17 September 2018
EMA/628683/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 17-20 September 2018

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

17 September 2018, 13:00 – 19:30, room 2A

18 September 2018, 08:30 – 19:30, room 2A

19 September 2018, 08:30 – 19:30, room 2A

20 September 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).

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

Table of contents

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 17-20 September 2018. See September 2018 CHMP minutes (to be published post October 2018 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 17-20 September 2018

1.3. Adoption of the minutes

CHMP minutes for 23-26 July 2018.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. paclitaxel - EMEA/H/C/004154

treatment of ovarian cancer

Scope: Oral explanation

Action: Oral explanation to be held on 18 September 2018 at time 14:30

List of Outstanding Issues adopted on 26.07.2018, 26.04.2018, 14.09.2017, 18.05.2017. List of Questions adopted on 23.06.2016.

See 3.1

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

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

Scope: Oral explanation

Action: Oral explanation to be held on 19 September 2018 at time 09:00

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

2.1.3. mexiletine hcl - Orphan - EMEA/H/C/004584

LUPIN (EUROPE) LIMITED; Treatment of myotonic disorders

Scope: Oral explanation, SAG report

Action: Oral explanation to be held on 18 September 2018 at time 11:00

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

2.1.4. volanesorsen - Orphan - EMEA/H/C/004538

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

Scope: Oral explanation

Action: Oral explanation to be held on 19 September 2018 at time 14:00

List of Outstanding Issues adopted on 28.06.2018, 26.04.2018. List of Questions adopted on 14.12.2017.

2.2. Re-examination procedure oral explanations

2.2.1. Exondys - eteplirsen - Orphan - EMEA/H/C/004355

AVI Biopharma International Ltd; treatment of Duchenne muscular dystrophy

Scope: Oral Explanation, SAG report, opinion

Action: Oral explanation to be held on 18 September 2018 at time 09:00

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

Opinion adopted on 31.05.2018.

Updated list of experts for SAG Neurology meeting held 7 September 2018 were adopted via written procedure on 4 September 2018.

See 3.5.

2.3. Post-authorisation procedure oral explanations

2.3.1. Xtandi - enzalutamide - EMEA/H/C/002639/II/0039/G

Astellas Pharma Europe B.V.

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Eva A. Segovia

Action: Oral explanation to be held on 18 September 2018 at time 16:30, SAG-Oncology report

The final list of experts for the SAG-Oncology meeting held on 6 September was adopted via written procedure on 4 September 2018.

Request for Supplementary Information adopted on 26.07.2018, 31.05.2018.

See 5.1.

2.4. Referral procedure oral explanations

2.4.1. 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: Oral explanation

Action: Oral explanation to be held on 19 September 2018 at time 12:00

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. brigatinib - EMEA/H/C/004248

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 25.01.2018, 12.10.2017. List of Questions adopted on 22.06.2017.

3.1.2. paclitaxel - EMEA/H/C/004154

treatment of ovarian cancer

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.07.2018, 26.04.2018, 14.09.2017, 18.05.2017. List of Questions adopted on 23.06.2016.

See 2.1.

3.1.3. buprenorphine - EMEA/H/C/004651

treatment of opioid dependence within a framework of medical, social and psychological treatment

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 25.01.2018.

3.1.4. doravirine - EMEA/H/C/004747

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.06.2018. List of Questions adopted on 22.03.2018.

3.1.5. 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: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.06.2018. List of Questions adopted on 22.03.2018.

3.1.6. galcanezumab - EMEA/H/C/004648

prophylaxis of migraine

Scope: Opinion

Action: For adoption

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

3.1.7. pegfilgrastim - EMEA/H/C/004915

treatment of neutropenia

Scope: Opinion

Action: For adoption

List of Questions adopted on 22.03.2018.

3.1.8. damoctocog alfa pegol - Orphan - EMEA/H/C/004054

Bayer AG; Treatment and prophylaxis of haemophilia A

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.06.2018. List of Questions adopted on 25.01.2018.

3.1.9. voretigene neparvovec - Orphan - ATMP - EMEA/H/C/004451

Spark Therapeutics Ireland Ltd; treatment of patients with vision loss due to Leber congenital amaurosis or retinitis pigmentosa inherited retinal dystrophy

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 20.07.2018, 25.05.2018. List of Questions adopted on 08.12.2017.

3.1.10. pegfilgrastim - EMEA/H/C/004700

treatment of neutropenia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.06.2018. List of Questions adopted on 25.01.2018.

3.1.11. mogamulizumab - Orphan - EMEA/H/C/004232

Kyowa Kirin Limited; treatment of cutaneous T-cell lymphoma

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.07.2018, List of Questions adopted on 22.02.2018.

3.1.12. meropenem / vaborbactam - EMEA/H/C/004669

treatment of urinary tract infection (cUTI), including pyelonephritis, intra-abdominal infection (cIAI), hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP), bacteraemia, infections due to bacterial organisms

Scope: Opinion

Action: For adoption

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

3.1.13. pegfilgrastim - EMEA/H/C/004802

treatment of neutropenia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 22.02.2018.

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

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

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

Scope: List of Outstanding Issues

Action: For adoption

List of Questions adopted on 08.09.2017.

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

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

Scope: List of Outstanding Issues

Action: For adoption

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

3.2.3. apalutamide - EMEA/H/C/004452

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.06.2018.

3.2.4. romosozumab - EMEA/H/C/004465

Treatment of osteoporosis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 26.04.2018.

3.2.5. fexinidazole - Article 58 - EMEA/H/W/002320

treatment of human African trypanosomiasis (HAT)

Scope: List of outstanding issues

List of experts for adoption via written procedure on 13.09.2018

Action: For adoption

List of Outstanding Issues adopted on 26.06.2018. List of Questions adopted on 24.04.2018.

3.2.6. macimorelin - EMEA/H/C/004660

Diagnosis of Adult growth hormone deficiency (AGHD)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.03.2018.

3.2.7. trastuzumab - EMEA/H/C/004916

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.03.2018.

3.2.8. lanadelumab - Orphan - EMEA/H/C/004806

Accelerated assessment

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 26.06.2018.

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

3.3.1. ambrisentan - EMEA/H/C/004985

treatment of pulmonary arterial hypertension (PAH)

Scope: List of questions

Action: For adoption

3.3.2. ambrisentan - EMEA/H/C/004955

treatment of pulmonary arterial hypertension (PAH)

Scope: List of questions

Action: For adoption

3.3.3. cabazitaxel - EMEA/H/C/004951

treatment of prostate cancer

Scope: List of questions

Action: For adoption

3.3.4. avatrombopag - EMEA/H/C/004722

treatment of thrombocytopenia

Scope: List of questions

Action: For adoption

3.3.5. etanercept - EMEA/H/C/004711

Rheumatoid arthritis, Juvenile idiopathic arthritis, Psoriatic arthritis, Axial spondyloarthritis, Ankylosing spondylitis, Non-radiographic axial spondyloarthritis, Plaque psoriasis, Paediatric plaque psoriasis

Scope: List of questions

Action: For adoption

3.3.6. febuxostat - EMEA/H/C/004773

treatment of hyperuricaemia

Scope: List of questions

Action: For adoption

3.3.7. levodopa - EMEA/H/C/004786

treatment of symptoms of OFF periods in Parkinson's disease

Scope: List of questions

Action: For adoption

3.3.8. posaconazole - EMEA/H/C/005005

treatment of fungal infections

Scope: List of questions

Action: For adoption

3.3.9. delafloxacin - EMEA/H/C/004860

treatment of Acute Bacterial Skin and Skin Structure Infection (ABSSSI) in adults

Scope: List of questions

Action: For adoption

3.3.10. edaravone - EMEA/H/C/004938

treatment of amyotrophic lateral sclerosis (ALS)

Scope: List of questions

Action: For adoption

3.3.11. risankizumab - EMEA/H/C/004759

treatment of psoriasis in adults

Scope: List of questions

Action: For adoption

3.3.12. crisaborole - EMEA/H/C/004863

treatment of mild to moderate atopic dermatitis

Scope: List of questions

Action: For adoption

3.3.13. ioflupane (123i) - EMEA/H/C/004745

indicated for detecting loss of functional dopaminergic neuron terminals in the striatum

Scope: List of questions

Action: For adoption

3.3.14. talazoparib - EMEA/H/C/004674

for the treatment of adult patients with germline breast cancer susceptibility gene (BRCA) mutated human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer.

Scope: List of questions

Action: For adoption

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

3.4.1. andexanet alfa - EMEA/H/C/004108

treatment of direct or indirect factor Xa(FXa) inhibitor when reversal of anticoagulation is needed

Scope: Request for an additional extension of clock-stop to respond to the 2nd List of Outstanding Issues adopted in February 2018.

Action: For adoption

List of Outstanding Issues adopted on 09.11.2017, 22.02.2018. List of Questions adopted on 15.12.2016

3.4.2. glutamine - Orphan - EMEA/H/C/004734

Emmaus Medical Europe Ltd; treatment of sickle cell disease

Scope: Request by the applicant dated 16.08.2018 for an extension to the clock stop to respond to the List of Questions adopted on 28.06.2018.

Action: For adoption

List of Questions adopted on 28.06.2018.

3.4.3. trientine dihydrochloride - Orphan - EMEA/H/C/004111

Univar BV; Treatment of Wilson's disease

Scope: Request by the applicant dated 06.09.2018 for an extension to the clock stop to respond to the List of Questions adopted on 28.06.2018.

Action: For adoption

List of Questions adopted on 28.06.2018.

3.4.4. cemiplimab - EMEA/H/C/004844

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

Scope: Request by the applicant dated 05.09.2018 for an extension to the clock stop to respond to the List of Questions adopted on 26.07.2018.

Action: For adoption

List of Questions adopted on 26.07.2018.

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

3.5.1. Exondys - eteplirsen - Orphan - EMEA/H/C/004355

AVI Biopharma International Ltd; treatment of Duchenne muscular dystrophy

Scope: Oral Explanation, SAG report, opinion

Action: For adoption

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

Opinion adopted on 31.05.2018.

Updated list of experts for SAG Neurology meeting held 7 September 2018 were adopted via written procedure on 4 September 2018.

See 2.2.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. treprostinil – Orphan - EMEA/H/C/004847

SciPharm Sarl, Treatment of chronic thromboembolic pulmonary hypertension

Scope: Letter dated 5.09.2018 informing EMA about the withdrawal of MAA

Action: For information

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. ELOCTA - efmoroctocog alfa - EMEA/H/C/003964/X/0021

Swedish Orphan Biovitrum AB (publ)

Rapporteur: Jan Mueller-Berghaus

Scope: “Extension application to introduce new strength of 4000 IU, 5000 IU and 6000 IU primarily enabling prophylactic dosing in adult patients.”

Action: For adoption

List of Questions adopted on 31.05.2018.

4.1.2. Gilenya - fingolimod - EMEA/H/C/002202/X/0044/G

Novartis Europharm Limited

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension application to introduce a new strength of hard capsules (0.25 mg) to the currently approved presentations of Gilenya, grouped with a type II variation (extension of indication) to add a new indication for the treatment of paediatric patients of 10 years of age and above with relapsing multiple sclerosis (RMS). As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 5.3, 6 and 8 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. In addition, Annex II is updated to be brought in line with the latest QRD template version 10."

Action: For adoption

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

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

Vertex Pharmaceuticals (Europe) Ltd.

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Rhea Fitzgerald

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

List of Questions adopted on 28.06.2018.

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. Simponi - golimumab - EMEA/H/C/000992/X/0083/G

Janssen Biologics B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ulla

Wändel Liminga

Scope: “Extension application to add a new strength of 100 mg/ml solution for injection for paediatric use.
C.I.6.a - Extension of indication to include paediatric patients from the age of 2 years and older for the treatment of polyarticular juvenile idiopathic arthritis (pJIA) with Simponi 100 mg/ml solution for injection. As a consequence, sections 4.1, 4.2, 5.1 and section 4.1 of the 50mg strength have been updated accordingly.
C.I.11.z - To update the RMP to version 18.0 to delete the following safety concerns: vasculitis, psoriasis (new onset or worsening of pre-existing), and sarcoidosis/sarcoid like reaction. This change has been agreed by the CHMP in the outcome of variation Type II/068.
C.I.11.z - To update the RMP to version 18.0 to change the due date of the category 3 study MK-8259-050. This change has been agreed by the CHMP in the outcome of MEA033.
In addition, the marketing authorisation holder took the opportunity to:
- update the Product Information in line with the latest QRD template (version 10);
- implement the recommendations stated in the revised Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' with regards to the excipient Sorbitol (E420);
- add a statement in Section 4.4 of the SmPC to record the name and the batch number of the administered product, in line with Good Pharmacovigilance Practice (GVP) Module PII: Biological medicinal products.”

Action: For adoption

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

Teva B.V.

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: “Extension application to add a new strength of 2 mg/ml (concentrate for solution for solution for infusion) in vials.
The RMP (version 2.0) is updated accordingly.”

Action: For adoption

4.3.3. Zykadia - ceritinib - EMEA/H/C/003819/X/0025

Novartis Europharm Limited

Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Ulla Wändel Liminga

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

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. Adcetris - brentuximab vedotin - Orphan - EMEA/H/C/002455/II/0055

Takeda Pharma A/S

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of the existing Hodgkin lymphoma (HL) indication to include the frontline treatment of adult patients with CD30+ advanced HL in combination with chemotherapy, based on data from ECHELON-1 (C25003), a phase 3 multi-centre, randomised, open-label study comparing the modified progression-free survival (mPFS) obtained with brentuximab vedotin, doxorubicin, vinblastine and dacarbazine versus the mPFS obtained with doxorubicin, bleomycin, vinblastine and dacarbazine. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Furthermore, the PI is brought in line with the latest QRD template version 10. The MAH also submitted an updated RMP version 13."

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018.

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

Ipsen Pharma

Rapporteur: Robert James Hemmings, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Menno van der Elst

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

Request for Supplementary Information adopted on 28.06.2018.

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

Vertex Pharmaceuticals (Europe) Ltd.

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

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

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018.

5.1.4. Kisqali - ribociclib - EMEA/H/C/004213/II/0004

Novartis Europharm Limited

Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver

Scope: "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- 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).
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.
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.
An updated RMP version 2.0 was submitted as part of the application."

Action: For adoption

5.1.5. 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 monotherapy 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

Request for Supplementary Information adopted on 28.06.2018.

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

AbbVie Deutschland GmbH & Co. KG

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

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

Action: For adoption

5.1.7. Ravicti - glycerol phenylbutyrate - Orphan - EMEA/H/C/003822/II/0019

Horizon Pharma Ireland Limited

Rapporteur: Greg Markey, Co-Rapporteur: Jayne Crowe

Scope: "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.
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."

Action: For adoption

5.1.8. Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0050

Novartis Europharm Limited

Rapporteur: Concepcion Prieto Yerro

Scope: “Change of the Revolade indication of immune thrombocytopaenic purpura to specify the duration of the disease. As a result the SmPC sections 4.1, 4.2, 4.4, 4.8 and 5.1 are being revised. The Package leaflet is being updated accordingly.”

Action: For adoption

5.1.9. 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

Request for Supplementary Information adopted on 28.06.2018.

5.1.10. Rubraca - rucaparib - Orphan - EMEA/H/C/004272/II/0001

Clovis Oncology UK Limited

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Ulla Wändel Liminga

Scope: “Extension of Indication to include new indication for Rubraca "Rubraca is indicated as monotherapy for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy". As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated with the expanded clinical eficacy and safety data. The Package Leaflet is also updated in accordance.
The updated RMP version 2.0 has also been submitted.
In addition, the applicant took the opportunity to propose the move of one paragraph from section 4.4 to 5.1 in the SmPC for consistency with other SmPC agents in this class with

this indication."

Action: For adoption

5.1.11. Sprycel - dasatinib - EMEA/H/C/000709/II/0059

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Fátima Ventura, PRAC Rapporteur: Doris Stenver

Scope: "Extension of Indication to include a paediatric indication for Philadelphia chromosome positive acute lymphoblastic leukaemia for Sprycel; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, and 5.2 of the SmPC are updated.
The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to the product information.
The RMP version 16.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018.

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

Roche Registration GmbH

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

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

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

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018.

5.1.13. 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

Request for Supplementary Information adopted on 28.06.2018.

5.1.14. Venclyxto - venetoclax - Orphan - EMEA/H/C/004106/II/0008

AbbVie Deutschland GmbH & Co. KG

Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty

Scope: "Extension of Indication to include Venclyxto in combination with rituximab for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy.
As a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated.
The Package Leaflet is updated in accordance.
This submission also fulfils the Annex II condition to submit the results of the MURANO study comparing venetoclax plus rituximab to bendamustine plus rituximab in patients with relapsed/refractory CLL.
In addition, RMP version 3.0 is submitted."

Action: For adoption

Request for Supplementary Information adopted on 26.04.2018.

5.1.15. Xtandi - enzalutamide - EMEA/H/C/002639/II/0039/G

Astellas Pharma Europe B.V.

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Eva A. Segovia

Scope: "C.I.4: Update of sections 4.4, 4.7, 4.8 and 5.2 of the SmPC in order to amend the warning on possible association with seizure, to amend the effects on driving or operating machines, to amend the identified adverse reactions and to amend the 'Race' subsection

regarding pharmacokinetic properties based on the results from the completed studies PROSPER, a Phase 3 Randomized Controlled Study, designed to investigate the Safety and Efficacy of Enzalutamide in Patients with Non-Metastatic Castration-Resistant Prostate Cancer; and Asian PREVAIL, a Multinational Phase 3, Randomized, Double-blind, Placebo-controlled Efficacy and Safety Study of Oral Enzalutamide in Chemotherapy-naive Subjects with Progressive Metastatic Prostate Cancer Who Have Failed Androgen Deprivation Therapy; and the updated integrated clinical safety database.
The Package Leaflet is updated in accordance.
C.I.6.a: Extension of Indication to include patients with non-metastatic castration-resistant prostate cancer (CRPC) for Xtandi;
as a consequence, sections 4.1 and 5.1 of the SmPC are updated, based on the supportive clinical study results of MDV3100-14 (PROSPER), a Phase 3 Randomized Controlled Study, designed to investigate the Safety and Efficacy of Enzalutamide in Patients with Non-Metastatic Castration-Resistant Prostate Cancer; MDV3100-09 (STRIVE), a Multicenter Phase 2 Study to investigate the Safety and Efficacy of Enzalutamide Versus Bicalutamide in Men With Non-Mtastatic or Metastatic Castration-Resistant Prostate Cancer; and based on supportive non-clinical data from 7 new reports.
The Package Leaflet is updated in accordance.
An updated RMP version 12.1 was submitted in order to include the changes related to the extension of indication."

Oral explanation to be held on 18 September 2018 at time 16:30, SAG-Oncology report

Action: For adoption

Request for Supplementary Information adopted on 26.07.2018, 31.05.2018.

See also 2.3

5.1.16. WS1369
Elebrato Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004781/WS1369/0001
Trelegy Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004363/WS1369/0001

GlaxoSmithKline Trading Services Limited

Lead Rapporteur: Peter Kiely, Lead Co-Rapporteur: Harald Enzmann, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "To modify the approved current COPD therapeutic indication to "maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD)".
As a consequence, the indication section (4.1), Undesirable effects section (4.8) and Pharmacodynamic Properties section (5.1), Pharmacokinetic properties section (5.2), Preclinical Safety data section (5.3) of the EU SmPC, and the Possible side effects section (4) of the package leaflet are updated accordingly. This is based on the result of study CTT116855 and study 200812 and the population PK report 208059.
The updated RMP (version 02) has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018.

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

5.2.1. Hemlibra - emicizumab - EMEA/H/C/004406/II/0002

Roche Registration GmbH

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

Scope: "Extension of Indication to include routine prophylaxis of bleeding episodes in patients with hemophilia A without factor VIII inhibitors, for Hemlibra. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated with efficacy and safety information of the pivotal trials:
- Study BH30071 (HAVEN 3) - an ongoing, multicenter, open-label, randomized Phase III clinical study evaluating the efficacy, safety and PK of emicizumab prophylaxis at doses of 1.5 mg/kg/week (QW) and 3 mg/kg/every 2 weeks (Q2W) versus no prophylaxis in adults and adolescent patients (age of 12 or above) with haemophilia A without inhibitors against factor VIII (FVIII).
- Study BO39182 (HAVEN 4) - an ongoing multicenter, open-label, non-randomized Phase III study evaluating the efficacy, safety and PK of emicizumab given as the dose of 6 mg/kg/every 4 weeks (Q4W) in adults and adolescent patients (age of 12 or above) with hemophilia A with or without FVIII inhibitors.
- Study BH29992 (HAVEN 2) - a multicenter, open-label, non-randomized Phase III study evaluating the efficacy, safety and PK of emicizumab at the QW dose in pediatric patients (<12 years old or 12-17 years old and <40kg) with hemophilia A with FVIII inhibitors.
The Package Leaflet and the Risk Management Plan (v.2.0) is updated in accordance.
In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor corrections and clarity to sections 4.4, 4.5 and 4.6 of the SmPC."

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

Action: For discussion

Letter from third party

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

5.3.1. Blincyto - blinatumomab - Orphan - EMEA/H/C/003731/II/0011

Amgen Europe B.V.

Scope: "Extension of Indication to include the treatment of adults with minimal residual disease (MRD) positive B-cell precursor acute lymphoblastic leukaemia (ALL)for BLINCYTO; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, and to update the safety information. The Labelling is updated in accordance.
RMP version 4.0 is included in this submission."

Re-examination timetable.

Action: For adoption

Opinion adopted on 26.07.2018. An oral explanation was held on 24.07.2018.

Request for Supplementary Information adopted on 26.04.2018, 14.12.2017, 22.06.2017.

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

6.2.1. human fibrinogen / human thrombin - EMEA/H/D/004308

to support the endogenous clotting process and increase of haemostasis in surgical procedures

Scope: Request by the applicant dated 10 September 2018 requesting an extension of clock stop to respond to the List of Questions adopted on 22 March 2018.

Action: For adoption

List of Questions adopted on 22.03.2018.

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. quizartinib –Orphan - H0004468

Daiichi Sankyo Europe GmbH, Treatment of adults with relapsed or refractory acute myeloid leukemia (AML) which is FLT3-ITD positive

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

Action: For adoption

8.2. Priority Medicines (PRIME)

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

8.2.1. List of applications received

Action: For information

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Onivyde - irinotecan hydrochloride trihydrate – Orphan - EMEA/H/C/004125/II/0008

Baxalta Innovations GmbH

Rapporteur: Filip Josephson, PRAC Rapporteur: David Olsen,

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

Action: For adoption

9.1.2. Orgalutran - ganirelix - EMEA/H/C/000274/II/0041

Merck Sharp & Dohme B.V.

Rapporteur: Outi Mäki-Ikola,

Scope: "Update of section 4.3 of the SmPC to expand the existing contraindication regarding hypersensitivity to include also wording regarding dry natural rubber/latex and sections 4.4 and 6.5 of the SmPC to clarify that this product is in contact with dry natural rubber/latex. The labelling and Package Leaflet have been updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representative in Belgium in the Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 26.07.2018.

10. Referral procedures

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

No items

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

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: Oral explanation

Action: Oral explanation to be held on 19 September 2018 at time 12:00

See 2.4

10.4.2. Syner-KINASE 10 000 IU - EMEA/H/A-29(4)/1472

Syner-Medica Ltd

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Sol Ruiz

Scope: Request for an extension to the clock stop to respond to the list of questions adopted in July 2018.

Action: For adoption

RMS: UK; CMS: DE, ES, FR, NL; Mutual Recognition Procedure number: UK/H/6520/01-05/MR, Disagreements regarding benefit/risk balance, safety and manufacturing.

List of questions adopted: 26.07.2018

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

No items

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

10.6.1. Metamizole containing medicinal products – metamizole sodium - EMEA/H/A-31/1469

MAH various

Rapporteur: Ewa Balkowiec, Co-rapporteur: Harald Enzmann

Scope: List of outstanding issues

Action: For adoption

The Polish National Competent Authority triggered a referral under Article 31 of Directive 2001/83 based on interest of the Union, requesting an opinion to CHMP on whether the scientific data regarding the maximum daily dose and contraindications concerning pregnancy and breastfeeding are adequately presented in the product information of metamizole containing medicinal products.

10.6.2. Valsartan-containing medicinal products - EMEA/H/A-31/1471

MAHs: various

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Martina Weise

Scope: List of outstanding issues

Action: For adoption

Referral notification from European Commission regarding an API manufacturer (Zhejiang

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

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

September 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

Minutes of ITF Briefing meeting held on 19th July 2018

Action: For information

13.2. Innovation Task Force briefing meetings

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Election of new CHMP chairperson

The election of a new Chairperson will take place **at the September 2018 CHMP plenary meeting** as previously communicated to the Committee.

Action: For adoption

14.1.2. Telematics strategy 2020-2025: Concept Paper

Action: For discussion

14.1.3. Concepts of significant benefit (follow-up to CHMP Work Plan 2017)

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 03-06 September 2018

Action: For information

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

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 12-14 September 2018
Action: For information

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 23-24 September 2018

Action: For information

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at September 2018 PDCO

Action: For information

Report from the PDCO meeting held on 25–27 July 2018

Action: For information

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

Action: For discussion/adoption

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 11-13 September 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 17-19 September 2018

Action: For information

CMDh questions to BWP on leeches (EMA/CMDh/270304/2018)

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 3-6 September 2018. Table of conclusions

Action: For information

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

14.3.2. Name Review Group (NRG)

No items

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP September 2018 meeting to CHMP for adoption:

- 10 reports on products in scientific advice and protocol assistance
- 15 reports on products in pre-authorisation procedures
- 1 report on products in plasma master file

Action: For adoption

14.3.4. Guideline Consistency Group (GCG)

Chair: Aranzazu Sancho-Lopez

Feedback from Barbara van Zwieten-Boot as previous GCG chair

Action: For information

14.3.5. Excipients Drafting Group

Chair: Dominique Masset

Information for the package leaflet regarding ethanol used as an excipient in medicinal products for human use (EMA/CHMP/43486/2018)
Action: For adoption

Information for the package leaflet regarding dextrans used as excipients in medicinal products for human use (EMA/CHMP/187129/2016)
Action: For adoption for 6-month public consultation

Information for the package leaflet regarding proline used as an excipient in medicinal products for human use (EMA/CHMP/108086/2016)
Action: For adoption for 6-month public consultation

Information for the package leaflet regarding lactose used as an excipient in medicinal products for human use (EMA/CHMP/186428/2016)
Action: For adoption for 6-month public consultation

Information for the package leaflet regarding polysorbates used as excipients in medicinal products for human use (EMA/CHMP/190743/2016)
Action: For adoption for 6-month public consultation

14.3.6. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus/Romaldas Mačiulaitis

Response from RIWP and PKWP to CMDh questions on Classification as Narrow Therapeutic Index (NTI) drug and advice on requirements for bioequivalence studies – colchicine

Action: For adoption

14.3.7. Safety Working Party (SWP)

Chair: Jan Willem Van der Laan

Response from SWP to PRAC regarding prenatal exposure to paracetamol and impact on the urogenital apparatus or impact on neurodevelopment

Action: For adoption

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

14.5.1. International Council on Harmonisation (ICH)

Clinical electronic Structured Harmonized Protocol (CeSHarP): Call for expression of interest of one expert

Action: For information

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. 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)*

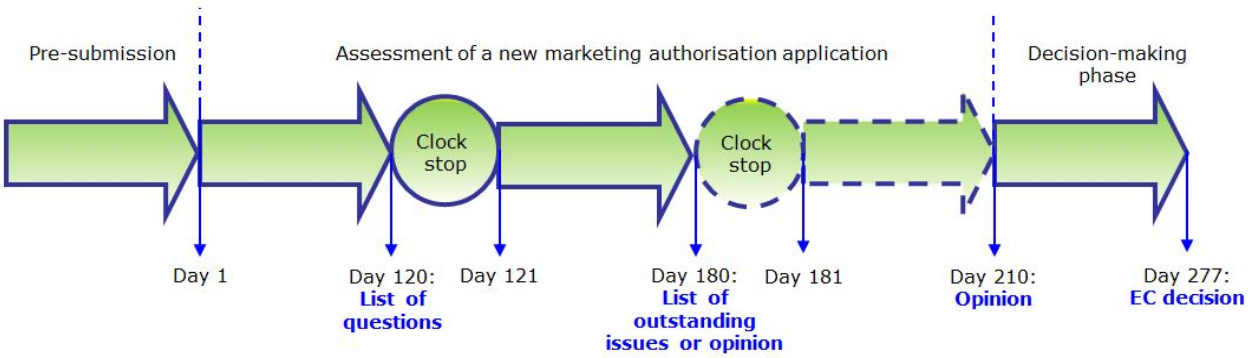
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

17 September 2018
EMA/628682/2018

Annex to 17-20 September 2018 CHMP Agenda

Pre submission and post authorisation issues

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

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

Final Outcome of Rapporteurship allocation for September 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

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

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

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
Request for Supplementary Information adopted on 28.06.2018.

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: Ulla Wändel Liminga

B.2.2. Renewals of Marketing Authorisations for unlimited validity

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

Bemfola - follitropin alfa -
EMEA/H/C/002615/R/0019
Gedeon Richter Plc., Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Menno van der Elst

Brintellix - vortioxetine -
EMEA/H/C/002717/R/0019
H. Lundbeck A/S, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Laurence de Fays
Request for Supplementary Information adopted on 26.07.2018.

Ixiaro - japanese encephalitis vaccine (inactivated, adsorbed) -
EMEA/H/C/000963/R/0091
Valneva Austria GmbH, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Brigitte Keller-Stanislawski

Izba - travoprost -
EMEA/H/C/002738/R/0011
Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Rhea Fitzgerald
Request for Supplementary Information adopted on 26.07.2018.

Levetiracetam Hospira - levetiracetam -
EMEA/H/C/002783/R/0018
Hospira UK Limited, Generic, Generic of Keppra, Rapporteur: Juris Pokrotnieks, PRAC Rapporteur: Laurence de Fays
Request for Supplementary Information adopted

on 26.07.2018.

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

Neuraceq - florbetaben (18F) -
EMEA/H/C/002553/R/0025
Life Radiopharma Berlin GmbH, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Patrick Batty
Request for Supplementary Information adopted on 26.07.2018.

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: Ulla Wändel Liminga

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, Co-Rapporteur: Harald Enzmann, 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.2.3. Renewals of Conditional Marketing Authorisations

OCALIVA - obeticholic acid -

EMEA/H/C/004093/R/0009, Orphan
Intercept Pharma Ltd, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 03-06 September 2018 PRAC:

Signal of cytomegalovirus (CMV) infection:

LEMTRADA - Alemtuzumab – EMEA/H/C/003718

Sanofi Belgium, Rapporteur: Mark Ainsworth, Co-Rapporteur: Filip Josephson

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

Signal of immune thrombocytopenic purpura, thrombocytopenia:

TECFIDERA - Dimethyl Fumarate – EMEA/H/C/002601

Biogen Idec Ltd, Rapporteur: Martina Weise, Co-Rapporteur: Robert James Hemmings

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

Signal of interstitial lung disease:

- Duloxetine -

ARICLAIM - EMEA/H/C/000552

Eli Lilly Nederland B.V., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Kristina Dunder

CYMBALTA - EMEA/H/C/000572

XERISTAR - EMEA/H/C/000573

YENTREVE - EMEA/H/C/000545

DULOXETINE LILLY - EMEA/H/C/004000

Eli Lilly Nederland B.V., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Filip Josephson

DULOXETINE MYLAN -

EMEA/H/C/003981

Mylan S.A.S, Rapporteur: John Joseph Borg

DULOXETINE ZENTIVA - EMEA/H/C/003935

Zentiva k.s., Rapporteur: Kristina Dunder

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

Signal of aortic aneurysm and dissection:

QUINSAIR – Fluoroquinolones - EMEA/H/C/002789

Chiesi Farmaceutici S.p.A., Rapporteur: Robert James Hemmings, Co-Rapporteur: Ondrej Slanar

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

Signal of skin cancer:

- Hydrochlorothiazide –

Actelsar HCT - telmisartan, hydrochlorothiazide – EMEA/H/C/002676

Actavis Group PTC ehf, Rapporteur: Alar Irs

Kinzalkomb - telmisartan, hydrochlorothiazide – EMEA/H/C/000415

PritorPlus - telmisartan, hydrochlorothiazide – EMEA/H/C/000414

Bayer AG, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Harald Enzmann

MicardisPlus - telmisartan, hydrochlorothiazide – EMEA/H/C/000413

Boehringer Ingelheim International, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Harald Enzmann

Ifirmacombi - irbesartan, hydrochlorothiazide - EMEA/H/C/002302

Krka, d.d., Novo mesto, Rapporteur: Concepcion Prieto Yerro

Tolucombi – telmisartan, hydrochlorothiazide – EMEA/H/C/0002549

Krka, d.d., Novo mesto, Rapporteur: Alar Irs

Rasilez HCT - aliskiren,

hydrochlorothiazide - EMEA/H/C/000964

Noden Pharma DAC, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Agnes Gyurasics

Copalia HCT - amlodipine, valsartan, hydrochlorothiazide - EMEA/H/C/001159

Dafiro HCT - amlodipine besylate, valsartan, hydrochlorothiazide - EMEA/H/C/0001160

Novartis Europharm Limited, Rapporteur: Mark Ainsworth, Co-Rapporteur: Alar Irs

Irbesartan Hydrochlorothiazide Zentiva - irbesartan, hydrochlorothiazide - EMEA/H/C/000783

Karvezide - irbesartan, hydrochlorothiazide - EMEA/H/C/000221

Sanofi-aventis groupe

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Outi Maki-Ikola

CoAprovel - irbesartan, hydrochlorothiazide - EMEA/H/C/000222

Sanofi Clir SNC, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Outi Maki-Ikola

Irbesartan/Hydrochlorothiazide Teva - irbesartan, hydrochlorothiazide - EMEA/H/C/001112

Teva B.V., Rapporteur: Concepcion Prieto Yerro

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

Signal of cytomegalovirus gastrointestinal infection:

YERVOY – Ipilimumab – EMEA/H/C/002213

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jorge Camarero Jiménez

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

Signal of pulmonary hypertension and fatal cases associated with use in an off-

label indication, early-onset intrauterine growth restriction:

REVATIO - Sildenafil – EMEA/H/C/000638

VIAGRA -Sildenafil – EMEA/H/C/000202

Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Concepcion Prieto Yerro

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

Signal of premature ending of the GALILEO5 study in patients who have received an artificial heart valve through a transcatheter aortic valve replacement (TAVR):

XARELTO – Rivaroxaban – EMEA/H/C/000944

Bayer AG, Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise

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

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

EMEA/H/C/PSUSA/00000985/201801
(dexamethasone (centrally authorised product indicated in uveitis and macular oedema))
CAPS:
Ozurdex (EMEA/H/C/001140) (dexamethasone), Allergan Pharmaceuticals Ireland, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, “28 Jan 2017 – 27 Jan 2018”

EMEA/H/C/PSUSA/00002169/201802
(nitisinone)
CAPS:
Orfadin (EMEA/H/C/000555) (nitisinone), Swedish Orphan Biovitrum International AB, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, “From 21 Feb 2017 - To 20 Feb 2018”

EMEA/H/C/PSUSA/00002499/201802
(prasugrel)
CAPS:

Efient (EMEA/H/C/000984) (prasugrel), Daiichi Sankyo Europe GmbH, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, “26-Feb-2017 to 25-Feb-2018”

EMEA/H/C/PSUSA/00002611/201801
(ranolazine)
CAPS:
Ranexa (EMEA/H/C/000805) (ranolazine), Menarini International Operations Luxembourg S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “27 Jan 2015 - 26 Jan 2018”

EMEA/H/C/PSUSA/00010022/201801
(axitinib)
CAPS:
Inlyta (EMEA/H/C/002406) (axitinib), Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: David Olsen, “27 January 2017 to 26 January 2018”

EMEA/H/C/PSUSA/00010043/201801
(meningococcal group-B vaccine (rDNA, component, adsorbed))
CAPS:
Bexsero (EMEA/H/C/002333) (meningococcal group B vaccine (recombinant, component, adsorbed)), GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “14/07/2017 - 13/01/2018”

EMEA/H/C/PSUSA/00010120/201802
(nalmefene)
CAPS:
Selincro (EMEA/H/C/002583) (nalmefene), H. Lundbeck A/S, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, “25 Feb 2017 - 24 Feb 2018”

EMEA/H/C/PSUSA/00010140/201801
(vismodegib)
CAPS:
Erivedge (EMEA/H/C/002602) (vismodegib), Roche Registration GmbH, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, “30 January 2017 to 29 January 2018”

EMEA/H/C/PSUSA/00010363/201801
(dasabuvir)
CAPS:
Exviera (EMEA/H/C/003837) (dasabuvir), AbbVie Deutschland GmbH & Co. KG,

Rapporteur: Filip Josephson, PRAC Rapporteur: Dolores Montero Corominas, “15 January 2017 to 14 January 2018”

EMEA/H/C/PSUSA/00010367/201801
(ombitasvir / paritaprevir / ritonavir)
CAPS:
Viekirax (EMEA/H/C/003839) (ombitasvir / paritaprevir / ritonavir), AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, PRAC Rapporteur: Maria del Pilar Rayon, “15 January 2017 – 14 January 2018”

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

Adcetris - brentuximab vedotin -
EMEA/H/C/002455/II/0056/G, Orphan
Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik
Request for Supplementary Information adopted on 05.07.2018.

Alprolix - eftrenonacog alfa -
EMEA/H/C/004142/II/0020, Orphan
Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop

Armisarte - pemetrexed -
EMEA/H/C/004109/II/0017/G
Actavis Group PTC ehf, Rapporteur: Alar Irs
Request for Supplementary Information adopted on 21.06.2018.

Bortezomib Accord - bortezomib -
EMEA/H/C/003984/II/0014
Accord Healthcare Limited, Generic, Generic of VELCADE, Rapporteur: Milena Stain

Bortezomib Hospira - bortezomib -
EMEA/H/C/004207/II/0008
Pfizer Europe MA EEIG, Generic, Generic of VELCADE, Rapporteur: Milena Stain

Cuprior - trientine -
EMEA/H/C/004005/II/0001/G
GMP-Orphan SA, Rapporteur: Jayne Crowe

Request for Supplementary Information adopted on 26.07.2018.

Cyramza - ramucirumab - EMEA/H/C/002829/II/0024/G

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

Request for Supplementary Information adopted on 26.07.2018.

Cyramza - ramucirumab - EMEA/H/C/002829/II/0025

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

Request for Supplementary Information adopted on 19.07.2018.

Daptomycin Hospira - daptomycin - EMEA/H/C/004310/II/0006/G

Hospira UK Limited, Generic, Generic of Cubicin, Rapporteur: Kolbeinn Gudmundsson

Request for Supplementary Information adopted on 22.02.2018.

Dupixent - dupilumab - EMEA/H/C/004390/II/0009/G

sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus

EXJADE - deferasirox - EMEA/H/C/000670/II/0061

Novartis Europharm Limited, Rapporteur: Alexandre Moreau

Request for Supplementary Information adopted on 26.07.2018.

Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0106

Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege

Gliolan - aminolevulinic acid - EMEA/H/C/000744/II/0015

medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Bruno Sepodes

Request for Supplementary Information adopted on 28.06.2018.

Herzuma - trastuzumab - EMEA/H/C/002575/II/0005

Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus

Request for Supplementary Information adopted

on 26.07.2018.

Kentera - oxybutynin -
EMEA/H/C/000532/II/0047
Nicobrand Limited, Rapporteur: Bart Van der Schueren

Keytruda - pembrolizumab -
EMEA/H/C/003820/II/0051/G
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri
Request for Supplementary Information adopted on 19.07.2018.

Kineret - anakinra -
EMEA/H/C/000363/II/0060
Swedish Orphan Biovitrum AB (publ), Rapporteur: Mark Ainsworth
Request for Supplementary Information adopted on 26.07.2018.

Kyntheum - brodalumab -
EMEA/H/C/003959/II/0004/G
LEO Pharma A/S, Rapporteur: Johann Lodewijk Hillege

Lemtrada - alemtuzumab -
EMEA/H/C/003718/II/0025/G
Sanofi Belgium, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth

Lonquex - lipegfilgrastim -
EMEA/H/C/002556/II/0041/G
Sicor Biotech UAB, Rapporteur: Greg Markey

MULTAQ - dronedarone -
EMEA/H/C/001043/II/0041
sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege

Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine -
EMEA/H/C/002226/II/0082
Pfizer Europe MA EEIG, Rapporteur: Greg Markey

NovoSeven - eptacog alfa (activated) -
EMEA/H/C/000074/II/0106
Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik

Ocrevus - ocrelizumab -
EMEA/H/C/004043/II/0004
Roche Registration GmbH, Rapporteur: Mark Ainsworth

Ongentys - opicapone - EMEA/H/C/002790/II/0009
Bial - Portela & Cª, S.A., Rapporteur: Greg Markey
Request for Supplementary Information adopted on 26.04.2018.

Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0136/G
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Reagila - cariprazine - EMEA/H/C/002770/II/0008
Gedeon Richter Plc., Rapporteur: Kristina Dunder

Rekovelle - follitropin delta - EMEA/H/C/003994/II/0008/G
Ferring Pharmaceuticals A/S, Rapporteur: Joseph Emmerich
Request for Supplementary Information adopted on 28.06.2018.

Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0052/G
Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro

Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0007
GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren

Somavert - pegvisomant - EMEA/H/C/000409/II/0086/G
Pfizer Europe MA EEIG, Rapporteur: Joseph Emmerich

Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0125
GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder
Request for Supplementary Information adopted on 14.06.2018.

Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0127/G
GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder
Request for Supplementary Information adopted

on 19.07.2018.

Tamiflu - oseltamivir -
EMEA/H/C/000402/II/0135
Roche Registration GmbH, Rapporteur: Outi Mäki-Ikola

Yervoy - ipilimumab -
EMEA/H/C/002213/II/0058/G
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik
Request for Supplementary Information adopted on 12.07.2018.

WS1404
Nuwiq-EMEA/H/C/002813/WS1404/0022
Vihuma-
EMEA/H/C/004459/WS1404/0004
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus
Request for Supplementary Information adopted on 05.07.2018.

WS1415
Blitzima-
EMEA/H/C/004723/WS1415/0015
Ritemvia-
EMEA/H/C/004725/WS1415/0015
Rituzena-
EMEA/H/C/004724/WS1415/0016
Truxima-
EMEA/H/C/004112/WS1415/0016
Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz
Request for Supplementary Information adopted on 26.07.2018.

WS1427
Nuwiq-EMEA/H/C/002813/WS1427/0024
Vihuma-
EMEA/H/C/004459/WS1427/0007
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus

WS1452
Rixathon-
EMEA/H/C/003903/WS1452/0013
Riximyo-
EMEA/H/C/004729/WS1452/0013
Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus

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

Afinitor - everolimus -
EMEA/H/C/001038/II/0058

Novartis Europharm Limited, Rapporteur: Harald Enzmann, “Submission of the final report from study CRAD001Y2201, listed as a category 1 study in the RMP. This is a three arm randomised study investigating the combination of everolimus with exemestane versus everolimus alone versus capecitabine in patients with oestrogen receptor positive metastatic breast cancer after recurrence or progression on letrozole or anastrozole. Consequently, Annex II of the Product Information was updated to remove this study.”
Request for Supplementary Information adopted on 31.05.2018.

Alecensa - alectinib -
EMEA/H/C/004164/II/0016

Roche Registration GmbH, Rapporteur: Filip Josephson, “Submission of the final study analysis on secondary ALK-mutation positive/negative samples and correlation with clinical outcome in fulfilment of a CHMP recommendation for alectinib, adopted during the initial Marketing Authorisation. The application is based on an additional analysis generated from two studies (NP28673 and NP28761).”

Atripla - efavirenz / emtricitabine / tenofovir disoproxil -
EMEA/H/C/000797/II/0130

Bristol-Myers Squibb and Gilead Sciences Ltd., Rapporteur: Martina Weise, “Update of sections 4.3 and 4.5 of the SmPC in order to include drug-drug interaction data between efavirenz (EFV) and grazoprevir/elbasvir based on a review of the antiviral product Zepatier.

The Marketing authorisation holder (MAH) has taken the opportunity to introduce changes to the sodium wording in Section 4.4 of the SmPC and to align the text in Section 4.6 (Fertility, pregnancy and lactation) for Atripla with the currently approved wording in the Eviplera SmPC.

The Package Leaflet (PIL) has been updated accordingly.

In addition, the MAH has also taken the opportunity to implement some minor linguistic amendments (MLAs) to the translations of the product information annexes for the following languages: DE, FI, FR, IT, NL and NO."

Baraclude - entecavir - EMEA/H/C/000623/II/0059

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to include information regarding the newly detected resistance information showing reduced susceptibility to entecavir for the rtA 181C substitution in combination with LVDr substitutions, rtL 180M + rtM204V. In addition, the Marketing authorisation holder (MAH) 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. The MAH also took the opportunity to add the sodium concentration for Baraclude 0.05 mg/ml oral solution in section 2 of the SmPC and section 2 of the PL according to the guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'."

Brilique - ticagrelor - EMEA/H/C/001241/II/0041

AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 4.4 of the SmPC in order to clarify the posology in patients having an acute coronary syndromes (ACS) event, to update the warning related to bradyarrhythmia based on already assessed studies and post-marketed use (clinical trials PLATO (D5130C05262), PEGASUS (D5132C00001), SOCRATES (D5134C00001) and EUCLID (D5135C00001)) and to introduce "stroke" as a possible even in case of premature discontinuation.
Furthermore the MAH took the opportunity to update the PI in relation to sodium content in line with QRD and to update the list of local representatives in the Package Leaflet."

Ceprotin - human protein C - EMEA/H/C/000334/II/0104

Baxter AG, Rapporteur: Jan Mueller-Berghaus, "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.

The Package Leaflet has been further updated."
Request for Supplementary Information adopted on 21.06.2018.

Coagadex - human coagulation factor X - EMEA/H/C/003855/II/0009, Orphan
Bio Products Laboratory Limited, Rapporteur: Andrea Laslop, "Update of section 5.2 of the SmPC in order to include data on long-term use based on final results from the study Ten05, a multicentre, retrospective data collection study on the use of BPL's high purity factor X in the treatment of patients with hereditary factor X deficiency on a compassionate use basis. In addition the Marketing authorisation holder (MAH) took the opportunity to update the number of patients treated with Coagadex in section 4.8 of the SmPC based on studies Ten01, Ten02 and Ten03 as well as to include some editorial changes in section 4.2 of the SmPC. Furthermore, the information on perioperative management in the Package Leaflet has been aligned with information in the SmPC."

Cyramza - ramucirumab - EMEA/H/C/002829/II/0023/G
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."
Request for Supplementary Information adopted on 14.06.2018.

Dacogen - decitabine - EMEA/H/C/002221/II/0035, Orphan
Janssen-Cilag International N.V., Rapporteur:

Alexandre Moreau, “Update of section 4.4, and 4.8 of the SmPC in order to add the adverse events "Hepatic Function abnormal" and "Hyperbilirubinaemia" with the frequency common and to include clinical recommendations in patients developing signs or symptoms of hepatic impairment based on a cumulative review of post-marketing data; the Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of the local representative in Portugal in the Package Leaflet. Furthermore, the term “(for pH adjustment)” has been removed from the Annex IIIA in accordance with the revision 2 of the European Commission guideline on Excipients in the labelling and package leaflet of medicinal products for human use.”
Request for Supplementary Information adopted on 26.07.2018.

ILARIS - canakinumab - EMEA/H/C/001109/II/0060

Novartis Europharm Limited, Rapporteur: Jan Mueller-Berghaus, “Update of section 5.1 of the SmPC based on the final clinical study report (CSR) from Study ACZ885G2306 (β-SPECIFIC 4 Patients: Study of Paediatric efficacy and safety with first-line use of canakinumab: An open-label canakinumab (ACZ885) dose reduction or dose interval prolongation efficacy and safety study in patients with Systemic Juvenile Idiopathic Arthritis (SJIA)). The submission of the final CSR addresses the post-authorisation measure MEA 036.3 (PAES) and the requirements of article 46 of the paediatric regulation.”

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

Merck Sharp & Dohme B.V., Rapporteur: Greg Markey, “Submission of the final reports from 3 in vitro studies evaluating the inhibitory effect of raltegravir at higher concentrations on OATP1B3, OCT1, OCT2, MATE1 and MATE2-K transporters and CYP2B6, CYP2D6, UGT2B7 enzyme activities, and a final CSR to assess the drug-drug interaction (DDI) potential of raltegravir at a 1,200 mg once daily clinical dose, according to the request from the CHMP

following the assessment of X/59."

Jinarc - tolvaptan -
EMEA/H/C/002788/II/0015
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).

The Package Leaflet is updated accordingly."
Request for Supplementary Information adopted on 21.06.2018.

Keytruda - pembrolizumab -
EMEA/H/C/003820/II/0054
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Update of section 5.1 of the SmPC based on the final clinical study report (CSR) for KEYNOTE-045 (KN045); a phase III randomized clinical trial of pembrolizumab (MK-3475) versus paclitaxel, docetaxel or vinflunine in subjects with recurrent or progressive metastatic urothelial cancer. The submission addresses the post-authorisation measure 'ANX 020' and Annex IID has been updated accordingly."

Kyprolis - carfilzomib -
EMEA/H/C/003790/II/0030, Orphan
Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of section 4.4 of the SmPC in order to include a warning of the increased risk of cardiac failure in Asian patients treated with carfilzomib based on postmarketing experience and 3 phase 3, randomized-controlled studies (CLARION-Study 2011-003; ENDEAVOR-Study 20130398 and A.R.R.O.W.-Study 20140355). In addition, the Marketing authorisation holder (MAH) took the opportunity to propose few minor typographical changes to SmPC."

Latuda - lurasidone -
EMEA/H/C/002713/II/0021
Aziende Chimiche Riunite Angelini Francesco S.p.A., Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC to add new paediatric data available in children and adolescent patients (10-17 years of age) with bipolar I

disorder, upon request by CHMP following the assessment of the paediatric study D1050326 submitted according to Art. 46 procedure (no. EMEA/H/C/002713/P46/008)."

Lemtrada - alemtuzumab - EMEA/H/C/003718/II/0023

Sanofi Belgium, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth, "Update of section 4.8 of the SmPC in order to update the table of frequencies of adverse reactions in accordance with the SmPC guideline following request from PRAC in procedure EMEA/H/C/PSUSA/00010055/201703. This procedure also included an update in section 4.4 to add warning on acute acalculous cholecystit following a cumulative review of the cases. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 12.07.2018.

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

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

Mircera - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/II/0067

Roche Registration GmbH, Rapporteur: Concepcion Prieto Yerro, "Update of sections 4.2., 5.1. and 5.2. of the SmPC in order to update the paediatric information based on results from phase II dose finding study NH 19707 (Dolphin): An Open-Label, Multi-Center, Multiple Dose Study to Determine the Optimum Starting Dose of Intravenous MIRCERA for Maintenance Treatment of Anemia in Pediatric Patients with Chronic Kidney Disease on Hemodialysis; listed as a category 3 study in the RMP. The Package Leaflet is updated accordingly."

Orgalutran - ganirelix - EMEA/H/C/000274/II/0041

Merck Sharp & Dohme B.V., Rapporteur: Outi Mäki-Ikola, "Update of section 4.3 of the SmPC to expand the existing contraindication regarding hypersensitivity to include also wording regarding dry natural rubber/latex and

sections 4.4 and 6.5 of the SmPC to clarify that this product is in contact with dry natural rubber/latex. The labelling and Package Leaflet have been updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representative in Belgium in the Package Leaflet."
Request for Supplementary Information adopted on 26.07.2018.

Otezla - apremilast - EMEA/H/C/003746/II/0021
Celgene Europe BV, Rapporteur: Peter Kiely, "Update of sections 4.2 and 5.1 of Otezla SmPC to include data (up to 5 years of treatment) from the following studies (CC-10004-PSA-002, -003, -004, -005 and CC-10004-PSOR-008, -009)) listed as a category 3 study in the RMP (MEA 002)."

Ozempic - semaglutide - EMEA/H/C/004174/II/0001
Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC in order to reflect final results from the SUSTAIN 7 trial (NN9535-4216), a 40-week open-label trial comparing the safety and efficacy of 0.5 mg of Ozempic to 0.75 mg of dulaglutide and 1 mg of Ozempic to 1.5 mg of dulaglutide in patients on metformin with type-2 diabetes."
Request for Supplementary Information adopted on 26.07.2018, 25.05.2018.

Praluent - alirocumab - EMEA/H/C/003882/II/0040
sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Submission of the final clinical study report of study R727-CL-1018 (study title: A Phase 2 Pilot Study with a Randomized Double-Blind Treatment Phase to Evaluate the Pharmacodynamics and Safety of Alirocumab in Patients with Autosomal Dominant Hypercholesterolemia and Gain-of-Function Mutations in 1 or Both Alleles of the PCSK9 Gene or Loss-of-Function Mutations in 1 or More Alleles of the Apolipoprotein B Gene), as per MEA012."
Request for Supplementary Information adopted on 19.07.2018.

Praluent - alirocumab - EMEA/H/C/003882/II/0041
sanofi-aventis groupe, Rapporteur: Johann

Lodewijk Hillege, “Submission of the final clinical study report of study R727-CL-1119 (study title: A Randomized, Double-Blind, Double-Dummy, Active-Controlled Study to Evaluate the Efficacy and Safety of REGN727/SAR236553 in Patients with Primary Hypercholesterolemia Who Are Intolerant to Statins), as per MEA011.”

Revestive - teduglutide - EMEA/H/C/002345/II/0043, Orphan

Shire Pharmaceuticals Ireland Limited, Rapporteur: Mark Ainsworth, “Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC based on the final CSR of study TED-C14-006 (“a 24-Week Double-blind, Safety, Efficacy, and Pharmacodynamic Study Investigating Two Doses of Teduglutide in Pediatric Subjects Aged 1 Year Through 17 Years With Short Bowel Syndrome who are Dependent on Parenteral Support”; a category 3 study in the RMP). The Package Leaflet is updated accordingly.”
Request for Supplementary Information adopted on 26.07.2018, 31.05.2018.

Skilarence - dimethyl fumarate - EMEA/H/C/002157/II/0008/G

Almirall S.A, Rapporteur: Robert James Hemmings, “Submission of the final report from study AML/27. This is an in vitro study aimed to assess the potential of dimethyl fumarate to inhibit human hepatic cytochrome P450 (CYP) enzymes.

Submission of the final report from study AML/28. This is an in vitro study aimed to assess the potential interaction of dimethyl fumarate with p-glycoprotein (P-gp).

Submission of the final report from study Almirall-15-05May2017. This is an in vitro study aimed to assess the interaction of dimethyl fumarate with human BCRP efflux (ABC) transporters.”

Soliris - eculizumab - EMEA/H/C/000791/II/0103, Orphan

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."
Request for Supplementary Information adopted on 28.06.2018.

Somavert - pegvisomant - EMEA/H/C/000409/II/0084

Pfizer Europe MA EEIG, Rapporteur: Joseph Emmerich, "Update of sections 4.2 and 4.4 of the SmPC to introduce posology recommendations to recommend an assessment of baseline levels of liver tests (LTs) [serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum total bilirubin (TBIL), and alkaline phosphatase (ALP)] prior initiation of treatment with Somavert following analysis of the interim result for study "A6291010 (ACROSTUDY) - A multicenter, post marketing surveillance study of pegvisomant therapy in patients with acromegaly – extension" as requested in procedure EMEA/H/C/000409/MEA 061.1. The PL has been updated accordingly."
Request for Supplementary Information adopted on 12.07.2018.

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, randomised, open-label, phase 2a study of Strensiq in patients with hypophosphatasia. The MAH took also the occasion to update the PI to QRD version 10.0."
Request for Supplementary Information adopted on 28.06.2018.

Sustiva - efavirenz - EMEA/H/C/000249/II/0145/G

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, “Update of sections 4.3 and 4.5 of the SmPC in order to add contraindication with elbasvir/grazoprevir due to the potential for significant decreases in plasma concentrations of elbasvir and grazoprevir, based on the post-approval and literature data, the Package Leaflet is updated accordingly.
Update of sections 4.4 and 4.5 to include warnings in relation to the co-administration of efavirenz and sofosbuvir/velpatasvir; efavirenz and vepatasvir/sofosbuvir/voxilaprevir and efavirenz and glecaprevir/pibrentasvir; based on the post-approval and literature data, the Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.”
Request for Supplementary Information adopted on 26.07.2018.

Translarna - ataluren -
EMEA/H/C/002720/II/0045, Orphan
PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.4 and 4.5 of the SmPC in order to include information on Drug-Drug Interaction with sensitive probe substrate of organic anion transporting polypeptide 1B3 (OATP1B3) based on study PTC124-GD-042-HV (MEA016). The package leaflet is updated accordingly.”

Translarna - ataluren -
EMEA/H/C/002720/II/0046, Orphan
PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update information on patients with moderate to severe renal impairment based on results from study PTC124-GD-032-HV (MEA010). In addition the MAH took the opportunity to amend section 5.2 to propose correction of the biotransformation statement. The Package leaflet is updated accordingly.”

VELCADE - bortezomib -
EMEA/H/C/000539/II/0090
Janssen-Cilag International NV, Rapporteur: Daniela Melchiorri, “Update of section 5.1 of the SmPC to update the information based on final long-term follow-up and overall survival data for

LYM-3002, a Randomized, Open-label, Multicenter Phase 3 Study of the Combination of Rituximab, Cyclophosphamide, Doxorubicin, VELCADE, and Prednisone (VcR-CAP) or Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (R-CHOP) in Patients With Newly Diagnosed Mantle Cell Lymphoma who are not Eligible for a Bone Marrow Transplant. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of Local representatives in the Package Leaflet."	
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." Request for Supplementary Information adopted on 28.06.2018.	
Venclyxto - venetoclax - EMEA/H/C/004106/II/0016, Orphan AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Submission of the report from study M13-982 listed as a category 3 study in the RMP. This is a Phase 2 Open-Label Study of the Efficacy of ABT199 (GDC-0199) in Subjects with Relapsed/Refractory or Previously Untreated Chronic Lymphocytic Leukemia Harboring the 17p Deletion."	
Xadago - safinamide - EMEA/H/C/002396/II/0027 Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 4.5 of the SmPC in order to implement information regarding interaction of safinamide and rosuvastatin, following results from study CRO-PK-17-318. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for	

Ireland in the Package Leaflet and to include editorial changes in the English, German and Spanish product information."	
XALKORI - crizotinib - EMEA/H/C/002489/II/0055 Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, "Update of section 4.2 of the SmPC in order to provide greater clarity in the crizotinib dosing regimen modification recommendations for patients who receive a reduced dose of crizotinib, either because of pre-existing moderate or severe hepatic impairment or severe renal impairment or because of a previous dose reduction while on treatment with crizotinib. The Package Leaflet has been updated accordingly."	
XALKORI - crizotinib - EMEA/H/C/002489/II/0057 Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, "Submission of a number of analysis pertaining to the mechanisms of tumor resistance to crizotinib due to secondary ROS1 kinase domain mutations in patients with ROS1-positive non-small cell lung cancer (NSCLC)."	
XALKORI - crizotinib - EMEA/H/C/002489/II/0058 Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, "Submission of the final study report for study A8081038, a multinational active safety surveillance study of crizotinib in Europe and the United States." Opinion adopted on 06.09.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xultophy - insulin degludec / liraglutide - EMEA/H/C/002647/II/0026 Novo Nordisk A/S, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to reflect data for use of Xulthopy in combination with sodium glucose co-transporter 2 inhibitors (SGLT2i) in patients inadequately controlled on SGLT2i ±other oral anti-diabetic drug. The update is based on data from the clinical trial: NN9068-4229: "A Clinical Trial Comparing Glycaemic Control and Safety of Insulin Degludec/Liraglutide (IDegLira) versus Insulin Glargine (IGlar) as Add-on Therapy to SGLT2i in Subjects with Type 2 Diabetes Mellitus"."	

Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0038

Pfizer Ireland Pharmaceuticals, Rapporteur: Greg Markey, "Update of section 4.2 of the SmPC to amend the recommended duration of ceftaroline fosamil intravenous (IV) infusion for standard dose regimens in adults and paediatrics to a range of 5 to 60 minutes from the currently recommended infusion duration of 1 hour. The PIL is updated accordingly. In addition the MAH has also taken the opportunity to reformat section 4.2 of the SmPC Posology and method of administration and to incorporate minor editorial updates to sections 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC."

Zostavax - shingles (herpes zoster) vaccine (live) - EMEA/H/C/000674/II/0117

MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.5 and 5.1 of the SmPC to include that Zostavax can be given concomitantly with pneumococcal vaccine and to reflect the results of an observational post-marketing study comparing the effectiveness of Zostavax when co-administrated with a 23-valent pneumococcal polysaccharide vaccine (Bruxvoort K et al. 2018). The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet."

WS1371
Rasilez-EMEA/H/C/000780/WS1371/0119
Rasilez HCT-EMEA/H/C/000964/WS1371/0086

Noden Pharma DAC, Lead Rapporteur: Daniela Melchiorri, "Update of section 4.8 and 5.1 of the Rasilez SmPC and section 4.8 of the Rasilez/HCTZ SmPC in order to reflect the results from paediatric study CSPP100A2365E2 (a multicenter, 52 to 104 week extension study to evaluate the long term growth and development of pediatric hypertensive patients 6–17 years of age treated previously with aliskiren) provided as per the requirement of article 46."
Request for Supplementary Information adopted on 31.05.2018.

WS1380
Ebymect-EMEA/H/C/004162/WS1380/0033

Edistride-
EMEA/H/C/004161/WS1380/0027
Forxiga-
EMEA/H/C/002322/WS1380/0046
Xigduo-EMEA/H/C/002672/WS1380/0045
AstraZeneca AB, Lead Rapporteur: Kristina Dunder, “Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to reflect the final study results from study D1690C00024 (DERIVE); A Multicentre, Double-Blind, Placebo-Controlled, Parallel Group, Randomized, Phase III Study to Evaluate the Glycaemic Efficacy and Renal Safety of Dapagliflozin in Patients with Type 2 Diabetes Mellitus and Moderate Renal Impairment (CKD 3A) Who Have Inadequate Glycaemic Control.
In addition, the Worksharing applicant took the opportunity to implement minor editorial changes in Edistride, Ebymect and Xigduo SmPCs, as well as Ebymect Labelling. The Package Leaflets for Xigduo and Ebymect are updated accordingly.”
Request for Supplementary Information adopted on 26.07.2018.

WS1392
ProQuad-
EMEA/H/C/000622/WS1392/0125
MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus, “Update of section 4.8 of the SmPC in order to add the adverse reaction (ADR) meningitis with a frequency “not known” and to add a clarifying foot note for immunocompromised or immunocompetent individuals applicable to the ADR meningitis, herpes zoster and encephalitis. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to make some editorial changes in the product information and to update the list of local representatives in the package leaflet.”
Request for Supplementary Information adopted on 05.07.2018.

WS1411/G
Aluvia-
EMEA/H/W/000764/WS1411/0105/G
Kaletra-
EMEA/H/C/000368/WS1411/0171/G
Norvir-
EMEA/H/C/000127/WS1411/0150/G
AbbVie Deutschland GmbH & Co. KG, Lead

Rapporteur: Joseph Emmerich, “Update of section 4.5 of the SmPC in order to update the safety information on the interaction with ibrutinib based on the company core data sheets. The Package Leaflet is updated accordingly.
Update of section 4.5 of the SmPC in order to update the safety information of ritonavir, lopinavir/ritonavir on the interaction with levothyroxine based on the PRAC signal final assessment report EMA/101535/2018 possibly leading to decreased levothyroxine efficacy and hypothyroidis.”

WS1417/G
Invega-
EMEA/H/C/000746/WS1417/0060/G
Trevicta-
EMEA/H/C/004066/WS1417/0013/G
Xeplion-
EMEA/H/C/002105/WS1417/0039/G
Janssen-Cilag International NV, Lead Rapporteur: Kristina Dunder, “Update of sections 4.4 and 4.5 of the SmPC in order to add information regarding concomitant use with psychostimulants (in line with the CMDh recommendations for risperidone) and of section 4.8 of the SmPC to add catatonia as a new side-effect categorised as `Rare'. The Package Leaflet is updated accordingly.”

WS1422
CONTROLOC Control-
EMEA/H/C/001097/WS1422/0030
PANTOLOC Control-
EMEA/H/C/001100/WS1422/0034
PANTOZOL Control-
EMEA/H/C/001013/WS1422/0032
SOMAC Control-
EMEA/H/C/001098/WS1422/0031
Takeda GmbH, Lead Rapporteur: Greg Markey, “Update of section 5.3 of the SmPC in order to update the safety information based on the final results of study 14GR325 “A pre- and postnatal developmental toxicity study of pantoprazole sodium (PF-05208751) by oral gavage in rats focused on postnatal evaluation of bone development” as required by the PRAC Recommendation of EMEA/H/C/PSUSA/00002285/201708.”

WS1429

Descovy-
EMEA/H/C/004094/WS1429/0032
Genvoya-
EMEA/H/C/004042/WS1429/0048
Odefsey-
EMEA/H/C/004156/WS1429/0033
Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings, “Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC with data in patients on chronic haemodialysis from the Study GS-US-292-1825; this is a Phase 3b Open-Label Study toEvaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of E/C/F/TAF Fixed Dose Combination (FDC) in HIV-1 Infected Subjects on Chronic Hemodialysis.
The Package Leaflet is updated accordingly.
In addition, the Worksharing applicant (WSA) took the opportunity to introduce changes to the lactose wording for Genvoya and Odefsey and an administrative correction to the Genvoya Patient information leaflet (PIL) in order to add “lurasidone” to the second list of contra-indicated drugs appearing in the PIL.
The WSA has also taken the opportunity to introduce some minor administrative amendments throughout the product information for all three products as well as to implement some minor linguistic amendments (MLAs) to the translations of the respective product information annexes:
- Genvoya: DE, ES, FI, HR, HU, IS, IT, NO, SL and SV languages
- Descovy: DA, DE, ES, FR, HR, NL, NO, PT and SL languages
- Odefsey: CS, DE, LV, MT, NL, PL, SL and SV languages.”

WS1433
Clopidogrel Zentiva-
EMEA/H/C/000975/WS1433/0061
Clopidogrel/Acetylsalicylic acid Zentiva-
EMEA/H/C/001144/WS1433/0051
DuoPlavin-
EMEA/H/C/001143/WS1433/0050
Iscover-
EMEA/H/C/000175/WS1433/0133
Plavix-EMEA/H/C/000174/WS1433/0130
Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, “In response to PRAC recommendation for the signal of insulin autoimmune syndrome

(EPITT ref 19155), update of section 4.8 of the SmPC to the new adverse reaction 'insulin autoimmune syndrome'. The Package Leaflet are updated accordingly. In addition, at the request of the Agency, MA numbers of Plavix and Iscover were reviewed and updated as per the current format. The Plavix and Iscover Annex A and PI were updated accordingly."	
WS1444 **Kisplyx-EMEA/H/C/004224/WS1444/0012** **Lenvima-** **EMEA/H/C/003727/WS1444/0016** Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren, "Update of Sections 4.4 and 4.8 of the SmPC to add pneumothorax and nephrotic syndrome. The PIL is updated accordingly."	
WS1449 **Relvar Ellipta-** **EMEA/H/C/002673/WS1449/0038** **Revinty Ellipta-** **EMEA/H/C/002745/WS1449/0035** Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, "Update of section 4.8 of the SmPC in order to add hyperglycaemia as an adverse reaction based on a cumulative review of hyperglycaemia/new onset diabetes associated with fluticasone/vilanterol (FF/VI); the Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to update the Package Leaflet with a clarification on the adverse event "blurred vision" already included in the SmPC (WS-1224)."	
WS1459 **Clopidogrel Zentiva-** **EMEA/H/C/000975/WS1459/0062** **Clopidogrel/Acetylsalicylic acid Zentiva-** **EMEA/H/C/001144/WS1459/0052** **DuoPlavin-** **EMEA/H/C/001143/WS1459/0051** **Iscover-** **EMEA/H/C/000175/WS1459/0134** **Plavix-EMEA/H/C/000174/WS1459/0131** Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, "Update of section 5.1 of the SmPC in order to reflect the clinical outcome data of 2 randomised investigator-sponsored studies	

regarding de-escalation of P2Y12 receptor inhibitor to clopidogrel in ACS.”	

B.5.3. CHMP-PRAC assessed procedures

Advate - octocog alfa - EMEA/H/C/000520/II/0092 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-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.” Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Aflunov - prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - EMEA/H/C/002094/II/0044/G Seqirus S.r.l, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, “Update of sections 4.4, 4.6, 4.8 and 5.1 of the SmPC following clinical study reports of studies V87_25 and V87_26 listed as post approval commitments; these are Phase 3, stratified, randomized, controlled, observer-blind, multicenter studies; the Package Leaflet and Labelling are updated accordingly. The updated RMP version 3.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement some amendments to the PI and make some additional minor editorial corrections.”	
Brilique - ticagrelor - EMEA/H/C/001241/II/0042 AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst,	

"Update of sections 4.2, 4.9 and 5.2 of the SmPC in order to update the safety information in relation to renal impairment based on the final results from study D5130L00067; this is a single dose, randomized, open label, parallel group study conducted to compare the pharmacokinetics (PK), pharmacodynamics (PD), safety and tolerability of ticagrelor in haemodialysis patients to subjects with normal renal function. The RMP version 11 has also been submitted."

Bydureon - exenatide - EMEA/H/C/002020/II/0050

AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "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."

Request for Supplementary Information adopted on 28.06.2018.

Cosentyx - secukinumab - EMEA/H/C/003729/II/0033/G

Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, PRAC Rapporteur: Eva A. Segovia, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to include information on dose up-titration for Psoriatic Arthritis (PsA) and update of the radiographic sub-section for Psoriatic Arthritis (PsA) based on results from the 24-week data from study CAIN457F2342, the pooled data from PsA Phase 3 studies, the pooled data from patients who up-titrated their secukinumab dose in studies CAIN457F2306E1, CAIN457F2312 and CAIN457F2318, and long-term study observations which demonstrate higher rates of discontinuation for patients on secukinumab 150 mg compared to patients on secukinumab 300 mg. the Package leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the Package leaflet

in line with the latest approved SmPC as per procedure (EMEA/H/C/003729/IB/0028). The RMP (v.3.0) has also been updated including suicidal ideation and behavior as an important potential risk in the RMP and including minor administrative/editorial changes (LEG 005.2).” Request for Supplementary Information adopted on 31.05.2018.	
CYLTEZO - adalimumab - EMEA/H/C/004319/II/0004 Boehringer Ingelheim International GmbH, Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga, “Submission of the final report from study 1297.3 listed as a category 3 study in the RMP. This is an interventional trial to generate long-term safety, efficacy, and immunogenicity data for the administration of the proposed biosimilar Cyltezo in patients with moderate to severe rheumatoid arthritis.” Request for Supplementary Information adopted on 06.09.2018.	Request for supplementary information adopted with a specific timetable.
Herzuma - trastuzumab - EMEA/H/C/002575/II/0006 Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski Request for Supplementary Information adopted on 26.07.2018.	
Kisqali - ribociclib - EMEA/H/C/004213/II/0003/G Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver, “C.I.4: Update of section 5.2 of the SmPC in order to reflect on results from study CLEE011A2109: A Phase I, open label, multi-centre, parallel cohort, single dose study to evaluate the pharmacokinetics of LEE011 in healthy subjects with normal hepatic function and subjects with impaired hepatic function; C.I.4: Update of section 4.2 and 5.2 of the SmPC in order to reflect on results from study CLEE011A2116-Part I: A phase I, open label, multicentre, parallel-group, single dose two-staged study to evaluate the pharmacokinetics and safety of a single 400 mg oral dose of LEE011 in subjects with varying degrees of impaired renal function compared to matched healthy volunteers with normal renal function. The RMP version 2.0 has also been submitted.”	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 06.09.2018.	
NovoMix - insulin aspart - EMEA/H/C/000308/II/0095 Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.2, 4.5 and 5.1 of the SmPC to include data on the use of NovoMix® 30 combination use with GLP-1 receptor agonists. The PIL is updated accordingly. The RMP is laso updated (version 3)"	
Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0002 Roche Registration GmbH, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Julie Williams, "Update of sections 4.4 and 4.5 of the SmPC in order to include information on vaccination based on interim results from study BN29739 listed as a category 3 study in the RMP; this is a phase IIIb, multicentre, randomised, parallel-group, open-label study to evaluate the effects of ocrelizumab on immune response in patients with relapsing forms of multiple sclerosis. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted." Request for Supplementary Information adopted on 06.09.2018, 12.07.2018, 17.05.2018.	Request for supplementary information adopted with a specific timetable.
OFEV - nintedanib - EMEA/H/C/003821/II/0021, Orphan Boehringer Ingelheim International GmbH, Rapporteur: Jayne Crowe, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of section 4.8 of the SmPC in order to include 'myocardial infarction' as a new adverse drug reaction with a frequency 'uncommon' in order to fulfil LEG 004.1, following the assessment of PSUSA/00010319/201704. The Package Leaflet is updated accordingly. The RMP version 6.0 (in revision 2 of the template) has also been submitted." Request for Supplementary Information adopted on 06.09.2018.	Request for supplementary information adopted with a specific timetable.
Oncaspar - pegaspargase - EMEA/H/C/003789/II/0016/G Baxalta Innovations GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Patrick Batty, "Update of sections 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1 5.2 and 5.3 of the SmPC with the final results from studies DFCI 11-001	Request for supplementary information adopted with a specific timetable.

and AALL07P4 listed as category 3 studies in the RMP; Study DFCI 11-001 is a Phase 2, open-label, randomized, multicenter study to determine the safety and feasibility of administering an investigational asparaginase product (asparaginase formulation) compared with Oncaspar in subjects aged 1 to <22 years with newly diagnosed ALL and lymphoblastic lymphoma. Study AALL07P4 is a multicenter, open label, randomized, active-controlled, parallel design clinical pilot study conducted to evaluate the PK, pharmacodynamics, safety, immunogenicity and efficacy of an investigational asparaginase product in comparison with Oncaspar in patients aged 1 to <31 years newly diagnosed with high risk B-precursor ALL. The Package Leaflet is proposed to be updated accordingly. The RMP version 3.0 has also been submitted." Request for Supplementary Information adopted on 06.09.2018, 17.05.2018.	
Onivyde - irinotecan hydrochloride trihydrate - EMEA/H/C/004125/II/0008, Orphan Baxalta Innovations GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: David Olsen, "Update of sections 1, 2, 4.2, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC in order to reflect the expression of strength based on irinotecan anhydrous free-base. The Labelling and Package Leaflet are updated accordingly. In addition the MAH took the opportunity to introduce minor editorial changes. The updated RMP version 2.1 has also been submitted."	See 9.1
Ovitrelle - choriogonadotropin alfa - EMEA/H/C/000320/II/0073/G 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 6.0 are updated accordingly. The RMP is also updated to extend the important potential risk of 'misuse' to 'weight loss and anabolic growth promoting	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

effect'. 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." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018.	
Plegridy - peginterferon beta-1a - EMEA/H/C/002827/II/0046 Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Julie Williams, "Update of sections 4.4 and 4.8 of the SmPC in order to add new warning and safety information about anaphylaxis. The RMP version 3.2 has also been submitted." Request for Supplementary Information adopted on 06.09.2018.	Request for supplementary information adopted with a specific timetable.
Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0161 Pfizer Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final study report from study B1851041, a phase 4 post marketing study to determine 'National trends in Ambulatory Care Visits for Otitis Media in Children Under the Age of Five in the United States.' Consequently, the RMP version 12 has been updated." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 12.04.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Remicade - infliximab - EMEA/H/C/000240/II/0214 Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the RMP (v 17.0) and Annex II-D of the Product Information to remove the Educational material for health care professionals. In addition, the MAH is taking the opportunity to update the package leaflet with some missing warnings and ADRs already reflected in the SmPC, as requested by CHMP, and to introduce some minor QRD related changes."	

Request for Supplementary Information adopted on 26.07.2018.	
Ryzodeg - insulin human - EMEA/H/C/002499/II/0028 Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 5.1 of the SmPC based on new clinical data from a cardiovascular outcome trial EX1250-4080 (DEVOTE) conducted for insulin degludec. DEVOTE was a randomised, double-blind and event-driven clinical trial with a median duration of 2 years comparing the cardiovascular safety of insulin degludec versus insulin glargine (100 units/mL) in patients with type 2 diabetes mellitus at high risk of cardiovascular events. Based on the long-term exposure and safety data from DEVOTE which are also relevant for insulin degludec/insulin aspart, the Ryzodeg SmPC is updated with data from the trial in alignment with a recent update of the SmPC for insulin degludec. Section 6.5 of the SmPC is also being amended for an editorial improvement to more precisely describe the nature of the plunger stopper. The RMP version 7 has also been submitted, with updates consequent to the data in support of the application." Opinion adopted on 06.09.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tamiflu - oseltamivir - EMEA/H/C/000402/II/0136 Roche Registration GmbH, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.2, 4.8, 5.1 and 5.2 to guide prescribers on the use of Tamiflu for treatment in immunocompromised (IC) patients based on studyt NV20234, a Phase III, double-blind, randomized, stratified, multicenter study of conventional and double dose oseltamivir for the treatment of influenza in IC patients. The PL and RMP (v15) have been updated accordingly. In addition, the MAH took the opportunity to correct some minor errors."	
Toujeo - insulin glargine - EMEA/H/C/000309/II/0105/G Sanofi-Aventis Deutschland GmbH, Duplicate, Duplicate of Lantus, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van	

der Elst	
Truberzi - eluxadoline - EMEA/H/C/004098/II/0005/G Allergan Pharmaceuticals International Ltd, Rapporteur: Harald Enzmann, PRAC Rapporteur: Adam Przybylkowski, "Update of sections 4.5 and 5.2 of the SmPC in order to update the drug interaction information based on the final report from study 3030-102-002: a single-center, non-randomized, open-label, single-sequence study to evaluate the effect of eluxadoline on the single-dose pharmacokinetics of midazolam in healthy subjects, listed as a category 3 study in the RMP. The package leaflet was updated accordingly. Submission of the final report from study ELX-PH-08: in vitro evaluation of eluxadoline as an inducer of cytochrome P450 (CYP) 1A2 and 3A4 expression in cultured human hepatocytes, listed as a category 3 study in the RMP. Following the assessment of EMEA/H/C/PSUSA/00010528/201703, the RMP was updated to version 2.1 to update the existing important identified risk "SO spasm" to "SO spasm (Sphincter of Oddi dysfunction, SOD)" and include pancreatitis as a new important identified risk." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 12.07.2018, 17.05.2018, 08.03.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Varuby - rolapitant - EMEA/H/C/004196/II/0007/G Tesaro UK Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adam Przybylkowski, "- Update of SmPC section 4.5 regarding interaction with OCT1 substrates following the submission of the non-clinical study: in vitro evaluation of the substrate and inhibitor potential of rolapitant for efflux and update of transporters (17TESAP2R1). - Update of SmPC section 4.5 regarding interaction with UGT substrates following the submission of the 2 non-clinical studies: evaluation of potential UGT inhibition by rolapitant in cryopreserved human hepatocytes (170594) and evaluation of potential rolapitant metabolism by recombinantly expressed human UGT enzymes (TSRP/REP/07CRD75486/2017) - Update of SmPC section 4.5 following the submission of the open-label, single-d0se study	Request for supplementary information adopted with a specific timetable.

to assess the effects of rolapitant (oral) on the pharmacokinetics of caffeine (CYP1A2) in healthy subjects (1000-01-001) The RMP version 1.2 has also been submitted." Request for Supplementary Information adopted on 06.09.2018, 12.07.2018.	
WS1390 **Levitra-EMEA/H/C/000475/WS1390/0062** **Vivanza-EMEA/H/C/000488/WS1390/0058** Bayer AG, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Maria del Pilar Rayon, "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. 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." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1396 **Kisplyx-EMEA/H/C/004224/WS1396/0011** **Lenvima-EMEA/H/C/003727/WS1396/0015** Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren, Lead PRAC Rapporteur: Annika Folin, "Update of section 4.5 of the SmPC to include that there is no significant drug-drug interaction risk with midazolam, based on the results of study E7080-A001-109 (A Phase 1 Study to determine DDI of lenvatinib and midazolam, a cytochrome P450 3A4 (CYP3A4) substrate, in subjects with advanced solid	

tumors). The RMP is updated (version 10.4)" Request for Supplementary Information adopted on 12.07.2018.	

B.5.4. PRAC assessed procedures

PRAC Led **Deltyba - delamanid - EMEA/H/C/002552/II/0030, Orphan** Otsuka Novel Products GmbH, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "Update of the RMP (finally approved version 2.11), 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 to add clarifications to the described additional pharmacovigilance activities to assess the effectiveness of risk minimisation measures and the set up date of an EU network of laboratories." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Humira - adalimumab - EMEA/H/C/000481/II/0182** AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 14.0 in order to include a thorough review of the currently specified safety concerns in the Humira RMP, to updated in regards of previously assessed safety concerns and to make associated updates in line with GVP Module V." Request for Supplementary Information adopted on 06.09.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Kengrexal - cangrelor - EMEA/H/C/003773/II/0015** Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of an updated RMP version 2.0 in order to update the requirements for a study listed as category 3 in the RMP. In addition, the	Request for supplementary information adopted with a specific timetable.

MAH took the opportunity to revise the RMP in line with the RMP template version 2.0." Request for Supplementary Information adopted on 06.09.2018.	
PRAC Led **MabThera - rituximab - EMEA/H/C/000165/II/0152** Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final study report of the non-interventional drug utilisation study (DUS) BA28478 (MabThera drug utilisation study and patient alert card evaluation in non-oncology patients in Europe: an infusion centre-based approach). Consequently, update of sections 4.2 and 4.4 of the SmPC and Annex II.E to remove the patient alert card as an additional risk minimisation measure for the risks of PML and infections, for the non-oncology indications. The Package leaflet is updated in accordance. The RMP is laso updated (version 18). This submission is done in fulfilment of FUM-68.1 and FUM-71." Request for Supplementary Information adopted on 06.09.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Mycamine - micafungin - EMEA/H/C/000734/II/0038** Astellas Pharma Europe B.V., Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "Submission of an updated RMP version 20.0 in order to streamline and improve the educational programme and communication to physicians prescribing Mycamine as requested in variation II/0035." Request for Supplementary Information adopted on 06.09.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Neofordex - dexamethasone - EMEA/H/C/004071/II/0008** Laboratoires CTRS, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 4.0 in order to propose the removal a category 3 activity 'removal of the score line for subdivision of the 40mg tablet and consequent deletion of the 20mg posology'. In addition, the	Request for supplementary information adopted with a specific timetable.

MAH updated the other category 3 activity 'Development of a 20mg oral dosage form'. The MAH implemented the RMP revision 2 format." Request for Supplementary Information adopted on 06.09.2018.	
PRAC Led **Pegasys - peginterferon alfa-2a - EMEA/H/C/000395/II/0101** Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "Submission of an updated RMP version 9.0 in order to remove the NV25361 study (category 3 study); in addition, the YV25718 (study to establish the efficacy and safety of PEG-IFN monotherapy in children from 3 to less than 18 years of age with CHB) long term follow up milestone is amended from Q3 2020 to Q4 2021. The classification of some risks is also amended as per revision 2 of Module V of GVP including updates in the epidemiology section." Opinion adopted on 06.09.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Resolor - prucalopride - EMEA/H/C/001012/II/0042** 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." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018, 12.04.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Revestive - teduglutide - EMEA/H/C/002345/II/0045, Orphan** Shire Pharmaceuticals Ireland Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 8 in order to include the safety	

information from the final CSR of study TED-C14-006 ("a 24-Week Double-blind, Safety, Efficacy, and Pharmacodynamic Study Investigating Two Doses of Teduglutide in Pediatric Subjects Aged 1 Year Through 17 Years With Short Bowel Syndrome who are Dependent on Parenteral Support"; a category 3 study in the RMP) that was submitted within variation EMEA/H/C/002345/II/0043."	
PRAC Led **Simponi - golimumab - EMEA/H/C/000992/II/0084** Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Update of the RMP to version 18.0, based upon the conclusion of the PSUR Assessment report (PSUSA/00001560/201704), in order to remove the Educational programme for prescribing healthcare professionals (HCPs) as an additional risk minimisation measure. The Patient Alert Card is maintained and renamed Patient Reminder Card across the SmPC, Annex II, Labelling and Package Leaflet. In addition, the Marketing authorisation holder took the opportunity to update the list of local representatives in the Package Leaflet." Opinion adopted on 06.09.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Thymanax - agomelatine - EMEA/H/C/000916/II/0038** 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." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Valdoxan - agomelatine - EMEA/H/C/000915/II/0039** Les Laboratoires Servier, Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Karen	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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.” Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018.	
PRAC Led **Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0186** Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Adrien Inoubli, 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’.” Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0188** Gilead Sciences Ireland UC, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Joseph Emmerich, “Submission of the final report from study GS-EU-174-0224 listed as a category 3 study in the RMP. This is a cross-sectional drug utilisation study in children and adolescents with Chronic Hepatitis B to assess whether physicians prescribing Viread to paediatric patients with Chronic Hepatitis B in the EU were following the relevant recommendations in the Viread SmPC and educational brochures.” Opinion adopted on 06.09.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0190** Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Joseph Emmerich, “Submission of an updated RMP version 22.1 (in	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

accordance with the revised guidance in the Guideline on good pharmacovigilance practices Module V) to propose removing the additional risk minimization activities for HIV and HBV adults associated with the renal safety concern from the RMP." Opinion adopted on 06.09.2018.	
PRAC Led **Votubia - everolimus - EMEA/H/C/002311/II/0055, Orphan** Novartis Europharm Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "Submission of the final report from the non-interventional study CRAD001MIC03, listed as a category 3 study in the RMP. This is an international disease registry collecting data on manifestations, interventions and outcomes in patients with tuberous sclerosis complex." Opinion adopted on 06.09.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Xeloda - capecitabine - EMEA/H/C/000316/II/0077** Roche Registration GmbH, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "To update the Xeloda RMP (version 9.1) in line with the product information changes recently approved within variation EMEA/H/C/000163/II/0074. The following updates are included: post-authorisation exposure updated, presentation of important identified risk dihydropyrimidine dehydrogenase deficiency (DPD) updated and inclusion of additional updates related to section 4.4 of the SmPC for DPD, revised as part of procedure EMEA/H/C/316/II/0074. In addition MAH took the opportunity to introduce the new EU RMP template."	
PRAC Led **WS1270 Enbrel-EMEA/H/C/000262/WS1270/0216 LIFMIOR-EMEA/H/C/004167/WS1270/0013** Pfizer Europe MA EEIG, Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Robert James Hemmings, "Submission of the final report from study B1801396, a non-interventional PASS listed as a category 3 study in the RMP. This is a	Request for supplementary information adopted with a specific timetable.

non-interventional, population-based, multi-country, observational cohort register study to evaluate the risk of adverse pregnancy outcomes in patients with rheumatoid arthritis and related inflammatory diseases, who were treated with etanercept compared to patients with the same diseases of interest who were treated with non-biologic systemic drugs, but without etanercept or other biologics during pregnancy, using merged data from Sweden, Denmark and Finland." Request for Supplementary Information adopted on 06.09.2018, 17.05.2018.	
PRAC Led **WS1357** **Efficib-EMEA/H/C/000896/WS1357/0089** **Janumet-EMEA/H/C/000861/WS1357/0089** **Januvia-EMEA/H/C/000722/WS1357/0063** **Ristaben-EMEA/H/C/001234/WS1357/0055** **Ristfor-EMEA/H/C/001235/WS1357/0076** **TESAVEL-EMEA/H/C/000910/WS1357/0063** **Velmetia-EMEA/H/C/000862/WS1357/0092** **Xelevia-EMEA/H/C/000762/WS1357/0067** Merck Sharp & Dohme B.V., Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 10 in order to remove "theoretic carcinogenic potential" form the list of safety concerns, currently classified as "missing information"." Request for Supplementary Information adopted on 06.09.2018, 12.04.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **WS1370** **Zoledronic acid Mylan-EMEA/H/C/002482/WS1370/0015** Mylan S.A.S, Generic, Generic of Zometa, Lead PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "The RMP has been updated to the latest template. In addition the MAH has included "and other anatomical sites" in addition to "Osteonecrosis of the jaw" as an important identified risk, to be in line with CHMP assessment report for zoledronic acid,	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

procedure number EMEA/H/C/PSUSA/00003149/201608, dated 21 April 2017."
Opinion adopted on 06.09.2018.
Request for Supplementary Information adopted on 10.07.2018.

PRAC Led
WS1402
Bretaris Genuair-
EMEA/H/C/002706/WS1402/0038
Eklira Genuair-
EMEA/H/C/002211/WS1402/0038
AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, Lead PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Robert James Hemmings, "Submission of an updated RMP version 7.0 in order to proposed changes in categorisation of safety concerns and missing information in the RMP as per the guidance provide for the revision 2 of the RMP and to provide the RMP under the revision 2 template."

PRAC Led
WS1403
Brimica Genuair-
EMEA/H/C/003969/WS1403/0023
Duaklir Genuair-
EMEA/H/C/003745/WS1403/0023
AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, Lead PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Robert James Hemmings, "Submission of an updated RMP version 4.0 in order to proposed changes in categorisation of safety concerns and missing information in the RMP as per the guidance provide for the revision 2 of the RMP and to provide the RMP under the revision 2 template."

B.5.5. CHMP-CAT assessed procedures

Imlygic - talimogene laherparepvec -
EMEA/H/C/002771/II/0024, ATMP
Amgen Europe B.V., Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen,

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

WS1324/G
Afinitor-
EMEA/H/C/001038/WS1324/0056/G
Votubia-
EMEA/H/C/002311/WS1324/0050/G
Novartis Europharm Limited, Lead Rapporteur: Harald Enzmann
Request for Supplementary Information adopted on 03.05.2018.

WS1353/G
Hexacima-
EMEA/H/C/002702/WS1353/0079/G
Hexaxim-
EMEA/H/W/002495/WS1353/0084/G
Hexyon-
EMEA/H/C/002796/WS1353/0083/G
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus
Request for Supplementary Information adopted on 19.07.2018, 17.05.2018.

WS1407
HyQvia-EMEA/H/C/002491/WS1407/0042
Kiovig-EMEA/H/C/000628/WS1407/0083
Baxalta Innovations GmbH, Lead Rapporteur: Jan Mueller-Berghaus

---

WS1409
Keppra-EMEA/H/C/000277/WS1409/0172
UCB Pharma S.A., Lead Rapporteur: Koenraad Norga

WS1410
Infanrix hexa-
EMEA/H/C/000296/WS1410/0243
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

---

WS1412
Blitzima-
EMEA/H/C/004723/WS1412/0016
Ritemvia-
EMEA/H/C/004725/WS1412/0016
Rituzena-
EMEA/H/C/004724/WS1412/0017
Truxima-
EMEA/H/C/004112/WS1412/0017

Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz

WS1416
Kisplyx-EMEA/H/C/004224/WS1416/0014
Lenvima-
EMEA/H/C/003727/WS1416/0018
Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren

WS1419
Abseamed-
EMEA/H/C/000727/WS1419/0073
Binocrit-
EMEA/H/C/000725/WS1419/0073
Epoetin alfa Hexal-
EMEA/H/C/000726/WS1419/0072
Sandoz GmbH, Lead Rapporteur: Alexandre Moreau

WS1424
Eviplera-
EMEA/H/C/002312/WS1424/0092
Odefsey-
EMEA/H/C/004156/WS1424/0032
Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings

WS1425
Nuwiq-EMEA/H/C/002813/WS1425/0023
Vihuma-
EMEA/H/C/004459/WS1425/0005
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus

WS1431
Ceprotin-
EMEA/H/C/000334/WS1431/0105
Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus

WS1437/G
Anoro Ellipta-
EMEA/H/C/002751/WS1437/0020/G
Elebrato Ellipta-
EMEA/H/C/004781/WS1437/0004/G
Incruse Ellipta-
EMEA/H/C/002809/WS1437/0019/G
Laventair Ellipta-
EMEA/H/C/003754/WS1437/0023/G
Rolufta Ellipta-
EMEA/H/C/004654/WS1437/0006/G
Trelegy Ellipta-

EMEA/H/C/004363/WS1437/0003/G
Glaxo Group Ltd, Lead Rapporteur: Peter Kiely

WS1440/G
Hirobriz Breezhaler-
EMEA/H/C/001211/WS1440/0050/G
Onbrez Breezhaler-
EMEA/H/C/001114/WS1440/0048/G
Oslif Breezhaler-
EMEA/H/C/001210/WS1440/0048/G
Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth

WS1443
Actos-EMEA/H/C/000285/WS1443/0080
Competact-
EMEA/H/C/000655/WS1443/0071
Glustin-EMEA/H/C/000286/WS1443/0079
Tandemact-
EMEA/H/C/000680/WS1443/0058
Takeda Pharma A/S, Lead Rapporteur: Peter Kiely

WS1448/G
Ultibro Breezhaler-
EMEA/H/C/002679/WS1448/0027/G
Ulunar Breezhaler-
EMEA/H/C/003875/WS1448/0026/G
Xoterna Breezhaler-
EMEA/H/C/003755/WS1448/0030/G
Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth

WS1463
Abseamed-
EMEA/H/C/000727/WS1463/0074
Binocrit-
EMEA/H/C/000725/WS1463/0074
Epoetin alfa Hexal-
EMEA/H/C/000726/WS1463/0073
Sandoz GmbH, Lead Rapporteur: Alexandre Moreau

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

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

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

ibalizumab - EMEA/H/C/004961 , treatment of adults infected with HIV-1 resistant to at least 1 agent in 3 different classes	**Accelerated review**
larotrectinib - EMEA/H/C/004919 , treatment of adult and paediatric patients with locally advanced or metastatic solid tumours	**Accelerated review**

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

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

adalimumab - EMEA/H/C/004475
, treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis
List of Questions adopted on 22.03.2018.

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

antithrombin alfa -
EMEA/H/C/000587/S/0035

asfotase alfa -
EMEA/H/C/003794/S/0032, Orphan
Alexion Europe SAS

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

CRYSVITA - burosumab -
EMEA/H/C/004275/R/0002, Orphan
Kyowa Kirin Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Brigitte Keller-Stanislawski

Ebilfumin - oseltamivir -
EMEA/H/C/003717/R/0012
Actavis Group PTC ehf, Generic, Generic of Tamiflu, Rapporteur: Milena Stain, PRAC

Rapporteur: Kirsti Villikka

SIRTURO - bedaquiline - EMEA/H/C/002614/R/0031, Orphan
Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

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

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

BiResp Spiromax - budesonide / formoterol - EMEA/H/C/003890/II/0026
Teva Pharma B.V., Duplicate, Duplicate of DuoResp Spiromax, Rapporteur: Nithyanandan Nagercoil

Cinryze - C1 esterase inhibitor (human) - EMEA/H/C/001207/II/0064
Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus

DuoResp Spiromax - budesonide / formoterol - EMEA/H/C/002348/II/0026
Teva Pharma B.V., Rapporteur: Nithyanandan Nagercoil

Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0108/G
Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege

Fasenra - benralizumab - EMEA/H/C/004433/II/0008
AstraZeneca AB, Rapporteur: Nithyanandan Nagercoil

Foclivia - influenza virus surface antigens (inactivated) of strain A/Vietnam/1194/2004 (H5N1) - EMEA/H/C/001208/II/0038/G
Seqirus S.r.l, Rapporteur: Daniela Melchiorri

Kovaltry - octocog alfa - EMEA/H/C/003825/II/0017/G
Bayer AG, Rapporteur: Kristina Dunder

Miglustat Gen.Orph - miglustat -

EMEA/H/C/004366/II/0003
Gen.Orph, Generic, Generic of Zavesca,
Rapporteur: Milena Stain

Mircera - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/II/0070
Roche Registration GmbH, Rapporteur:
Concepcion Prieto Yerro

Obizur - susoctocog alfa - EMEA/H/C/002792/II/0021
Baxalta Innovations GmbH, Rapporteur:
Nithyanandan Nagercoil

PREVYMIS - letermovir - EMEA/H/C/004536/II/0005, Orphan
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson

SIRTURO - bedaquiline - EMEA/H/C/002614/II/0030, Orphan
Janssen-Cilag International NV, Rapporteur:
Filip Josephson

Trazimera - trastuzumab - EMEA/H/C/004463/II/0002
Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus

Ucedane - carglumic acid - EMEA/H/C/004019/II/0002/G
Lucane Pharma, Generic, Generic of Carbaglu,
Rapporteur: Eleftheria Nikolaidi

Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0040
MCM Vaccine B.V., Rapporteur: Bart Van der Schueren

WS1420
Ambirix-
EMEA/H/C/000426/WS1420/0092
Twinrix Adult-
EMEA/H/C/000112/WS1420/0126
Twinrix Paediatric-
EMEA/H/C/000129/WS1420/0127
GlaxoSmithkline Biologicals SA, Lead
Rapporteur: Jan Mueller-Berghaus

WS1432
Ambirix-
EMEA/H/C/000426/WS1432/0093

Twinrix Adult-
EMEA/H/C/000112/WS1432/0127
Twinrix Paediatric-
EMEA/H/C/000129/WS1432/0128
GlaxoSmithkline Biologicals SA, Lead
Rapporteur: Robert James Hemmings

WS1456
Infanrix hexa-
EMEA/H/C/000296/WS1456/0247
GlaxoSmithkline Biologicals SA, Lead
Rapporteur: Bart Van der Schueren

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

Bronchitol - mannitol -
EMEA/H/C/001252/II/0034, Orphan
Pharmaxis Pharmaceuticals Limited,
Rapporteur: Nithyanandan Nagercoil, "Update of sections 4.8 and 5.1 of the SmPC in order to update the frequency of certain adverse events and to update the clinical safety and efficacy information based on the results of the clinical data from Study CF 303. This is a phase 3 safety and efficacy clinical trial in adult cystic fibrosis subjects. The package leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in the product information and correct the Annex A."

Fluenz Tetra - influenza vaccine (live attenuated, nasal) -
EMEA/H/C/002617/II/0084
AstraZeneca AB, Rapporteur: Bart Van der Schueren, "Update of section 4.6 of the SmPC to include new information from a publication on breast-feeding. (Brady et al., 2018). The variation also includes recommendations from the Renewal procedure (EMEA/H/C/002617/0079) which included removal of the additional monitoring section, as well as updates from recommendations in the new EMA Guidelines for Vaccines. The Package Leaflet is updated accordingly.
In addition, the Marketing Authorisation Holder (MAH) took the opportunity to introduce minor editorial changes to the Product Information."

Remicade - infliximab - EMEA/H/C/000240/II/0217

Janssen Biologics B.V., Rapporteur: Kristina Dunder, “Update of section 4.8 of the SmPC in order to add the adverse drug reaction “acute generalised exanthematous pustulosis (AGEP)” with a frequency rare. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet.”

Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0011

Pfizer Limited, Rapporteur: Johann Lodewijk Hillege, “Update of section 4.4 of the SmPC in order to add a warning about concomitant use of treatments inhibiting terminal complement activation.”

Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/II/0067

Bial - Portela & Cª, S.A., Rapporteur: Martina Weise, “Update of sections 4.8 and 5.1 of the SmPC in order to reflect the long-term safety and efficacy data obtained from the open-label extensions (parts II to V) of the phase III study BIA-2093-305. The study was assessed in procedure EMA/H/C/988/P46 025.”

Zostavax - shingles (herpes zoster) vaccine (live) - EMEA/H/C/000674/II/0120

MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, “Update of section 4.8 of the SmPC in order to add the adverse reactions Guillain-Barré syndrome and facial paralysis with frequency “very rare” following a review post-marketing cases; the Package Leaflet is updated accordingly.”

WS1477

Lixiana-EMEA/H/C/002629/WS1477/0019

Roteas-EMEA/H/C/004339/WS1477/0007

Daiichi Sankyo Europe GmbH, Lead Rapporteur: Concepcion Prieto Yerro, “Update of sections 4.4, 4.8 and 5.1 of the SmPC for Lixiana and Roteas to update the clinical efficacy and safety information based on the final results from study DUI176b-D-U311, a phase IIIB prospective, randomised, open-label, blinded evaluator study to evaluate the efficacy and safety of low molecular weight heparin/edoxaban versus dalterparin in venous

thromboembolism associated with cancer. In addition, the Worlsharing applicant (WSA) took the opportunity to combine the 15 mg, 30 mg and 60 mg strengths SmPCs, to delete 'aspirin' from section 2 of the Package Leaflet, to update the contact details of the Portuguese local representative in the Package Leaflet for Lixiana only, and to make some corrections to the German, Finnish, Italian, Lithuanian, Maltese and Portuguese translations."

B.6.10. CHMP-PRAC assessed procedures

Dificlir - fidaxomicin - EMEA/H/C/002087/II/0033

Astellas Pharma Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of an updated RMP version 10 in order to reflect the final outcome (Year 5) of the ClosER study (study AG2012-3459, Clostridium difficile European Resistance surveillance study).
The ClosER study was a prospective, longitudinal, pan-European, in vitro sentinel surveillance study of susceptibility of Clostridium difficile to fidaxomicin and other antibiotics. The study is an additional pharmacovigilance activity (Category 3, MEA 002.4) included in the Dificlir RMP."

Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0036

GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jean-Michel Dogné, "Update of section 4.4 of the SmPC in order to modify the warning related to the waning of protection against Plasmodium falciparum malaria over time. This update is based on final results from study MALARIA-076 listed as a category 3 study in the RMP. This was an open extension to the phase III, multi-centre study MALARIA-055 PRI (110021) to evaluate long-term efficacy, safety and immunogenicity of the GSK Biologicals' candidate malaria vaccine in infants and children. The RMP version 4.1 has also been submitted."

SIRTURO - bedaquiline -
EMEA/H/C/002614/II/0028, Orphan
Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.4 of the SmPC in order to update the safety information with inclusion of a statement on bedaquiline resistance, further to a request by the PRAC in the context of the assessment of PSUR procedure EMEA/H/C/PSUSA/00010074/201709 (LEG 011).
The RMP version 3.0 has also been submitted, updated based on the data triggering the SmPC update and to reflect completion of studies which were assessed in previous procedures.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."

Toujeo - insulin glargine -
EMEA/H/C/000309/II/0106
Sanofi-Aventis Deutschland GmbH, Duplicate, Duplicate of Lantus, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Submission of the final report from a completed Phase 3b study, EFC13799: "A randomized, open-label, 2-arm, parallel-group, multicenter, 26-week study assessing the safety and efficacy of HOE901-U300 versus Lantus (insulin glargine 100 U/mL) in patients ≥ 65 years with treatment of diabetes mellitus type II (T2DM) inadequately controlled on antidiabetic regimens either including no insulin, or with basal insulin as their only insulin". The RMP (version 5) is updated to reflect the exposure data in elderly patients."

B.6.11. PRAC assessed procedures

PRAC Led
Abraxane - paclitaxel -
EMEA/H/C/000778/II/0092
Celgene Europe BV, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 17.0 in order to propose the reclassification and/or renaming of known safety concerns associated with the use of paclitaxel in

accordance with the new Guideline on Good Pharmacovigilance Practices (GVP) Module V version 2”

PRAC Led

Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0072

UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, “Submission of an updated RMP (version 14.0) in order to revise the distribution’s list of educational materials (addition of dermatologists) and to revise the RMP in line with the new RMP template (GVP Module V rev.2) including the update of the important identified risks and important potential risks. The PASS protocol for Study UP0038 designed to assess the effectiveness of the educational material is updated to add dermatologists to the healthcare professional study population, to remove Italy and Spain from study participation and to make additional administrative changes. In addition, the MAH took the opportunity to make some administrative changes in the RMP.”

PRAC Led

Colobreathe - colistimethate sodium - EMEA/H/C/001225/II/0039

Teva B.V., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, “Submission of the final report from study CLB-MD-08, a Category 3, non-interventional PASS. This is a Safety, Cross-sectional survey study to evaluate the effectiveness of the Colobreathe risk minimisation educational programme among healthcare professionals and patients. This submission also fulfils MEA 012.1.”

PRAC Led

Eurartesim - piperaquine tetraphosphate / artenimol - EMEA/H/C/001199/II/0032

Alfasigma S.p.A., Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, “Submission of an updated RMP version 15.2 (in line with the revision 2 of the RMP template) in order to close the Pregnancy Registry. In addition, the Marketing authorisation holder (MAH) took the opportunity to:

- Distribution of a new version of the

educational material.
- Addition of two important potential risks: `Delayed haemolytic anaemia' and `Severe skin reactions´, such as Stevens- Johnson syndrome and Toxic Epidermal Necrolysis.
- Limitation of the reproductive risk to the first trimester of pregnancy.
- Update on several studies.
- Inclusion of Eurartesim into the WHO Essential Medicines List.
- Update the MAH details."

PRAC Led

Herceptin - trastuzumab - EMEA/H/C/000278/II/0147

Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from the pregnancy registry (H4621g, MotHER) study listed as a category 3 study in the RMP. This is an observational study of pregnancy and pregnancy outcome in women with breast cancer treated with trastuzumab, pertuzumab in combination with trastuzumab, or ADO-trastuzumab emtansine during Pregnancy or within 7 months prior to conception. The RMP is being updated accordingly (version 20.0) and in response to comments discussed and received in procedure EMEA/H/C/000278/II/140."

PRAC Led

Nulojix - belatacept - EMEA/H/C/002098/II/0050/G

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "Submission of the final report from studies (IM103074 and IM103077) listed as category 3 studies in the RMP. Study IM103074 is an observational study designed to assess the pattern of use of balatacept in US transplant recipients in routine clinical practice. Study IM103077 is an observational study designed to assess the patterns of use of belatacept in renal transplantation using the collaborative transplant study.
An updated RMP (version 16.0) is submitted in order to reflect the results of the above studies. In addition, the MAH took the opportunity to update the RMP in line with the new RMP

template (GVP Module V rev.2), to reflect minor editorial changes and to reflect the earlier completion dates for two remaining studies (IM103075 and IM103076) listed as category 3 studies in the RMP."	
PRAC Led **Otezla - apremilast -** **EMEA/H/C/003746/II/0023** Celgene Europe BV, Rapporteur: Peter Kiely, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Concepcion Prieto Yerro, "Submission of an updated RMP version 11.0 in order to reclassify and/or rename the known safety concerns associated with the use of apremilast in accordance with the new Guideline on GVP Module V. In addition, the RMP is converted to the RMP template Revision 2."	
PRAC Led **Tasmar - tolcapone -** **EMEA/H/C/000132/II/0061** Meda AB, Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, "Submission of an updated RMP version 7 in order to: - reflect currently available data from post-marketing experience and patient exposure data; - align the RMP with the new GVP RMP template rev.2; - remove the important identified risk 'dopaminergic effects due to increased bioavailability of co-administered levodopa (e.g. dyskinesia)' and the potential risk 'drug interactions with significant clinical consequence including sudden sleep onset'."	

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

WS1469
Glyxambi-
EMEA/H/C/003833/WS1469/0016
Jentadueto-
EMEA/H/C/002279/WS1469/0046
Trajenta-
EMEA/H/C/002110/WS1469/0034
Boehringer Ingelheim International GmbH, Lead
Rapporteur: Johann Lodewijk Hillege

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

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

B.7.2. Monthly Line listing for Type I variations

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

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

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

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

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

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

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES

Information related to plasma master files cannot be released at the present time as these contain commercially confidential information.

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

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

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

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

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

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

G. ANNEX G

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

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

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 17-20 September 2018 CHMP plenary:

G.3.2. List of procedures starting in September 2018 for October 2018 CHMP adoption of outcomes

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