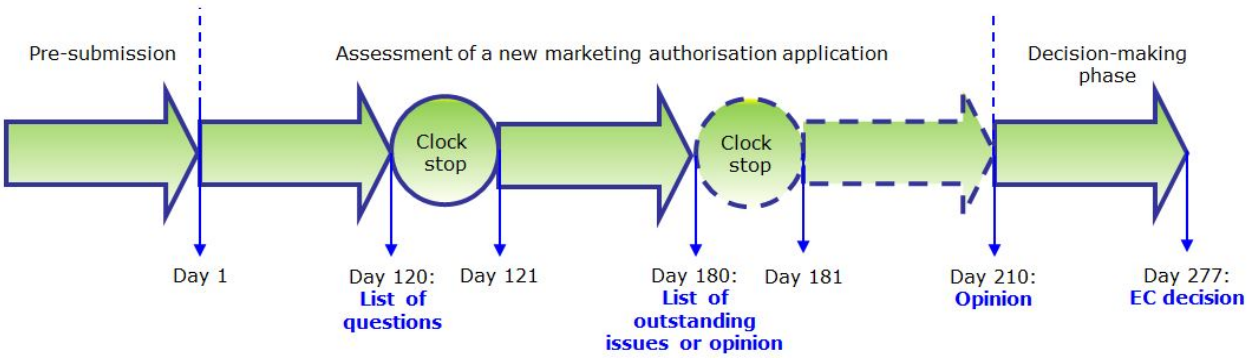
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

**Initial applications** *(section 3)*

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

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

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




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

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

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

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

Extensions of marketing authorisations are applications for the change or addition of new strengths,

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

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

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

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

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

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

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

**Re-examination procedures** *(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/

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 June 2018
EMA/CHMP/427802/2018

# Annex to 25-28 June 2018 CHMP Agenda

Pre submission and post authorisations issues

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## A. PRE SUBMISSION ISSUES

### A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for June 2018: **For adoption**

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

Final Outcome of Rapporteurship allocation for June 2018: **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

**Firdapse - amifampridine - EMEA/H/C/001032/S/0053, Orphan**
BioMarin Europe Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams

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

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

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

**Abilify Maintena - aripiprazole - EMEA/H/C/002755/R/0025**
Otsuka Pharmaceutical Europe Ltd, Rapporteur: Bruno Sepodes, Co-Rapporteur: Eleftheria Nikolaidi, PRAC Rapporteur: Qun-Ying Yue
Request for Supplementary Information adopted on 31.05.2018.

**Evicel - human fibrinogen / human thrombin - EMEA/H/C/000898/R/0054**
Omrix Biopharmaceuticals N. V., Rapporteur:

Jan Mueller-Berghaus, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Brigitte Keller-Stanislawski
Request for Supplementary Information adopted on 26.04.2018.

**Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/R/0079**
AstraZeneca AB, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Jean-Michel Dogné

**INTELENCE - etravirine - EMEA/H/C/000900/R/0052**
Janssen-Cilag International NV, Rapporteur: Joseph Emmerich, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Caroline Laborde
Request for Supplementary Information adopted on 31.05.2018.

**Memantine Accord - memantine - EMEA/H/C/002766/R/0010**
Accord Healthcare Limited, Generic, Generic of Axura, Rapporteur: Milena Stain, PRAC Rapporteur: Dolores Montero Corominas

**Opsumit - macitentan - EMEA/H/C/002697/R/0027, Orphan**
Actelion Registration Limited, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Dolores Montero Corominas
Request for Supplementary Information adopted on 31.05.2018.

**Rasilez HCT - aliskiren / hydrochlorothiazide - EMEA/H/C/000964/R/0087**
Noden Pharma DAC, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Amelia Cupelli
Request for Supplementary Information adopted on 31.05.2018.

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

**Bavencio - avelumab - EMEA/H/C/004338/R/0003, Orphan**
Merck Serono Europe Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine

Stark
Request for Supplementary Information adopted on 31.05.2018.

## B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

**Kalydeco – Ivacraftor – EMEA/H/C/PSR/S/0014**

Vertex Pharmaceuticals

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Dolores Montero Corominas

Scope: PASS results for an observational study to evaluate the long-term safety of ivacaftor in patients with cystic fibrosis.

An update to the RMP resulting from the data presented in this PASS final study report was submitted.

An update to the Product Information resulting from the data presented in this PASS final study report was submitted.

PRAC recommendation to CHMP

**Action:** For adoption

**Signal detection**

PRAC recommendations on signals adopted at the PRAC meeting held on 11-14 June 2018 PRAC:

**Signal of loss of consciousness**

**Champix - Varenicline – EMEA/H/C/000699**

Pfizer Limited, Rapporteur: Mark Ainsworth, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Anette Kirstine Stark

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

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

**EMEA/H/C/PSUSA/00001467/201712**
(fondaparinux)
CAPS:
**Arixtra** (EMEA/H/C/000403) (fondaparinux sodium), Aspen Pharma Trading Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "07 December 2016 to 06 December 2017
Update of section 4.4 and 5.1 of the SmPC to add information on potential cross-reactivity of fondaparinux to sera from patients with Heparin Induced Thrombocytopenia (HIT) type II, and remove the present statement that a causal association between treatment with fondaparinux and the occurrence of HIT has not been established. The Package leaflet is updated accordingly."

**EMEA/H/C/PSUSA/00009261/201711**
(pixantrone)
CAPS:
**Pixuvri** (EMEA/H/C/002055) (pixantrone), CTI Life Sciences Limited, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, "11-May-2017 to 10-Nov-2017"

**EMEA/H/C/PSUSA/00010134/201712**
(sofosbuvir)
CAPS:
**Sovaldi** (EMEA/H/C/002798) (sofosbuvir), Gilead Sciences International Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Julie Williams, "06 June 2017 to 05 December 2017"

**EMEA/H/C/PSUSA/00010180/201711**
(cabozantinib)
CAPS:
**CABOMETYX** (EMEA/H/C/004163) (cabozantinib), Ipsen Pharma, Rapporteur: Robert James Hemmings
**Cometriq** (EMEA/H/C/002640) (cabozantinib), Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "29 November 2016 - 28 November 2017"

**EMEA/H/C/PSUSA/00010186/201711**
(vedolizumab)
CAPS:
**Entyvio** (EMEA/H/C/002782) (vedolizumab), Takeda Pharma A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Adam Przybylkowski, "20 May 2017 to 19 November 2017"

**EMEA/H/C/PSUSA/00010301/201711**
(ibrutinib)
CAPS:
**Imbruvica** (EMEA/H/C/003791) (ibrutinib), Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, "13 May 2017 to 12 November 2017"

**EMEA/H/C/PSUSA/00010455/201711**
(lumacaftor / ivacaftor)
CAPS:
**Orkambi** (EMEA/H/C/003954) (lumacaftor / ivacaftor), Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Almath Spooner, "20 May 17 to 19 Nov 2017"

**EMEA/H/C/PSUSA/00010533/201711**
(etelcalcetide)
CAPS:
**Parsabiv** (EMEA/H/C/003995) (etelcalcetide), Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, "11/05/2017 - 10/11/2017"

**EMEA/H/C/PSUSA/00010556/201712**
(venetoclax)
CAPS:
**Venclyxto** (EMEA/H/C/004106) (venetoclax), AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, "05 June 2017 to 04 December 2017"

## B.4. EPARs / WPARs

## 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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| **Armisarte - pemetrexed - EMEA/H/C/004109/II/0017/G**<br>Actavis Group PTC ehf, Rapporteur: Alar Irs | |
| **BiResp Spiromax - budesonide / formoterol - EMEA/H/C/003890/II/0024/G**<br>Teva Pharma B.V., Duplicate, Duplicate of DuoResp Spiromax, Rapporteur: Nithyanandan Nagercoil<br>Request for Supplementary Information adopted on 21.06.2018. | Request for supplementary information adopted with a specific timetable. |
| **Cosentyx - secukinumab - EMEA/H/C/003729/II/0031/G**<br>Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen<br>Opinion adopted on 07.06.2018.<br>Request for Supplementary Information adopted on 25.01.2018. | Positive Opinion adopted by consensus on 07.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Dacogen - decitabine - EMEA/H/C/002221/II/0034/G, Orphan**<br>Janssen-Cilag International N.V., Rapporteur: Alexandre Moreau | |
| **DuoResp Spiromax - budesonide / formoterol - EMEA/H/C/002348/II/0024/G**<br>Teva Pharma B.V., Rapporteur: Nithyanandan Nagercoil<br>Request for Supplementary Information adopted on 21.06.2018. | Request for supplementary information adopted with a specific timetable. |
| **Elaprase - idursulfase - EMEA/H/C/000700/II/0077/G**<br>Shire Human Genetic Therapies AB, Rapporteur: Greg Markey<br>Opinion adopted on 21.06.2018. | Positive Opinion adopted by consensus on 21.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Eptifibatide Accord - eptifibatide - EMEA/H/C/004104/II/0004**<br>Accord Healthcare Limited, Generic, Generic of Integrilin, Rapporteur: Jayne Crowe<br>Request for Supplementary Information adopted on 07.06.2018. | Request for supplementary information adopted with a specific timetable. |
| **Flixabi - infliximab - EMEA/H/C/004020/II/0020**<br>Samsung Bioepis UK Limited, Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 07.06.2018.<br>Request for Supplementary Information adopted | Positive Opinion adopted by consensus on 07.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| on 08.02.2018. | |
| **Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0082**<br>AstraZeneca AB, Rapporteur: Bart Van der Schueren | |
| **Gliolan - aminolevulinic acid - EMEA/H/C/000744/II/0015**<br>medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Bruno Sepodes | |
| **Inhixa - enoxaparin sodium - EMEA/H/C/004264/II/0031**<br>Techdow Europe AB, Duplicate, Duplicate of Thorinane, Rapporteur: Andrea Laslop<br>Opinion adopted on 07.06.2018. | Positive Opinion adopted by consensus on 07.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Kevzara - sarilumab - EMEA/H/C/004254/II/0006/G**<br>sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 21.06.2018. | Positive Opinion adopted by consensus on 21.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Keytruda - pembrolizumab - EMEA/H/C/003820/II/0046**<br>Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri<br>Request for Supplementary Information adopted on 21.06.2018. | Request for supplementary information adopted with a specific timetable. |
| **Lemtrada - alemtuzumab - EMEA/H/C/003718/II/0021/G**<br>Genzyme Therapeutics Ltd, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth<br>Request for Supplementary Information adopted on 07.06.2018. | Request for supplementary information adopted with a specific timetable. |
| **MabThera - rituximab - EMEA/H/C/000165/II/0151**<br>Roche Registration GmbH, Rapporteur: Sinan B. Sarac<br>Opinion adopted on 21.06.2018. | Positive Opinion adopted by consensus on 21.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **NexoBrid - concentrate of proteolytic enzymes enriched in bromelain - EMEA/H/C/002246/II/0035, Orphan**<br>MediWound Germany GmbH, Rapporteur: Harald Enzmann<br>Opinion adopted on 07.06.2018.<br>Request for Supplementary Information adopted | Positive Opinion adopted by consensus on 07.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| on 12.04.2018. | |
| **Rekovelle - follitropin delta - EMEA/H/C/003994/II/0008/G**<br>Ferring Pharmaceuticals A/S, Rapporteur: Joseph Emmerich | |
| **Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0023/G**<br>CSL Behring GmbH, Rapporteur: Kristina Dunder | |
| **Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0001**<br>GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren | |
| **Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0125**<br>GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder<br>Request for Supplementary Information adopted on 14.06.2018. | Request for supplementary information adopted with a specific timetable. |
| **Xolair - omalizumab - EMEA/H/C/000606/II/0084**<br>Novartis Europharm Limited, Rapporteur: Kristina Dunder<br>Request for Supplementary Information adopted on 03.05.2018. | |
| **WS1376/G**<br>**Blitzima-EMEA/H/C/004723/WS1376/0013/G**<br>**Ritemvia-EMEA/H/C/004725/WS1376/0013/G**<br>**Rituzena-EMEA/H/C/004724/WS1376/0014/G**<br>**Truxima-EMEA/H/C/004112/WS1376/0014/G**<br>Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz<br>Opinion adopted on 21.06.2018. | Positive Opinion adopted by consensus on 21.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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

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| **Ceprotin - human protein C - EMEA/H/C/000334/II/0104**<br>Baxter AG, Rapporteur: Jan Mueller-Berghaus, | Request for supplementary information adopted with a specific timetable. |

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| "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information of Ceprotin based on an update of the Company Core Safety Information.<br>The Package Leaflet has been further updated."<br>Request for Supplementary Information adopted on 21.06.2018. | |
| **Cyramza - ramucirumab - EMEA/H/C/002829/II/0023/G**<br>Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik, "Submission of the final report from study Study I4T-MC-JVCZ Randomized Phase 2 Trial Evaluating Alternative Ramucirumab Doses in Combination with Paclitaxel in Second-Line Metastatic or Locally Advanced, Unresectable Gastric or Gastroesophageal Junction Adenocarcinoma and Study I4T-MC-JVDB Randomized Phase 2 Trial Evaluating Pharmacokinetics and Safety of Four Ramucirumab Dosing Regimens in Second Line Gastric or Gastroesophageal Junction Adenocarcinoma in fulfilment with Annex II condition linked to Cyramza Marketing Authorisation. Annex II of the product information has been updated accordingly."<br><br>Request for Supplementary Information adopted on 14.06.2018. | Request for supplementary information adopted with a specific timetable. |
| **Daklinza - daclatasvir - EMEA/H/C/003768/II/0028**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC to include the final results of study ALLY-3C (AI444379), an interventional open-label phase 3 study evaluating daclatasvir and sofobuvir with ribavirin in cirrhotic subjects with genotype 3 chronic hepatitis C infection to demonstrate the sustained virologic response at follow-up Week 12 (SVR12) rate, defined as hepatitis C virus (HCV) ribonucleic acid (RNA) < lower limit of quantification (LLOQ) target detected (TD) or target not detected (TND) at follow-up Week 12 in subjects treated with 24 weeks of daclatasvir (DCV) + sofosbuvir (SOF) + ribavirin (RBV) therapy was greater than the historical threshold sustained virologic response (SVR) rate. In addition the MAH took the opportunity to include a new statement regarding the amount of sodium contained in the medicinal product in section 4.4 of the | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| SmPC and section 2 of the Package Leaflet in line with the revised 'Guideline on excipients in the labelling and package leaflet of medicinal products for human use', and to update the contact details of the Bulgarian, Estonian, Hungarian, Icelandic, Latvian, Lithuanian and Romanian local representatives in the Package Leaflet."<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 12.04.2018. | |
| **Dynastat - parecoxib - EMEA/H/C/000381/II/0072**<br>Pfizer Limited, Duplicate, Duplicate of Xapit (SRD), Rapporteur: Jayne Crowe, "Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to update the information on the use of parecoxib beyond 3 days based on a recent publication on the 'Safety of parecoxib when used for more than 3 days for the management of postoperative pain'; this is an observatory study of the Pfizer clinical trial database to identify randomized, double-blind, placebo controlled trials in which patients could have, potentially, received parecoxib for longer than 3 days for the management of postoperative pain. The Package Leaflet is updated accordingly.<br><br>In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the Package Leaflet in line with the SmPC with the inclusion of diazepam and omeprazole in section 2 of the Package Leaflet."<br>Opinion adopted on 21.06.2018.<br>Request for Supplementary Information adopted on 17.05.2018. | Positive Opinion adopted by consensus on 21.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Elaprase - idursulfase - EMEA/H/C/000700/II/0076**<br>Shire Human Genetic Therapies AB, Rapporteur: Greg Markey, "Update of section 4.8 of the SmPC to update the frequency category of the following adverse drug reactions: hypertension, tachypnoea, dyspepsia, erythema and infusion-site swelling, following a review of the frequencies and incidence categories for adverse drug reactions reported with Elaprase, based on integrated data from all relevant completed studies (i.e. studies TKT024, TKT024EXT and HGT-ELA-038). The Package Leaflet is updated accordingly. In addition, the Marketing | Positive Opinion adopted by consensus on 21.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| Authorisation Holder (MAH) took the opportunity to implement some minor corrections to the SmPC."<br>Opinion adopted on 21.06.2018. | |
| **Genvoya - elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004042/II/0046**<br>Gilead Sciences Ireland UC, Rapporteur: Robert James Hemmings, "Update of sections 4.8 and 5.1of the SmPC for Genvoya in order to amend the safety and pharmacodynamic information based on the final results from study Study GS-US-292-1515, listed as a category 3 study in the RMP;<br>this is A Phase 2/3, Open-Label Study to Evaluate the Safety and Efficacy of E/C/F/TAF in HIV-1 Infected Virologically Suppressed Adolescents.<br>The MAH also took the opportunity to make administrative updates to Section 4.5 and 5.1 of the SmPC." | |
| **Giotrif - afatinib - EMEA/H/C/002280/II/0028**<br>Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to update the efficacy section with data in EGFR TKI-naïve NSCLC patients whose tumours harbour uncommon EGFR mutations based on a meta-analysis across three trials (1200.22, 1200.32 and 1200.34). In addition, the Marketing authorisation holder (MAH) took the opportunity to implement minor linguistic amendments to the translations of the product information annexes: BG, CZ, DE, DK, FI, IS, IT, NO, PT, SE and SK." | |
| **Humira - adalimumab - EMEA/H/C/000481/II/0170**<br>AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, "Update of section 4.6 of the SmPC in order to update information on pregnancy and lactation based on results from pregnancy registry (OTIS; study number M03-604) and supported by relevant published literature. The Package Leaflet is updated accordingly."<br>Request for Supplementary Information adopted on 22.02.2018, 30.11.2017. | |
| **Jinarc - tolvaptan -** | Request for supplementary information adopted |

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| **EMEA/H/C/002788/II/0015**<br>Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information on acute liver failure requiring liver transplantation, based post-marketing experience with tolvaptan in autosomal dominant polycystic kidney disease (ADPKD).<br>The Package Leaflet is updated accordingly."<br>Request for Supplementary Information adopted on 21.06.2018. | with a specific timetable. |
| **Keytruda - pembrolizumab - EMEA/H/C/003820/II/0044**<br>Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Update of section 5.1 of the SmPC in order to reflect the final overall survival efficacy data from study Keynote-024; a randomized, open-label phase III trial of pembrolizumab versus platinum based chemotherapy in 1L subjects with PD-L1 strong metastatic non-small cell lung cancer (NSCLC)."<br>Request for Supplementary Information adopted on 31.05.2018. | |
| **Keytruda - pembrolizumab - EMEA/H/C/003820/II/0048**<br>Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Update of sections 4.2, 5.1 and 5.3 of the SmPC in order to align the posology of Keytruda for the melanoma -and 2nd line NSCLC indications to a 200 mg Q3W fixed dose regimen already approved for more recent indications (1st line NSCLC, classical Hodgkin lymphoma and urothelial carcinoma) based on the available overall PK and exposure data. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representative in Belgium in the Package Leaflet." | |
| **Kuvan - sapropterin - EMEA/H/C/000943/II/0059, Orphan**<br>BioMarin International Limited, Rapporteur: Peter Kiely, "As requested following the Art 46 procedure assessment, update of section 5.1 of the SmPC to reflect the data of the final clinical study report for the long term extension phase of the SPARK study. Sections 4.2 and 4.4 are also updated." | Positive Opinion adopted by consensus on 07.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| Opinion adopted on 07.06.2018. | |
| **Lokelma - sodium zirconium cyclosilicate - EMEA/H/C/004029/II/0003/G**<br>AstraZeneca AB, Rapporteur: Romaldas Mačiulaitis, "1) type II (C.I.4): Update of sections 4.8 and 5.1 of the SmPC in order to update the information based on final results from study ZS-005 (category 3 PASS study in the RMP). This is an open-label, multicentre, multi-dose, prospective maintenance study to investigate the long-term safety and efficacy of Lokelma (sodium zirconium cyclosilicate) in subjects with hyperkalaemia.<br>2) type II (C.I.4): Update of section 4.5 of the SmPC in order to add information regarding the use with drugs that have the potential for drug-drug interaction based on an increase in gastric PH.<br>The Package Leaflet has been updated accordingly." | |
| **Lucentis - ranibizumab - EMEA/H/C/000715/II/0069**<br>Novartis Europharm Limited, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to include information on the diabetic retinopathy score (DRSS) in diabetic macular edema patients (DME) based on pooled data from studies RFB002D2301 (RESTORE), RFB002D2303 (REVEAL) and RFB002D2305 (REFINE)."<br>Request for Supplementary Information adopted on 22.02.2018. | |
| **Samsca - tolvaptan - EMEA/H/C/000980/II/0030**<br>Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information on acute liver failure requiring liver transplantation, based on post-marketing experience with tolvaptan in autosomal dominant polycystic kidney disease (ADPKD).<br>The Package Leaflet is updated accordingly." | |
| **Savene - dexrazoxane - EMEA/H/C/000682/II/0036**<br>Clinigen Healthcare Ltd, Rapporteur: Alexandre Moreau, "Update of section 4.4 and 4.6 of the SmPC in order to add a warning on mutagenic activity of dexrazoxane and to update the | Request for supplementary information adopted with a specific timetable. |

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| contraception recommendations based on toxicological data and literature review, the Package Leaflet is updated accordingly.<br><br>In addition the MAH took the opportunity to make an administrative amendment to the description of the pharmaceutical form for Savene in order to align with the relevant EDQM standard terms."<br>Request for Supplementary Information adopted on 14.06.2018. | |
| **Saxenda - liraglutide - EMEA/H/C/003780/II/0018**<br>Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update the safety information based on the conclusions of the assessment of two PK Clinical trial reports (NN8022-3967 and NN8022-4181), previously submitted in accordance with Article 46 of Regulation (EC) No1901/2006, as amended, and assessed by the CHMP (P46 016)." | |
| **Soliris - eculizumab - EMEA/H/C/000791/II/0103, Orphan**<br>Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez, "To update SmPC section 4.4 describing reports of serious infections with Neisseria species (other than Neisseria meningitidis), including disseminated gonococcal infections, SmPC section 4.5 describing the theoretical potential for drug-drug interaction between eculizumab and intravenous human immunoglobulin (IVIg), SmpC section 4.6 clarifying that there is currently insufficient data to adequately characterize the safety of eculizumab in pregnant women with refractory gMG and SmPC section 4.8, clarifying sepsis as the most common presentation of Neisseria meningococcal infections. The annex II and the package leaflet are updated accordingly. The MAH took the opportunity to align the Product information with the QRD template." | |
| **Spinraza - nusinersen - EMEA/H/C/004312/II/0004, Orphan**<br>Biogen Idec Ltd, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Qun-Ying Yue, "Update of section 4.8 of the SmPC to include new safety information related to hydrocephalus. The PIL | Request for supplementary information adopted with a specific timetable. |

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| and the RMP (new version 7.0) are proposed to be updated accordingly. In addition, the MAH took the opportunity to correct some typographical errors in section 5.1 of the SmPC" Request for Supplementary Information adopted on 14.06.2018, 12.04.2018, 08.02.2018. | |
| **Stocrin - efavirenz - EMEA/H/C/000250/II/0114** Merck Sharp & Dohme B.V., Duplicate, Duplicate of Sustiva, Rapporteur: Bruno Sepodes, "Update of sections 4.3 and 4.5 of the SmPC in order to add contraindication with elbasvir/grazoprevir and to update information on interactions between efavirenz and elbasvir/grazoprevir, sofosbuvir/velpatasvir, sofosbuvir/velpatasvir/voxilaprevir, and etonogestrel implant; based on the post-approval and literature data. The Package Leaflet is updated accordingly." | |
| **Strensiq - asfotase alfa - EMEA/H/C/003794/II/0029, Orphan** Alexion Europe SAS, Rapporteur: Greg Markey, "Update of annex II after submission of the final report from study AA-HPP-208 listed as a category 1 study in the RMP (ANX001.2). This is a multicentre, randomized, open-label, Phase 2a study of Strensiq in patients with hypophosphatasia." | |
| **Venclyxto - venetoclax - EMEA/H/C/004106/II/0011, Orphan** AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Submission of the interim report from study M14-032 a phase II open-label study investigating efficacy and safety of venetoclax in patients with CLL with relapse or refractory to B-cell receptor signalling pathway inhibitor therapy, listed as a category 2 study in the RMP. Consequently, the remaining SOB is fulfilled and Annex II E is updated accordingly." | |
| **Vimpat - lacosamide - EMEA/H/C/000863/II/0070/G** UCB Pharma S.A., Rapporteur: Filip Josephson, "C.I.4 - Update of sections 4.8, 5.1, and 5.2 of the SmPC in order to update clinical efficacy and safety data in the paediatric population with the results from study SP0969: a phase 3, multicentre, double-blind, randomized, placebo-controlled, parallel-group study to evaluate the | Request for supplementary information adopted with a specific timetable. |

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| efficacy and safety of lacosamide as adjunctive therapy in subjects with epilepsy ≥4 years to <17 years of age with uncontrolled partial-onset seizures; 3 new ADRs (nasopharyngitis, pharyngitis, and pyrexia) have been added based on the results of the above mentioned study;<br>C.I.4 - Update of section 5.2 of the SmPC in order to update the pharmacokinetic data in the paediatric population based on results from the CL0430 population pharmacokinetic (PK) analyses;<br>C.I.4 - Update of section 4.8 of the SmPC in order to update the incidence of decreased appetite, lethargy, and abnormal behaviour in the paediatric population based on results from the updated safety data for Pool SPX-1 with clinical cut-off date of 01 November 2016.<br>The Package Leaflet and Labelling are updated accordingly.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some editorial changes in the PI. The MAH also took the opportunity to revise Annex A as requested."<br>Request for Supplementary Information adopted on 21.06.2018, 22.03.2018. | |
| **XALKORI - crizotinib - EMEA/H/C/002489/II/0054**<br>Pfizer Limited, Rapporteur: Alexandre Moreau, "Update of section 5.1 of the SmPC to reflect the final analysis of overall survival (OS), a secondary endpoint, in Study A8081014, a randomized phase 3 trial comparing oral crizotinib to first line chemotherapy in patients with ALK-positive advanced non-squamous non-small cell lung cancer (NSCLC)."<br>Opinion adopted on 21.06.2018.<br>Request for Supplementary Information adopted on 19.04.2018. | Positive Opinion adopted by consensus on 21.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Xeljanz - tofacitinib - EMEA/H/C/004214/II/0008**<br>Pfizer Limited, Rapporteur: Robert James Hemmings, "Update of sections 4.4, and 5.1 of the SmPC are being updated to add a warning regarding the increased risk of infection when corticosteroids are used concomitantly and to reflect information from study A3921187 (ORAL Strategy), respectively. This study is a phase 3b/4 randomized double-blind study of 5 mg of | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| Tofacitinib with and without methotrexate in comparison to adalimumab with methotrexate in subjects with moderately to severely active rheumatoid arthritis. The Package Leaflet is updated accordingly."<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 19.04.2018. | |
| **Xeljanz - tofacitinib - EMEA/H/C/004214/II/0011**<br>Pfizer Limited, Rapporteur: Robert James Hemmings, "To update section 4.4 of the SmPC to indicate that post-marketing cases of HB reactivation have been reported following routine pharmacovigilance review."<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 19.04.2018. | Negative Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Xofigo - radium-223 - EMEA/H/C/002653/II/0029**<br>Bayer AG, Rapporteur: Harald Enzmann, "Submission of Clinical Study Report for study 16506. This is an interventional re-treatment safety study of radium-223 dichloride in subjects with castration-resistant prostate cancer with bone metastases who received an initial course of six doses of radium-223 dichloride 50 kBq/kg every four weeks."<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 15.03.2018. | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Xydalba - dalbavancin - EMEA/H/C/002840/II/0021**<br>Allergan Pharmaceuticals International Ltd, Rapporteur: Filip Josephson, "Update to sections 4.4 and 4.8 of the product information in order to include back-pain as a symptom of infusion-related reactions in alignment with the last version Company Core Data Sheet (CCDS).<br><br>In addition, the MAH took the opportunity to add a precautionary statement to Section 6.6 to include flushing of the intravenous lines before and after dalbavancin infusion, to bring the PI in line with the latest QRD template version 10 and to update the local representatives in the PL"<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted | Negative Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| on 12.04.2018. | |
| **Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/II/0009**<br>Pfizer Ireland Pharmaceuticals, Rapporteur: Robert James Hemmings, “Update of sections 4.2 and 4.8 of the SmPC in order to reflect the availability of final CSR for the paediatric study C3591004 (D4280C00015). Study D4280C00015 is a single blind, randomised, multi-centre, active controlled, trial to evaluate safety, tolerability, pharmacokinetics and efficacy of ceftazidime and avibactam when given in combination with metronidazole, compared with meropenem, in children from 3 months to less than 18 years of age with complicated intra-abdominal infections (cIAIs). In addition, the MAH has updated the sodium statements in the SmPC (section 4.4) and Package Leaflet to align with the Annex to the European Commission guideline on ‘Excipients in the labelling and package leaflet of medicinal products for human use’.<br>The legal status ‘medicinal product subject to medical prescription’ is proposed to be removed from Annex IIIA, as per the QRD template Moreover, the MAH is introducing a correction in the Polish annexes (from ZAVICEFTA 2 g + 0.5g to ZAVICEFTA 2 g/0.5g).”<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 19.04.2018. | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1289**<br>**Komboglyze-**<br>**EMEA/H/C/002059/WS1289/0039**<br>**Onglyza-**<br>**EMEA/H/C/001039/WS1289/0045**<br>AstraZeneca AB, Lead Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to reflect the new saxagliptin renal cut-off value based on post hoc analysis of pooled data from 9 saxagliptin clinical trials.<br>In addition, the Worksharing applicant proposed to combine SmPCs of different strengths, for both Onglyza and Komboglyze.<br>Furthermore, the Worksharing applicant took the opportunity to include required information on two excipients, sodium and lactose, in sections 2 and 4.4 of the SmPC for Onglyza. The Package Leaflet is updated accordingly.” | |

Request for Supplementary Information adopted on 22.02.2018.

**WS1322**
**Genvoya-EMEA/H/C/004042/WS1322/0042**
**Stribild-EMEA/H/C/002574/WS1322/0090**
**Tybost-EMEA/H/C/002572/WS1322/0042**
Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings, "Update of Section 4.5 of the SmPC for Genvoya, Tybost and Stribild based on data on Drug-drug Interaction between cobicistat containing products and Direct Oral Anticoagulants (DOACs).

The Patient Leaflet (PIL) has been updated for all three products as a consequence.

The Worksharing MAH has taken this opportunity to introduce some minor administrative amendments throughout the product information for all three products respectively, as needed (i.e., correction of abbreviations, correction of formatting errors and correction of spelling mistakes). Minor administrative update is also made to Annex III for all three products.

The MAH has also taken this opportunity to implement some minor linguistic amendments (MLAs) to the translations of the respective product information annexes:

- Genvoya: CS, DA, DE, FI, HR, HU, IS, NO, PT and RO languages
- Tybost: DA, ES and HU languages
- Stribild: DA, DE, ES, FI, FR, IS, LV, MT, NO and RO languages"

Request for Supplementary Information adopted on 17.05.2018, 22.02.2018.

**WS1346**
**Aprovel-EMEA/H/C/000141/WS1346/0170**
**CoAprovel-EMEA/H/C/000222/WS1346/0185**
**Irbesartan Hydrochlorothiazide Zentiva-EMEA/H/C/000783/WS1346/0099**
**Irbesartan Zentiva-EMEA/H/C/000785/WS1346/0078**
**Karvea-EMEA/H/C/000142/WS1346/0174**
**Karvezide-**

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| **EMEA/H/C/000221/WS1346/0187**<br>Sanofi Clir SNC, Lead Rapporteur: Concepcion Prieto Yerro, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information for irbesartan and for irbesartan/ hydrochlorothiazide linked to irbesartan INN by adding "Psoriasis : the use of irbesartan in patients with psoriasis or a history of psoriasis should be carefully weighed as it may exacerbate psoriasis" and include new undesirable effects "anaphylactic reaction including anaphylactic shock", "psoriasis", "photosensitivity"; and update of the corresponding section of PL.<br>In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10."<br>Request for Supplementary Information adopted on 25.05.2018. | |
| **WS1363**<br>**Kisplyx-EMEA/H/C/004224/WS1363/0010**<br>**Lenvima-EMEA/H/C/003727/WS1363/0013**<br>Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren, "Update of sections 4.4 and 4.8 of the SmPC to add wound healing and aortic dissection. The PIL is updated accordingly."<br>Opinion adopted on 21.06.2018.<br>Request for Supplementary Information adopted on 17.05.2018. | Positive Opinion adopted by consensus on 21.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1381**<br>**Leganto-EMEA/H/C/002380/WS1381/0027**<br>**Neupro-EMEA/H/C/000626/WS1381/0082**<br>UCB Pharma S.A., Informed Consent of Neupro, Lead Rapporteur: Bruno Sepodes, "Update of section 4.8 of the SmPC in order to add an adverse drug reaction: Dropped Head Syndrome based on new pharmacovigilance data; The Package Leaflet is updated accordingly.<br>In addition, the Worksharing applicant (WSA) took the opportunity to correct some discrepancies found within the PIL of Greece, Cyrus and Romania and to update the Neupro Annex A in alignment with Leganto Annex A for the description of the multipack size." | Positive Opinion adopted by consensus on 07.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| Opinion adopted on 07.06.2018. | |
| **WS1391**<br>**Epclusa-**<br>**EMEA/H/C/004210/WS1391/0026**<br>**Vosevi-EMEA/H/C/004350/WS1391/0014**<br>Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, "Update of section 5.3 of the SmPC based on data from a 2-year rat carcinogenicity study TX-281-2030. In addition, the MAH took the opportunity to update the ATC code in line with the new classification of antivirals for treatment of HCV infections and to introduce minor linguistic amendments and typographical corrections throughout the Product Information."<br>Opinion adopted on 14.06.2018. | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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

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| **Advate - octocog alfa -**<br>**EMEA/H/C/000520/II/0091**<br>Baxter AG, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 4.2 of the SmPC in order to remove a statement that the use of 2 ml presentations has not been documented for paediatric subjects below 2 years of age. This update follows final results from study 061101 listed as a category 3 study in the RMP; this was a prospective, non-interventional, post-marketing surveillance study that assessed the safety and efficacy of Advate reconstituted in 2 ml of sterile water for injection during routine clinical practice in the EU.<br>The Package Leaflet is updated accordingly. The RMP version 15.1 has also been submitted."<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 12.04.2018. | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Advate - octocog alfa -**<br>**EMEA/H/C/000520/II/0092**<br>Baxter AG, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 5.1 of the SmPC in order to add new data on immune tolerance induction (ITI). This update follows final results from study PASS-INT-004; this was a prospective, multi-centre, uncontrolled, open-label, non- | Request for supplementary information adopted with a specific timetable. |

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| interventional postauthorization safety surveillance study conducted to evaluate Advate in ITI therapy in subjects with moderate or severe hemophilia A (baseline factor VIII ≤ 2%) and a high titer (> 5 BU) inhibitor to FVIII. The RMP version 16.0 has also been submitted." Request for Supplementary Information adopted on 14.06.2018. | |
| **Bydureon - exenatide - EMEA/H/C/002020/II/0050** AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "Update of sections 4.1, 4.2, 4.4 and 5.1 of the SmPC based on the final CSR of study EXSCEL (EXenatide Study of Cardiovascular Event Lowering; 'A randomized, placebo controlled clinical trial to evaluate cardiovascular outcomes after treatment with exanatide once weekly in patients with type 2 diabetes mellitus ') in fulfilment of PAM (LEG 009). The Package Leaflet is updated accordingly. In addition, RMP version 31 has been submitted as part of this application." | |
| **Defitelio - defibrotide - EMEA/H/C/002393/II/0027, Orphan** Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, "Submission of an updated RMP version 4.0 in order to re-classify the imposed non-interventional PASS listed as a category 2 study in the RMP (specific obligation) to a study listed as a category 3 in the RMP (required additional pharmacovigilance activities). This study is an observational registry (DF-VOD2013-03-REG) which aims to record safety and outcome data in patients diagnosed with severe VOD following HSCT treated or not with defitelio. The Annex II of the product information is updated accordingly." Request for Supplementary Information adopted on 26.04.2018, 22.02.2018, 09.11.2017. | |
| **Eylea - aflibercept - EMEA/H/C/002392/II/0045** Bayer AG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of sections 4.2 and 5.1 of the SmPC in order to add information for the Health Care Professional related to earlier treatment extension and related increments intervals based on final | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| results from phase 4 study ALTAIR. This is an interventional study evaluating the efficacy and safety of repeated doses of intravitreal (IVT) aflibercept with variable treatment intervals in Japanese subjects with neovascular AMD. The Package Leaflet is updated accordingly. The RMP version 24.1 has also been submitted."<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 17.05.2018. | |
| **Olumiant - baricitinib - EMEA/H/C/004085/II/0006**<br>Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Patrick Batty, "Update of section 4.8 of the SmPC in order to include pneumonia as adverse drug reaction with frequency 'common' following PRAC outcome on signal of pneumonia. The Package Leaflet is updated accordingly. The RMP version 6.0 has also been submitted as part of this application." | |
| **Ovitrelle - choriogonadotropin alfa - EMEA/H/C/000320/II/0073/G**<br>Merck Serono Europe Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of section 4.8 of the SmPC in order to indicate that thromboembolism can also occur without the presence of ovarian hyperstimulation syndrome (OHSS). The package leaflet and risk management plan (RMP) (version 5.1) are updated accordingly.<br>The RMP is also updated to extend the important potential risk of 'misuse' to 'weight loss and anabolic growth promoting effect'.<br>In addition, the marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the package leaflet, to make editorial changes in the product information and in the Annex A (list of authorised presentations). The MAH also took the opportunity to make some revisions in the RMP."<br>Request for Supplementary Information adopted on 14.06.2018. | Request for supplementary information adopted with a specific timetable. |
| **Sivextro - tedizolid phosphate - EMEA/H/C/002846/II/0027**<br>Merck Sharp & Dohme Limited, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Dolores | Request for supplementary information adopted with a specific timetable. |

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| Montero Corominas, “Update of section 4.8 of the SmPC in order to add safety information based on the final results from Bayer study 16099, listed as Post-Authorisation Efficacy Study (PAES) in the RMP; this is a prospective, randomized, open-label, active-controlled, multicenter study to evaluate the efficacy and safety of tedlizolid in Japanese patients with MRSA infections (skin and soft tissue infection [SSTI] and SSTI-related bacteremia).<br><br>The updated RMP version 4.0 is also being submitted, reflecting the new, second revision of the RMP template, issues by the EMA on 30 March 2017.”<br>Request for Supplementary Information adopted on 14.06.2018. | |
| **Soliris - eculizumab - EMEA/H/C/000791/II/0102, Orphan**<br>Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia, “Submission of the Clinical Study Report of the study C11-003 listed as Cat 3 study in the RMP. This is an observational, multi-center, multinational long term follow up study of atypical hemolytic uremic syndrome (aHUS) patients treated with eculizumab in a prior clinical study. The Risk Management Plan is updated to version 18.3 in order to:<br>- remove the missing information “Long term safety in aHUS patients” from the RMP.<br>- merge the important identified risks “serious infections” and “sepsis” into one important identified risk of “serious infections (including sepsis)”.<br>- align the frequency of the submission of the reports on the HCP survey, the controlled distribution and the aHUS registry to the PSUR submission every 2 years.<br>- convert the RMP into the EU RMP template Rev. 2.<br>- Section 'SV.1 Post-authorisation exposure' was updated according to PSUR 15 data.” | |
| **Stayveer - bosentan - EMEA/H/C/002644/II/0023**<br>Marklas Nederlands BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Caroline Laborde, “Update of Annex II.D and the RMP following the submisison of the final (13th) study report | Request for supplementary information adopted with a specific timetable. |

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| for the DUO Registry (a Category 3 non-interventional post-approval safety study and additional risk minimisation measure in the bosentan European Risk Management Plan)."<br>Request for Supplementary Information adopted on 14.06.2018. | |
| **Stribild - elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil - EMEA/H/C/002574/II/0087**<br>Gilead Sciences Ireland UC, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Julie Williams, "Submission of the final study report for Study GS-EU-236-0141, listed as a category 3 study in the Risk Management Plan, in order to fulfil a post-authorisation measure (PAM) MEA 006 for Stribild; This study is an Observational Drug Utilization Study of Stribild in Adults with HIV-1 Infection.<br><br>With this application and as agreed with the EMA, Gilead is also taking this opportunity to address the outstanding questions from MEA 002.3."<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 12.04.2018, 11.01.2018. | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **TAGRISSO - osimertinib - EMEA/H/C/004124/II/0021**<br>AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Sabine Straus, "Update of SmPC sections 4.5, 4.6 and 5.2 to reflect the results of Study D5160C00036, undertaken to assess the effect of single and multiple oral doses of osimertinib on the pharmacokinetics of a P-glycoprotein probe drug (Fexofenadine) in patients with advanced EGFRm NSCLC that have progressed on a prior EGFR-TKI regimen. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make a minor correction in Annex II and to implement minor editorial and/or QRD-template related changes in the SmPC and Package Leaflet. A revised RMP version 9 was provided as part of the application."<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 17.05.2018. | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| **TAGRISSO - osimertinib - EMEA/H/C/004124/II/0024**<br>AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Sabine Straus, "Update of sections 4.2 and 5.2 of the SmPC based on the results from Study D5160C00008, undertaken to determine the pharmacokinetics, safety and tolerability of AZD9291 following a single oral dose to patients with advanced solid tumours and normal hepatic function or mild or moderate hepatic impairment. An updated RMP version 9 was provided as part of the application."<br>Request for Supplementary Information adopted on 14.06.2018, 17.05.2018. | Request for supplementary information adopted with a specific timetable. |
| **Tasigna - nilotinib - EMEA/H/C/000798/II/0095, Orphan**<br>Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Update of section 4.6 of the SmPC following a review of information on pregnancy, lactation, female and male infertility and embryo-foetal developmental toxicity from the published literature, the MAH's safety database and preclinical safety data from reproductive animal studies. The Package Leaflet has been updated accordingly.<br>In addition, upon request by EMA, the MAH is proposing a potential update of Annex II section D (Key Elements of the Educational Material) in order to align the wording in Annex II with the current safety concerns outlined in the Tasigna EU RMP Education Materials.<br>Further, the MAH took the opportunity to implement minor editorial changes, corrections and/or additions in the SmPC and Package Leaflet based on data already submitted and assessed previously, including the alignment of section 4 of the Package Leaflet with section 4.8 of the SmPC and completeness of the list of excipients in SmPC section 6.1 and changes to SmPC sections 4.4 and 4.5. Finally, the MAH also took the opportunity to update the contact details in the list of local representatives in the Package Leaflet."<br>Request for Supplementary Information adopted on 14.06.2018. | Request for supplementary information adopted with a specific timetable. |
| **Tecentriq - atezolizumab - EMEA/H/C/004143/II/0004**<br>Roche Registration GmbH, Rapporteur: Sinan B. | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP |

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| Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Update of section 4.8 of the SmPC in order to update the safety information based on the primary results from study IMvigor211 in order to fulfil ANX 002. This is a phase III, open-label, multicentre, randomized study to investigate the efficacy and safety of atezolizumab (anti- PD-L1 antibody) compared with chemotherapy in patients with locally advanced or metastatic urothelial bladder cancer after failure with platinum-containing chemotherapy. The annex II.D, the Package Leaflet and the RMP (version 3.2, according to GVP module V revision 2) are updated accordingly. Some editorial changes throughout the Product Information are also made. In addition the MAH took the opportunity of including the ATC code in section 5.1 of the SmPC.”<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 12.04.2018. | recommendation. |
| **Tracleer - bosentan - EMEA/H/C/000401/II/0086**<br>Actelion Registration Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Caroline Laborde, “Update of Annex II.D and the RMP following the submisison of the final (13th) study report for the DUO Registry (a Category 3 non-interventional post-approval safety study and additional risk minimisation measure in the bosentan European Risk Management Plan).”<br>Request for Supplementary Information adopted on 14.06.2018. | Request for supplementary information adopted with a specific timetable. |
| **Volibris - ambrisentan - EMEA/H/C/000839/II/0054, Orphan**<br>Glaxo Group Ltd, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Dolores Montero Corominas, “Update of sections 4.2 and 5.2 of the SmPC based on results of a juvenile nonclinical toxicology study. The Risk Management Plan version 7.5 (in version 2 of the RMP template) has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct typographical errors including the rash frequency in section 4.8 of the SmPC and the date of renewal; and to introduce minor update in the braille section. Moreover, the MAH | Request for supplementary information adopted with a specific timetable. |

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| took the opportunity to propose combined version of the SmPCs for the different strengths."<br>Request for Supplementary Information adopted on 14.06.2018. | |
| **Yervoy - ipilimumab - EMEA/H/C/002213/II/0054**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "Update of section 5.1 of the SmPC to update the overall survival data of ipilimumab 3mg/kg monotherapy pooled across studies based on the final results of studies CA184332 and CA184338 listed as category 3 studies in the RMP, in order to fulfil MEA 035 and MEA 030.1 respectively. Study CA184332 is a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab as first line therapy in a community practice setting and study CA184438 is a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab as first line therapy. The RMP version 22.0 (according to revision 2 of the template) has also been submitted. In addition the MAH has taken the opportunity to correct some typographical errors throughout the SmPC and to update the contact details of the Bulgarian, Estonian, Icelandic, Latvian, Lithuanian, Hungarian and Romanian local representatives in the Package Leaflet."<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 12.04.2018. | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1343**<br>**Relvar Ellipta-**<br>**EMEA/H/C/002673/WS1343/0036**<br>**Revinty Ellipta-**<br>**EMEA/H/C/002745/WS1343/0032**<br>Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, "Submission of final results of study HZA115150 (SLS-Asthma, Salford Asthma); this is an interventional post-authorisation safety Category 1 study to further investigate the risk of pneumonia (ANX005). Consequently, Annex II condition of the product information is updated. Moreover, an updated RMP version 10 is submitted to add information | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| from the study, to update the important identified risk of pneumonia based on findings from the study, and to provide justifications for removal of the important potential risk of asthma related intubations and deaths and of missing information related to long term use in asthma (>1 year)."<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 12.04.2018. | |
| **WS1390**<br>**Levitra-EMEA/H/C/000475/WS1390/0062**<br>**Vivanza-EMEA/H/C/000488/WS1390/0058**<br>Bayer AG, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, "Update of sections 4.4 and 4.8 of the SmPC to reflect data from two post-marketing observational studies indicating an increased risk of Non-arteritic Anterior Ischaemic Optic Neuropathy (NAION) when using phosphodiesterase 5 (PDE5) inhibitors. The MAH is also terminating the Bayer NAION study 12912 and the RMP is updated accordingly to version 5.0.<br>In addition, the PI is brought in line with version 10.0 of the QRD template and the contact details of the Bulgarian local representative are updated in the Package Leaflets. The Package Leaflets for the 5 mg, 10 mg and 20 mg film-coated tablets strengths are combined into a single Package Leaflet and the PI for the 10 mg orodispersible tablet is updated for aspartame and sorbitol, according to the annex to the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. Some editorial amendments are also made to the PI."<br>Request for Supplementary Information adopted on 14.06.2018. | Request for supplementary information adopted with a specific timetable. |

### B.5.4. PRAC assessed procedures

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| PRAC Led<br>**Bemfola - follitropin alfa - EMEA/H/C/002615/II/0016**<br>Gedeon Richter Plc., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Update of the RMP version 2 based on the phase-3 multicentre study conducted to compare the efficacy and safety of two r-hFSH formulations in normal ovulatory women 35 to 42 years of age undergoing in vitro fertilisation (IVF) (CSR FIN3002).”<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 12.04.2018. | |
| PRAC Led<br>**Deltyba - delamanid - EMEA/H/C/002552/II/0030, Orphan**<br>Otsuka Novel Products GmbH, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, “Update of the RMP (verison 2.10), as requested by PRAC following the assessment of the Annual renewal to revise the risk re-categorisation justifications and lay language wording, as well as addition of clarifications to the described additional pharmacovigilance activities to assess the effectiveness of risk minimisation measures and set up date of EU network of laboratories.”<br>Request for Supplementary Information adopted on 14.06.2018. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**Edarbi - azilsartan medoxomil - EMEA/H/C/002293/II/0021**<br>Takeda Pharma A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of the final report from the drug utilisation study listed as a category 3 study in the RMP. This post-authorisation safety study is a retrospective non-interventional cohort study using a patient level electronic medical records database in Germany aimed to describe the prescription of azilsartan medoxomil in patients with essential hypertension and those prescribed azilsartan medoxomil for other reasons. The RMP version 5.1 has also been approved.”<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 12.04.2018. | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**Lucentis - ranibizumab - EMEA/H/C/000715/II/0070/G** | Request for supplementary information adopted with a specific timetable. |

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| Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder,<br>"1. Type II- C.I.13: Submission of the final report from study LUMINOUS study (CRFB002A2406), an observational, multicenter study to assess the long term safety and effectiveness of ranibizumab in routine clinical practice, in fulfilment of the post-authorisation measures MEA 036, MEA 048 and MEA 054. Consequentially, the RMP has been updated to reflect these changes.<br>2. Type II-C.I.11: Submission of an updated RMP version 17.0 (RMP template Rev. 2) according to GVP Module V to include changes not consequential to LUMINOUS study. In addition, the MAH is proposing the removal of the use of educational materials and targeted follow-up checklists listed in Annex II-D of the Product Information."<br>Request for Supplementary Information adopted on 14.06.2018, 12.04.2018. | |
| PRAC Led<br>**Mycamine - micafungin - EMEA/H/C/000734/II/0035**<br>Astellas Pharma Europe B.V., Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann,<br>"Submission of the final survey report regarding Educational tools in the RMP and Educational tools as a LEG (39) and updated RMP version 18.0."<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 12.04.2018, 11.01.2018. | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**Pergoveris - follitropin alfa / lutropin alfa - EMEA/H/C/000714/II/0055**<br>Merck Serono Europe Limited, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey,<br>"Update of the Pergoveris Risk Management Plan to version 5.2 in order to:<br>· Align the RMP template with Good Pharmacovigilance Practice (GVP) Module V, revision 1.<br>· Add the reference to Pergoveris solution for injection in pre-filled pen (300IU/150IU, 450IU/225IU and 900IU/450IU) following the approval in the European Union (EU) on the 8th | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| of May 2017.<br>Additionally, minor updates have been introduced to the safety specification sections based on the data reviewed until the most recent data lock point."<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 12.04.2018. | |
| PRAC Led<br>**Resolor - prucalopride - EMEA/H/C/001012/II/0042**<br>Shire Pharmaceuticals Ireland Limited, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "Submission of the final clinical study report for the post-authorization drug utilization study SHP555-804 in fulfilment of MEA 006.11 A drug utilisation study to examine characteristics of patients prescribed prucalopride (Resolor) and a pharmacoepidemiological study of the occurrence of major cardiovascular events, pregnancy, and pregnancy outcomes in the UK CPRD Database. The RMP (v 14.0) has also been updated to reflect the study results."<br>Request for Supplementary Information adopted on 14.06.2018, 12.04.2018. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**TAGRISSO - osimertinib - EMEA/H/C/004124/II/0022**<br>AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Sabine Straus, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 9 in order to remove the category 3 PASS Study D5165C00001 (CAURAL) from the Pharmacovigilance Plan."<br>Opinion adopted on 14.06.2018.<br>Request for Supplementary Information adopted on 17.05.2018. | Positive Opinion adopted by consensus on 14.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**TAGRISSO - osimertinib - EMEA/H/C/004124/II/0023**<br>AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Sabine Straus, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 9 in order to remove the category 3 PASS Study D5160C00022 (ASTRIS) from the Pharmacovigilance plan." | Request for supplementary information adopted with a specific timetable. |

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| Request for Supplementary Information adopted on 14.06.2018, 17.05.2018. | |
| PRAC Led<br>**Thymanax - agomelatine - EMEA/H/C/000916/II/0038**<br>Servier (Ireland) Industries Ltd., Duplicate, Duplicate of Valdoxan, Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Karen Pernille Harg, PRAC-CHMP liaison: Svein Rune Andersen, "Submission of the final report from study CLE-20098-096 listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study: drug utilisation study (DUS) to assess effectiveness of risk-minimisation measures."<br>Request for Supplementary Information adopted on 14.06.2018. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**Valdoxan - agomelatine - EMEA/H/C/000915/II/0039**<br>Les Laboratoires Servier, Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Karen Pernille Harg, PRAC-CHMP liaison: Svein Rune Andersen, "Submission of the final report from study CLE-20098-096 listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study: drug utilisation study (DUS) to assess effectiveness of risk-minimisation measures."<br>Request for Supplementary Information adopted on 14.06.2018. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0186**<br>Gilead Sciences International Limited, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Caroline Laborde, PRAC-CHMP liaison: Joseph Emmerich, "Submission of the final report from study GS-EU-174-1846, listed as a category 3 study in the RMP, in fulfilment of MEA 273. This is a 'Multicenter, Non-Interventional, Retrospective, Matched Cohort Study of Patients Monoinfected with Chronic Hepatitis B and with Moderate or Severe Renal Impairment Treated with Viread or Baraclude'."<br>Request for Supplementary Information adopted on 14.06.2018. | Request for supplementary information adopted with a specific timetable. |

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

**Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0002/G, ATMP**

CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder, , "Update of sections 4.8 and 5.1 of the SmPC in order to revise the wording and to update the safety and efficacy information based on the interim results from studies 16 HS 13 (24-month follow-up data) and 16 HS 14 (48-month follow-up data); the Package leaflet is updated accordingly.

Study 16 HS 13 is listed as a specific obligation post-authorisation efficacy study (PAES) in Annex II. It is a phase III, randomised, open label study aimed to evaluate the long-term efficacy and safety of Spherox vs. microfracture in patients with cartilage defects of the knee with a defect size between 1 and 4 cm2.

Study 16 HS 14 is listed as a category 3 study in the RMP. It is a phase II, randomised, open label study, aimed to evaluate the efficacy and safety of the treatment of large defects (4-10 $cm^2$) with 3 different doses of Spherox (ACT3D-CS) in subjects with cartilage defects of the knee.
Clarifications and editorial changes have been made to sections 4.2 and 4.7 of the SmPC and the package leaflet."
Opinion adopted on 22.06.2018.
Request for Supplementary Information adopted on 25.05.2018, 20.04.2018.

### 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

**WS1350**
**Hexacima-**
**EMEA/H/C/002702/WS1350/0078**
**Hexaxim-**
**EMEA/H/W/002495/WS1350/0083**
**Hexyon-**

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| **EMEA/H/C/002796/WS1350/0082**<br>Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus,<br>Request for Supplementary Information adopted on 26.04.2018. | |
| **WS1361**<br>**AZILECT-**<br>**EMEA/H/C/000574/WS1361/0079**<br>**Rasagiline ratiopharm-**<br>**EMEA/H/C/003957/WS1361/0012**<br>Teva B.V., Lead Rapporteur: Bruno Sepodes,<br>“To change the storage conditions for the finished product from "Do not store above 25 °C" to "Do not store above 30 °C".<br>The applicant took the opportunity to introduce editorial changes in the product information by correcting minor spelling mistakes and to align with QRD template (EN, CS, DA, EL, ET, FI, HR, HU, IS, IT, LT, LV, NO, PT, SK, SL and SV).”<br>Request for Supplementary Information adopted on 12.04.2018. | |
| **WS1368/G**<br>**Aflunov-**<br>**EMEA/H/C/002094/WS1368/0043/G**<br>**Foclivia-**<br>**EMEA/H/C/001208/WS1368/0037/G**<br>Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri<br>Request for Supplementary Information adopted on 17.05.2018. | |
| **WS1383**<br>**Renagel-**<br>**EMEA/H/C/000254/WS1383/0110**<br>**Renvela-**<br>**EMEA/H/C/000993/WS1383/0044**<br>**Sevelamer carbonate Zentiva-**<br>**EMEA/H/C/003971/WS1383/0015**<br>Genzyme Europe BV, Lead Rapporteur: Outi Mäki-Ikola<br>Opinion adopted on 07.06.2018. | Positive Opinion adopted by consensus on 07.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1384/G**<br>**PegIntron-**<br>**EMEA/H/C/000280/WS1384/0134/G**<br>**ViraferonPeg-**<br>**EMEA/H/C/000329/WS1384/0127/G**<br>Merck Sharp & Dohme Limited, Lead Rapporteur: Filip Josephson | Positive Opinion adopted by consensus on 07.06.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| Opinion adopted on 07.06.2018. | |
| **WS1385**<br>**Izba-EMEA/H/C/002738/WS1385/0009**<br>**Travatan-**<br>**EMEA/H/C/000390/WS1385/0058**<br>Novartis Europharm Limited, Lead Rapporteur: Concepcion Prieto Yerro, "To provide an updated Environmental Risk Assessment (ERA) dossier for travoprost-containing products Travatan and Izba, pursuant to the post-authorisation recommendation provided by the Agency in the framework of the following procedures:<br>· Travatan extension of indication - Procedure No. EMEA/H/C/000390/II/0046<br>· Izba initial MAA - Procedure No. EMEA/H/C/002738/0000<br>Based on the updated ERA results, the MAH also proposes to update sections 5.3 Preclinical safety data in both Izba and Travatan SmPC as well as section 6.6 Special precautions for disposal in Travatan SmPC." | |
| **WS1395**<br>**Fluenz Tetra-**<br>**EMEA/H/C/002617/WS1395/0081**<br>**Pandemic influenza vaccine H5N1**<br>**AstraZeneca-**<br>**EMEA/H/C/003963/WS1395/0014**<br>AstraZeneca AB, Lead Rapporteur: Bart Van der Schueren, | |

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

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| **Privigen - human normal immunoglobulin -**<br>**EMEA/H/C/000831/II/0129**<br>CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 4.3 of the SmPC to remove the hyperprolineamia contraindication. The package leaflet and RMP (version 6.0) are updated accordingly."<br>Request for Supplementary Information adopted on 12.04.2018.<br>Withdrawal request submitted on 13.06.2018. | The MAH withdrew the procedure on 13.06.2018. |
| **Zelboraf - vemurafenib -**<br>**EMEA/H/C/002409/II/0049**<br>Roche Registration GmbH, Rapporteur: Filip Josephson, "Update of the section 4.8 to add | The MAH withdrew the procedure on 12.06.2018. |

the sarcoidosis with the frequency 'common'.
The PL has been updated accordingly."
Withdrawal request submitted on 12.06.2018.

### 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

**angiotensin ii - EMEA/H/C/004930**, treatment of hypotension in adults with distributive or vasodilatory shock who remain hypotensive despite fluid and vasopressor therapy

**enasidenib - EMEA/H/C/004324, Orphan**
Celgene Europe Limited, treatment of acute myeloid leukaemia (AML)

**l-lysine hydrochloride / l-arginine hydrochloride - EMEA/H/C/004541**, reduction of renal radiation exposure during Peptide-Receptor Radionuclide Therapy (PRRT) with lutetium (177Lu) oxodotreotide

**posaconazole - EMEA/H/C/005028**, treatment of fungal infections in adults

**rituximab - EMEA/H/C/004807**, treatment of Non-Hodgkin's lymphoma (NHL), Chronic lymphocytic leukaemia (CLL) and Rheumatoid arthritis

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

**Vihuma - simoctocog alfa - EMEA/H/C/004459/X/0006/G**
Octapharma AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga, "Extension application to add new strengths of 2500 IU, 3000 IU and 4000 IU, powder and solvent for solution for injection.
The above line extension is grouped with the following variations:
- C.I.4 - to update sections 4.2, 4.8 and 5.1 of the SmPC to reflect available data from Previously Untreated Patients (PUP) from GENA-05 (interim report) study

- C.I.11.b - to update the Risk Management Plan (version 10) to align the content in a single harmonised worldwide version for simocotocg alfa (rFVIII).
- C.I.1.b - to update the Product Information with the wording agreed in the Art. 31 referral (EMEA/H/A-31/1448)."

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

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

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

**Adempas - riociguat -**
**EMEA/H/C/002737/R/0026, Orphan**
Bayer AG, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Martina Weise, PRAC
Rapporteur: Julie Williams

**Entyvio - vedolizumab -**
**EMEA/H/C/002782/R/0032**
Takeda Pharma A/S, Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC
Rapporteur: Adam Przybylkowski

**Latuda - lurasidone -**
**EMEA/H/C/002713/R/0020**
Aziende Chimiche Riunite Angelini Francesco S.p.A., Rapporteur: Filip Josephson, Co-Rapporteur: Robert James Hemmings, PRAC
Rapporteur: Qun-Ying Yue

**Mirvaso - brimonidine -**
**EMEA/H/C/002642/R/0021**
Galderma International, Rapporteur: Filip Josephson, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Julie Williams

**Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) -**
**EMEA/H/C/000973/R/0128**
GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Qun-Ying Yue

**Thymanax - agomelatine -**

**EMEA/H/C/000916/R/0040**
Servier (Ireland) Industries Ltd., Duplicate, Duplicate of Valdoxan, Rapporteur: Svein Rune Andersen, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Karen Pernille Harg

**Valdoxan - agomelatine - EMEA/H/C/000915/R/0042**
Les Laboratoires Servier, Rapporteur: Svein Rune Andersen, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Karen Pernille Harg

**Vimizim - elosulfase alfa - EMEA/H/C/002779/R/0024, Orphan**
BioMarin Europe Ltd, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Patrick Batty

**Zoledronic Acid Accord - zoledronic acid - EMEA/H/C/002667/R/0006**
Accord Healthcare Limited, Generic, Generic of Zometa, Rapporteur: Alar Irs, PRAC Rapporteur: Doris Stenver

### 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

**Kisqali - ribociclib - EMEA/H/C/004213/II/0004**
Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver, "Extension of Indication to include treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant. In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist for Kisqali. The proposed extension to the indication is based upon data from study CLEE011E2301 (A Phase III randomized, double-blind, placebo-controlled study of LEE011 or placebo in combination with tamoxifen and goserelin or a non-steroidal aromatase inhibitor (NSAI) and goserelin for the treatment of premenopausal women with hormone receptor positive, HER2-

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| negative, advanced breast cancer) and study CLEE011F2301 (A randomized double-blind, placebo-controlled study of ribociclib in combination with fulvestrant for the treatment of men and postmenopausal women with hormone receptor positive, HER2 negative, advanced breast cancer who have received no or only one line of prior endocrine treatment).<br>As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC have been updated and the Package Leaflet has been updated accordingly.<br>In addition, the MAH took the opportunity to make some editorial changes in the SmPC and to make an administrative update to the Estonian and Latvian local representatives addresses in the Package Leaflet.<br>An updated RMP version 2.0 was submitted as part of the application." | |
| **RAVICTI - glycerol phenylbutyrate - EMEA/H/C/003822/II/0019, Orphan**<br>Horizon Pharma Ireland Limited, Rapporteur: Greg Markey, "C.I.6 - Extension of indication to include in the authorised indication the new paediatric population from 0 to 2 months for RAVICTI based on the final results from study HPN-100-009, an Open Label Study of the Safety, Efficacy and Pharmacokinetics of Glycerol Phenylbutyrate in Pediatric Subjects under Two Years of Age with Urea Cycle Disorders (UCDs); 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.<br>This submission covers as well the requirement to submit clinical studies in the paediatric population in accordance with Article 46 of Regulation (EC) No 1901/2006 (the 'Paediatric Regulation') for study HPN-100-009." | |

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

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

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

**B.6.11. PRAC assessed procedures**

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

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

**B.6.14. PRAC assessed ATMP procedures**

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

**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**

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

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

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

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

**G. ANNEX G**

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

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

**Qualification of Biomarkers:**

**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 25-28 June 2018 CHMP plenary:**

**G.3.2. List of procedures starting in June 2018 for July 2018 CHMP adoption of outcomes**

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