19 March 2018
EMA/170926/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 19-22 March 2018

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

19 March 2018, 13:00 – 19:30, room 2A

20 March 2018, 08:30 – 19:30, room 2A

21 March 2018, 08:30 – 19:30, room 2A

22 March 2018, 08:30 – 15:00, room 2A

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

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

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1. Introduction

1.1. Welcome and declarations of interest of members, alternates and experts

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 19-22 March 2018. See March 2018 CHMP minutes (to be published post April 2018 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 19-22 March 2018

1.3. Adoption of the minutes

CHMP minutes for 19-22 February 2018

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. masitinib - Orphan - EMEA/H/C/004398

AB Science; treatment of amyotrophic lateral sclerosis

Scope: Oral explanation

Action: Oral explanation to be held on 21 March 2018 at time 11:00

List of Outstanding Issues adopted on 12.10.2017. List of Questions adopted on 26.01.2017.

2.1.2. abaloparatide - EMEA/H/C/004157

treatment of osteoporosis

Scope: Oral explanation

Action: Oral explanation to be held on 20 March 2018 at time 14:30

List of Outstanding Issues adopted on 14.12.2017, 20.07.2017, 15.12.2016. List of Questions adopted on 01.04.2016.

2.2. Re-examination procedure oral explanations

2.2.1. Aplidin - plitidepsin - Orphan - EMEA/H/C/004354

Pharma Mar, S.A.; treatment of multiple myeloma

Scope: Oral explanation

Action: Oral explanation to be held on 21 March 2018 at time 09:00

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

Opinion 14.12.2017

2.3. Post-authorisation procedure oral explanations

2.3.1. Keytruda - pembrolizumab - EMEA/H/C/003820

Merck Sharp & Dohme Limited; treatment of melanoma

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

Scope: Possible oral explanation, update on Keytruda"

Action: Possible oral explanation to be held on 21 March 2018 at time 14:00

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. betrixaban - EMEA/H/C/004309

treatment of prophylaxis of venous thromboembolism (VTE)

Scope: Opinion

Action: For adoption

Oral explanation held on 20.02.2018. List of Outstanding Issues adopted on 14.12.2017, 12.10.2017. List of Questions adopted on 21.04.2017.

3.1.2. dolutegravir / rilpivirine - EMEA/H/C/004427

treatment of HIV

Scope: Opinion

Action: For adoption

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

3.1.3. trastuzumab - EMEA/H/C/004361

treatment of metastatic breast cancer, early breast cancer, metastatic gastric cancer

Scope: Opinion

Action: For adoption

Oral explanation held on 24.01.2018. List of Outstanding Issues adopted on 22.02.2018, 09.11.2017. List of Questions adopted on 20.07.2017.

3.1.4. pemetrexed - EMEA/H/C/003958

treatment of malignant pleural mesothelioma and non-small cell lung cancer

Scope: Opinion

Action: For adoption

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

3.1.5. prasugrel - EMEA/H/C/004644

prevention of atherothrombotic events

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 22.02.2018, 14.12.2017. List of Questions adopted on 14.09.2017.

3.1.6. rucaparib - Orphan - EMEA/H/C/004272

Clovis Oncology UK Ltd; treatment of ovarian cancer

Scope: Opinion

Action: For adoption

Oral explanation held on 19.02.2018. List of Outstanding Issues adopted on 23.02.2018 (written procedure), 14.12.2017, 09.11.2017, 14.09.2017. List of Questions adopted on, 23.03.2017.

3.1.7. abaloparatide - EMEA/H/C/004157

treatment of osteoporosis

Scope: Opinion, SAG report from the SAG Cardiology meeting held on 1 March 2018

Action: For adoption

List of Outstanding Issues adopted on 14.12.2017, 20.07.2017, 15.12.2016. List of Questions adopted on 01.04.2016.

3.1.8. infliximab - EMEA/H/C/004647

treatment of rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, psoriasis and ulcerative colitis

Scope: Opinion

Action: For adoption

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

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

3.2.1. brexpiprazole - EMEA/H/C/003841

treatment of schizophrenia

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 20.07.2017.

3.2.2. tezacaftor / ivacaftor - Orphan - EMEA/H/C/004682

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

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.12.2017.

3.2.3. vonicog alfa - Orphan - EMEA/H/C/004454

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

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 12.10.2017.

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

3.3.1. 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: List of questions

Action: For adoption

3.3.2. doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746

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

Scope: List of questions

Action: For adoption

3.3.3. galcanezumab - EMEA/H/C/004648

prophylaxis of migraine

Scope: List of questions

Action: For adoption

3.3.4. pegfilgrastim - EMEA/H/C/004915

treatment of neutropenia

Scope: List of questions

Action: For adoption

3.3.5. pegfilgrastim - EMEA/H/C/004556

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

Scope: List of questions

Action: For adoption

3.3.6. adalimumab - EMEA/H/C/004475

treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis

Scope: List of questions

Action: For adoption

3.3.7. tisagenlecleucel - Orphan - ATMP - EMEA/H/C/004090

Accelerated assessment

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

Scope: List of questions

Action: For information

3.3.8. macimorelin - EMEA/H/C/004660

Diagnosis of Adult growth hormone deficiency (AGHD)

Scope: List of questions

Action: For adoption

3.3.9. trastuzumab - EMEA/H/C/004916

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

Scope: List of questions

Action: For adoption

3.3.10. buprenorphine - EMEA/H/C/004743

Substitution treatment for opioid drug dependence

Scope: List of questions

Action: For adoption

3.3.11. 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: List of questions

Action: For adoption

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

3.4.1. carmustine - EMEA/H/C/004326

treatment of brain tumours, multiple myeloma, Hodgkin's disease and non-Hodgkin's lymphomas

Scope: Letter from applicant dated 1 March 2018 requesting for an extension of clock stop to respond to the list of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 22.02.2018, 12.10.2017, 20.07.2017. List of Questions adopted on 13.10.2016.

3.4.2. dapivirine - Article 58 - EMEA/H/W/002168

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

Scope: Letter from applicant dated 9 March 2018 requesting for an extension of clock stop to respond to the list of questions.

Action: For adoption

List of Questions adopted on 09.11.2017.

3.4.3. - doxorubicin hydrochloride - EMEA/H/C/004110

treatment of breast and ovarian cancer

Scope: Letter from the applicant dated 9 March 2018 requesting an extension of clock stop to respond to the list of questions

Action: For adoption

List of Questions adopted on 14.09.2017.

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

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

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

Scope: Appointment of re-examination rapporteurs, draft timetable, SAG involvement

Action: For discussion

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

Opinion adopted on 22 February 2018.

Letter from the applicant dated 7 March 2018 requesting a re-examination of the Opinion adopted on 22 February 2018

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

4.1.1. Bortezomib Accord - bortezomib - EMEA/H/C/003984/X/0008

Accord Healthcare Ltd

Rapporteur: Milena Stain, PRAC Rapporteur: Carmela Macchiarulo

Scope: "Extension application to add a new strength of powder for solution for injection (1 mg) to the currently approved strength (3.5 mg) of Bortezomib Accord."

Action: For adoption

List of Outstanding Issues adopted on 25.01.2018. List of Questions adopted on 20.07.2017.

4.1.2. Bosulif - bosutinib - Orphan - EMEA/H/C/002373/X/0026

Pfizer Limited

Rapporteur: Harald Enzmann

Scope: "Extension application to add a new strength of 400mg film-coated tablets."

Action: For adoption

List of Questions adopted on 14.12.2017.

4.1.3. Votubia - everolimus - Orphan - EMEA/H/C/002311/X/0045

Novartis Europharm Limited

Rapporteur: Harald Enzmann, Co-Rapporteur: Greg Markey

Scope: "Extension application to add a new strength of 1 mg everolimus dispersible tablet."

Action: For adoption

List of Questions adopted on 09.11.2017.

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

No items

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

4.3.1. 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

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

Techdow Europe AB

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

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

Action: For adoption

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

No items

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

No items

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

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

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

Amgen Europe B.V.

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Eva Jirsová

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

Action: For adoption

Request for Supplementary Information adopted on 12.10.2017.

5.1.2. Briviact - brivaracetam - EMEA/H/C/003898/II/0010/G

UCB Pharma S.A.

Rapporteur: Filip Josephson, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension of Indication to include adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in patients with epilepsy 4 years of age and older for Briviact. As a consequence, sections 4.1, 4.2, 4.7, 5.1 and 5.2 of the SmPC are updated.
In addition, the Marketing authorisation holder (MAH) submitted a 5ml oral syringe and adaptor for the paediatric population.

The Package Leaflet and Labelling are updated in accordance.

Submission of the final Environmental Risk Assessment for the inclusion of the paediatric population in accordance with the new indication sought."

Action: For adoption

Request for Supplementary Information adopted on 12.10.2017.

5.1.3. Cabometyx - cabozantinib - EMEA/H/C/004163/II/0003

Ipsen Pharma

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

Scope: "Extension of indication to include for the treatment of advanced renal cell carcinoma the 'treatment-naïve adults with intermediate or poor risk per IMDC criteria' for CABOMETYX; as a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated in order to add a warning on dose reductions and dose interruptions and to update the safety information. The final report of the randomised phase II study comparing cabozantinib with commercially supplied sunitinib in subjects with previously untreated locally advanced or metastatic renal cell carcinoma (study A031203) is submitted in support of this application. The Package Leaflet is updated accordingly. The risk management plan (version 3.0) is also submitted.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make some editorial changes in the product information."

Action: For adoption

Request for Supplementary Information adopted on 14.12.2017.

5.1.4. Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0065

UCB Pharma S.A.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of Indication to include plaque psoriasis in adult patients for Cimzia; 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. The RMP version 13 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 09.11.2017.

5.1.5. Darzalex - daratumumab - Orphan - EMEA/H/C/004077/II/0011

Janssen-Cilag International NV

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of Indication to include the combination with bortezomib, melphalan and prednisone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant for Darzalex; 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. The RMP version 3.1 (in version 2 of the RMP template) has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of the Lithuanian and Slovenian local representatives in the Package Leaflet."

Action: For adoption

5.1.6. Ivemend - fosaprepitant - EMEA/H/C/000743/II/0037

Merck Sharp & Dohme Limited

Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of Indication to include adolescents, infants, toddlers and children aged 6 months and older for prevention of nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy.
As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.
The RMP version 5.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 25.01.2018.

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

Vertex Pharmaceuticals (Europe) Ltd

Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Dolores Montero Corominas

Scope: "1) C.I.6.a (type II) - Extension of Indication to include the combination regimen of the ivacaftor 150 mg evening dose and Symkevi (tezacaftor/ivacaftor);
2) B.IIe.5.a.2 (type IB) - to add a blister card pack presentation containing 28-tablets for the 150 mg film-coated tablets (EU/1/12/782/005);
3) B.IIe.5.a.2 (type IB) - to add a blister pack presentation containing 28-tablets for the 150 mg film-coated tablets (EU/1/12/782/006).
As a consequence, section4.1, 4.2, 4.4, 4.5, 4.8, 6.5 and 8 of the SmPC are updated.
Annex A, the Package Leaflet and Labelling are updated in accordance.
An updated RMP (version 6.0) is included."

Action: For adoption

Request for Supplementary Information adopted on 14.12.2017.

5.1.8. Nucala - mepolizumab - EMEA/H/C/003860/II/0013/G

GlaxoSmithKline Trading Services Limited

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Type II-C.I.6-Extension of Indication to include children and adolescents aged 6 to 17 years for Nucala; as a consequence, Sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC and Sections 1, 2, 3, 4 and Information for Healthcare Professionals in the Package Leaflet are updated accordingly.
In addition to the proposed SmPC/PL updates specific to the paediatric indication, as Nucala is a biological medicine, GSK is including wording in the NUCALA SmPC (Section 4.4) and PL (Information for Health Care Professionals) that the name and batch number of the administered product should be clearly recorded in the patient file.

In addition, editorial changes are introduced in section P.5.5."

Action: For adoption

5.1.9. Repatha - evolocumab - EMEA/H/C/003766/II/0017/G

Amgen Europe B.V.

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension of Indication to include reduction of atherosclerotic cardiovascular disease risk in adults with high cardiovascular risk for Repatha based on the results from Study 20110118 (a category 3 PV activity in the Risk Management Plan, MEA 004); as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 5.1 of the SmPC to include important mechanistic information for healthcare professionals based on Study 20120153 (a category 3 PV activity, MEA 006).
Submission of an updated RMP version 2.0 in order to add two category 3 studies in the RMP (Study 20160250 and Study 20150338), as well as to update the milestones of five category 3 studies (20110110, 20110271, 20120138, 20130286, 20130295)"

Action: For adoption

Request for Supplementary Information adopted on 22.02.2018, 14.12.2017, 14.09.2017.

5.1.10. Tyverb - lapatinib - EMEA/H/C/000795/II/0051

Novartis Europharm Limited

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

Scope: "Update of sections 4.1 and 5.1 of the SmPC based on results from study EGF114299/LAP016A2307 listed as a condition (ANX027.4) in the Annex II; a Phase III trial to compare the safety and efficacy of lapatinib plus trastuzumab plus an aromatase inhibitor (AI) versus trastuzumab plus an AI versus lapatinib plus an AI as first- or second-line therapy in postmenopausal subjects with hormone receptor positive, HER2-positive metastatic breast cancer (MBC) who have received prior trastuzumab and endocrine therapies. Annex II has been updated accordingly. A revised RMP version 34.0 has also been submitted as part of the application."

Action: For adoption

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

No items

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

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

Pfizer Limited

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Carmela Macchiarulo

Scope: Letter from the applicant dated 14 March 2018 requesting a re-examination of the opinion adopted on 22 February 2018, timetable, appointment of re-examination rapporteurs

Action: For adoption

Opinion adopted on 22 February 2018.

6. Ancillary medicinal substances in medical devices

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

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

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

Scope: Day 120 list of questions

Action: For adoption

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. avatrombopag maleate - H0004722

Proposed indication:

Avatrombopag is indicated for the treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure.

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. Opdivo - nivolumab - EMEA/H/C/003985/II/0036/G

Bristol-Myers Squibb Pharma EEIG

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

Scope: "C.I.4 (Type II) - Update of sections 4.2, 5.1, 5.2 and 6.6 of the SmPC in order to introduce new dosing regimens and schedule.

C.I.4 (Type II) - Update of sections 4.2, 5.1, 5.2 and 6.6 of the SmPC in order to introduce change the infusion time from 60 minutes to 30 minutes

These changes are based on interim results from study CA209153; this is a phase IIIb/IV safety trial of nivolumab in subjects with advanced or metastatic non-small cell Lung cancer who have progressed during or after receiving at least one prior systemic regimen; The

Package Leaflet is updated accordingly. The RMP version 10.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 22.02.2018, 14.09.2017.

9.1.2. WS1312
Prezista-EMEA/H/C/000707/WS1312/0093
Rezolsta-EMEA/H/C/002819/WS1312/0023
Symtuza-EMEA/H/C/004391/WS1312/0005

Janssen-Cilag International NV

Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst

Scope: "Update of sections 4.2, 4.4, 4.6, 5.1 and 5.2 of the SmPCs for Prezista, Rezolsta and Symtuza to reflect the data of the category 3 study TMC114HIV3015 in HIV-1 infected pregnant women. The PL of Symtuza is also updated.
Updated RMPs (version 25.3 for Prezista, 4.3 for Rezolsta and 2.1 for Symtuza) are proposed accordingly.
In addition, the MAH took the opportunity to implement the template version 2 for the Prezista and Rezolsta RMPs, removal of the fulfilled category 4 DAD study from the Prezista and Rezolsta RMPs, removal of observational study on growth in children and 'growth abnormalities in the paediatric population' as important potential risk in the Prezista RMP and addition of the missing information 'Safety in patients with cardiac conduction disorders' in the Rezolsta RMP (alignement with Tybost RMP)."

Action: For adoption

9.1.3. Keytruda - pembrolizumab - EMEA/H/C/003820

Merck Sharp & Dohme Limited; treatment of melanoma

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

Scope: Possible oral explanation, update on Keytruda"

Action: For adoption

See 2.3

9.1.4. Vibativ – telavancin - EMEA/H/C/001240

Theravance Biopharma Ireland Ltd

Rapporteurs: Greg Markey, Co-Rapporteur: Martina Weise

Scope: Withdrawal of marketing authorisation

Action: For information

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

Hospira UK Limited

Rapporteur: Kolbeinn Gudmundsson

Scope: Letter from applicant requesting for an extension of clock stop to respond to the request for supplementary information.

Action: For adoption

Request for Supplementary Information adopted on 22.02.2018.

9.1.6. Zykadia - ceritinib - EMEA/H/C/003819/II/0015

Novartis Europharm Limited

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

Scope: "Update of sections 4.2, 4.4, 4.5, 4.8 and 5.2 of the SmPC in order to update the safety information based on the primary PK and preliminary safety results of the food effect study CLDK378A2112. The Package Leaflet is updated accordingly.

The RMP version 9.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 14.12.2017, 12.10.2017, 22.06.2017.

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

No items

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

No items

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

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

MAH: various

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

Action: For adoption

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

10.6.2. Retinoids: acitretin (NAP); adapalene (NAP); alitretinoin - PANRETIN (CAP); bexarotene – TARGRETIN (CAP); isotretinoin (NAP); tazarotene (NAP); tretinoin (NAP) - EMEA/H/A-31/1446

Eisai Ltd (Panretin, Targretin), various

PRAC Rapporteur: Ana Sofia Diniz Martins; PRAC Co-rapporteur: Julie Williams

Panretin – Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri
Targretin – Rapporteur: Alexandre Moreau, Co-Rapporteur: Greg Markey

Scope: Opinion

Action: For discussion

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

March 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

Action: For information

13.2. Innovation Task Force briefing meetings

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

13.2.1. ITF Briefing Meeting

ITF briefing meeting

Meeting date: 23 March 2018

Action: For adoption

ITF briefing meeting

Meeting date: 20 March 2018

Action: For adoption

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Change to timing of Scientific Committee Chair and Vice-Chair elections

Action: For information

14.1.2. Referral Roadmap

Action: For discussion

14.1.3. Joint CHMP-PDCO-CAT Strategic review and Learning meeting to be held in Oslo, Norway under the Bulgarian Presidency of the Council of the European Union

Scope: Discussion on topics to be added on the agenda of the upcoming Strategic Review and Learning meeting 7-9 May 2018

Action: For discussion

14.1.4. Review of CHMP assessment reports templates

Scope: Review of CHMP assessment reports templates for initial MAA, Generics (Spring 2018 Roll out)

Action: For adoption

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 5-8 March 2018

Action: For information

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

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 14-16 March 2018
Action: For information

Guideline on the quality, non-clinical and clinical aspects of gene therapy medicinal products (EMA/CAT/143641/2017)

Action: For adoption

14.2.3. Paediatric Committee (PDCO)

PIPs reaching D30 at March 2018 PDCO

Action: For information

Report from the PDCO meeting held on 20-23 March 2018

Action: For information

Joint CHMP/PDCO session

Agenda for joint session

Action: For discussion

14.2.4. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 13-15 March 2018
Action: For information

14.2.5. 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 19-21 March 2018

Action: For information

Questions to PKWP re 'Clarification on product specific bioequivalence guideline on paliperidone'

Action: For adoption

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 5-8 March 2018. Table of conclusions

Action: For information

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

14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 21 February 2018.

Action: For adoption

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse,

Reports from BWP March 2018 meeting to CHMP for adoption:

- 05 reports on products in scientific advice and protocol assistance

- 10 reports on products in pre-authorisation procedures
- 00 reports on products in post-authorisation procedures
- 03 reports on products in plasma master file

Action: For adoption

Final minutes from January face-to-face meeting held 15-17 January 2018

Action: For information

Draft agenda for BWP face-to-face meeting to be held 16-18 April 2018

Action: For information

Draft Meeting Report - Workshop on Prior Knowledge held 23 November 2017

Action: For information

14.3.4. Biosimilar Medicinal Products Working Party (BMWP)

Draft minutes of Interested Parties meeting with the BMWP held on 21 September 2017 at EMA

Action: For information

14.3.5. Biostatistics Working Party (BSWP)

Chair: Anja Schiel/Jörg Zinserling

Invitation to 1.5-day workshop on the “draft reflection paper on statistical methodology for the comparative assessment of quality attributes in drug development” on 3-4 May 2018

A multi-disciplinary scientific workshop touching upon quality, manufacturing, statistics, and methodology areas will be held at EMA and interested CHMP members are invited to participate. The main focus of the workshop will lie on better understanding challenges seen by industry stakeholders and discussion of methodological approaches in relation to comparisons at quality level for biosimilars, generics and pre-post manufacturing changes. Topics for discussion will be based on comments received during the public consultation phase of the “draft reflection paper on statistical methodology for the comparative assessment of quality attributes in drug development”.

Programme details and preliminary topic suggestions for discussion are attached. Interested CHMP members can express interest to participate in the workshop by 23 March 2018.

Action: For information

Nomination of additional assessor to BSWP

Action: For adoption

14.3.6. Cardiovascular Working Party (CVSWP)

Chair: Kristina Dunder

Vice-chair election – Nominations should be sent by 13 April 2018.

Action: For information

14.3.7. European Medicines Agency Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (PCWP) and Healthcare Professionals' Organisations (HCPWP)

PCWP Co-chair: Kaisa Immonen, HCPWP Co-chair: Gonzalo Calvo

Draft Agenda of the PCWP/HCPWP joint meeting 17-18 April 2018

Action: For information

Draft PCWP/HCPWP Work Plan for 2018-2019

Action: For adoption

14.3.8. Infectious Diseases Working Party (IDWP)

Chair: Maria Jesus Fernandez Cortizo,

Addendum to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections to address paediatric-specific clinical data requirements.

Action: For adoption

Concept paper on preparation of a revised guideline on the evaluation of medicinal products indicated for treatment of bacterial infections

Action: For adoption

14.3.9. Coordination with EMA Working Parties/Working Groups/Drafting Groups on ICH E9 (R1) addendum on estimands

BSWP Chair: Anja Schiel, CHMP: Robert James Hemmnings

Reflection of the ICH E9 (R1) addendum on estimands and sensitivity analysis in clinical trials to the guideline on statistical principles for clinical trials in the CHMP scientific guidelines – feedback from WPs and DGs

Action: For discussion

14.3.10. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink/Henrike Potthast

PKWP proposal for a Q & A to clarify requirements in Appendix 1 of the MR guideline on sensitisation and irritation tests for transdermal products.

Action: For adoption

Nomination of additional assessor to PKWP

Action: For adoption

14.3.11. Quality Working Party (QWP)

Chair: Keith Pugh/Blanka Hirschlerova

QWP response to CMDh questions to on Paclitaxel Hetero (PT/H/1256/001/DC)

Action: For adoption

14.3.12. Rheumatology Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus

Nominations for experts/members to support the development of the following guidelines by 16 March 2018.

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

Two new members are envisaged, for the development of a “Concept paper on the need for guidance on the development of medicinal products for acute kidney injury” experts with regulatory and/or clinical expertise for this topic are sought.

Action: For adoption

Nomination of members to RIWP

Nomination of additional assessor to RIWP

Action: For adoption

14.3.13. Vaccines Working Party (VWP)

Chair: Mair Powell/Svein Rune Andersen

Nomination of additional assessor (observer) to VWP

Action: For adoption

14.3.14. Discussion on additional assessors (so called observers) to working parties and drafting groups

CHMP: Tomas Salmonson

Action: For discussion

14.3.15. Oncology Working Party (ONCWP)

Chair: Pierre Demolis/Paolo Foggi

Nomination of additional assessor (observer) to ONCWP

Action: For adoption

14.3.16. Ad-hoc Influenza Working Group

Chair: Ton van der Stappen

Scope: EU Strain selection for the Influenza Vaccines for the Season 2018/2019: Report from the Ad Hoc Influenza working group to the BWP

Action: For adoption

Scope: EU Recommendation for the Seasonal Influenza Vaccine Composition for the Season 2019/2019

Action: For adoption

Presentation by Ton van der Stappen

14.3.17. Safety Working Party (SWP)

Chair: Jan Willem Van der Laan

Scope: SWP Response to LoQ on 'Acceptable levels of histamine in human and veterinary solution for injection and eye drop solution medicinal products'

Action: For adoption

Scope: SWP response to CMDh Question on acceptability of statement on potential residues of latex in the Product information of products packed in containers with synthetic rubber stopper

Adopted via written procedure on 16 March 2018

Action: For information

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

No items

16. Explanatory notes

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

Oral explanations *(section 2)*

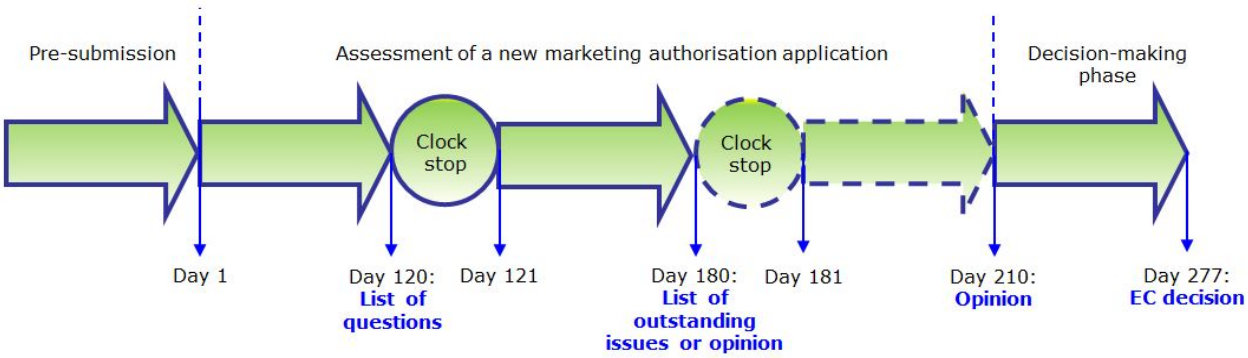
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

Initial applications *(section 3)*

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

Re-examination procedures *(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

19 March 2018
EMA/162410/2018 Corr[1]

Annex to 19-22 March 2018 CHMP Agenda

Pre submission and post authorisation issues

[1] Correction in section 6.1

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

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

Final Outcome of Rapporteurship allocation for
March 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

Defitelio - defibrotide -
EMEA/H/C/002393/S/0029, Orphan
Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams

Kolbam - cholic acid -
EMEA/H/C/002081/S/0025, Orphan
Retrophin Europe Ltd, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Patrick Batty

Vyndaqel - tafamidis -
EMEA/H/C/002294/S/0044, Orphan
Pfizer Limited, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Ghania Chamouni

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Atosiban SUN - atosiban -
EMEA/H/C/002329/R/0012
Sun Pharmaceutical Industries Europe B.V., Generic, Generic of Tractocile, Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli
Request for Supplementary Information adopted

on 22.02.2018.

Giotrif - afatinib -
EMEA/H/C/002280/R/0026
Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Ulla Wändel Liminga

Ovaleap - follitropin alfa -
EMEA/H/C/002608/R/0023
Teva B.V., Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 22.02.2018.

Stivarga - regorafenib -
EMEA/H/C/002573/R/0025
Bayer AG, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus
Request for Supplementary Information adopted on 22.02.2018.

Ultibro Breezhaler - indacaterol / glycopyrronium -
EMEA/H/C/002679/R/0024
Novartis Europharm Limited, Rapporteur: Mark Ainsworth, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Doris Stenver

Xoterna Breezhaler - indacaterol / glycopyrronium -
EMEA/H/C/003755/R/0027
Novartis Europharm Limited, Duplicate, Duplicate of Ultibro Breezhaler, Rapporteur: Mark Ainsworth, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Doris Stenver

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Aubagio - teriflunomide -
EMEA/H/C/002514/R/0016
sanofi-aventis groupe, Rapporteur: Martina Weise, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber

Cholib - fenofibrate / simvastatin -
EMEA/H/C/002559/R/0017
Mylan Products Limited, Rapporteur: Robert James Hemmings, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Julie Williams

Incresync - alogliptin / pioglitazone - EMEA/H/C/002178/R/0023

Takeda Pharma A/S, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst

Lemtrada - alemtuzumab - EMEA/H/C/003718/R/0020

Genzyme Therapeutics Ltd, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver

Maci - matrix applied characterised autologous cultured chondrocytes - EMEA/H/C/002522/R/0017, ATMP

Vericel Denmark ApS, Rapporteur: Christiane Niederlaender, Co-Rapporteur: Johannes Hendrikus Ovelgonne, PRAC Rapporteur: Julie Williams

Request for Supplementary Information adopted on 19.01.2018.

Procysbi - mercaptamine - EMEA/H/C/002465/R/0019, Orphan

Chiesi Orphan B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Qun-Ying Yue

Tybost - cobicistat - EMEA/H/C/002572/R/0041

Gilead Sciences International Limited, Rapporteur: Robert James Hemmings, Co-Rapporteur: Joseph Emmerich, PRAC Rapporteur: Julie Williams

Vipdomet - alogliptin / metformin - EMEA/H/C/002654/R/0024

Takeda Pharma A/S, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst

Vipidia - alogliptin - EMEA/H/C/002182/R/0019

Takeda Pharma A/S, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst

Xarelto - rivaroxaban - EMEA/H/C/000944/R/0060

Bayer AG, Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Qun-Ying Yue

B.2.3. Renewals of Conditional Marketing Authorisations

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection
PRAC recommendations on signals adopted at the PRAC meeting held on 5-8 March 2018 PRAC:
PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its March 2018 meeting:
EMEA/H/C/PSUSA/00001712/201707 (ibuprofen (indicated in ductus arteriosus)) CAPS: **Pedea** (EMEA/H/C/000549) (ibuprofen), Orphan Europe SARL, Rapporteur: Jayne Crowe, PRAC Rapporteur: Almath Spooner, “30 July 2014 - 29 July 2017”
EMEA/H/C/PSUSA/00002003/201708 (metformin hydrochloride / sitagliptin) CAPS: **Efficib** (EMEA/H/C/000896) (sitagliptin / metformin hydrochloride), Merck Sharp & Dohme Limited, Rapporteur: Johann Lodewijk Hillege **Janumet** (EMEA/H/C/000861) (sitagliptin / metformin hydrochloride), Merck Sharp & Dohme Limited, Rapporteur: Johann Lodewijk Hillege **Ristfor** (EMEA/H/C/001235) (sitagliptin / metformin hydrochloride), Merck Sharp & Dohme Limited, Rapporteur: Johann Lodewijk Hillege **Velmetia** (EMEA/H/C/000862) (sitagliptin / metformin hydrochloride), Merck Sharp & Dohme Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, “04/08/2015 - 03/08/2017”

EMEA/H/C/PSUSA/00002711/201708 (sitagliptin) CAPS: **Januvia** (EMEA/H/C/000722) (sitagliptin), Merck Sharp & Dohme Limited, Rapporteur: Johann Lodewijk Hillege **Ristaben** (EMEA/H/C/001234) (sitagliptin), Merck Sharp & Dohme Limited, Rapporteur: Johann Lodewijk Hillege **TESAVEL** (EMEA/H/C/000910) (sitagliptin), Merck Sharp & Dohme Limited, Rapporteur: Johann Lodewijk Hillege **Xelevia** (EMEA/H/C/000762) (sitagliptin), Merck Sharp & Dohme Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "04-August-2014 to 03-August-2017"	
EMEA/H/C/PSUSA/00010081/201708 (cobicistat) CAPS: **Tybost** (EMEA/H/C/002572) (cobicistat), Gilead Sciences International Limited, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Julie Williams, "27 August 2016 to 26 August 2017"	
EMEA/H/C/PSUSA/00010082/201708 (cobicistat / elvitegravir / emtricitabine / tenofovir disoproxil) CAPS: **Stribild** (EMEA/H/C/002574) (elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil), Gilead Sciences International Limited, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Julie Williams, "27 August 2016 to 26 August 2017"	
EMEA/H/C/PSUSA/00010340/201708 (ospemifene) CAPS: **Senshio** (EMEA/H/C/002780) (ospemifene), Shionogi Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Julie Williams, "27/02/2017 – 26/08/2017"	

B.4. EPARs / WPARs

Alpivab - peramivir - EMEA/H/C/004299 Biocryst UK Limited, treatment of influenza, New active substance (Article 8(3) of Directive	For information only.

No 2001/83/EC)	
Amglidia - glibenclamide - EMEA/H/C/004379, Orphan Ammtek, treatment of neonatal diabetes, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	For information only.
Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204, Orphan Pfizer Limited, combination therapy with daunorubicin (DNR) and cytarabine (AraC) for the treatment of adult patients with previously untreated, de novo acute myeloid leukaemia (AML)., New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only.
Riarify - beclometasone dipropionate anhydrous / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004836 Chiesi Farmaceutici S.p.A., symptomatic treatment and reduction of exacerbations in adult patients with chronic obstructive pulmonary disease (COPD) with airflow limitation and who are at risk of exacerbations, Informed Consent of Trimbow, Informed consent application (Article 10c of Directive No 2001/83/EC)	For information only.
Trydonis - beclometasone dipropionate anhydrous / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004702 Chiesi Farmaceutici S.p.A., symptomatic treatment and reduction of exacerbations in adult patients with chronic obstructive pulmonary disease (COPD) with airflow limitation and who are at risk of exacerbations, Informed Consent of Trimbow, Informed consent application (Article 10c of Directive No 2001/83/EC)	For information only.

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

Aloxi - palonosetron - EMEA/H/C/000563/II/0045/G Helsinn Birex Pharmaceuticals Ltd, Rapporteur: Peter Kiely

Request for Supplementary Information adopted on 22.02.2018.

Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0068/G
UCB Pharma S.A., Rapporteur: Kristina Dunder

Cinryze - C1 esterase inhibitor (human) - EMEA/H/C/001207/II/0058/G
Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus
Request for Supplementary Information adopted on 18.01.2018.

Dupixent - dupilumab - EMEA/H/C/004390/II/0002
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus

Gardasil - human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) - EMEA/H/C/000703/II/0075
MSD Vaccins, Rapporteur: Kristina Dunder

Imraldi - adalimumab - EMEA/H/C/004279/II/0005/G
Samsung Bioepis UK Limited (SBUK), Rapporteur: Outi Mäki-Ikola

Infanrix hexa - diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and Haemophilus influenzae type b (Hib) conjugate vaccine (adsorbed) - EMEA/H/C/000296/II/0237/G
GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren

Lojuxta - lomitapide - EMEA/H/C/002578/II/0028
Aegerion Pharmaceuticals Limited, Rapporteur: Johann Lodewijk Hillege
Request for Supplementary Information adopted on 18.01.2018.

Memantine ratiopharm - memantine - EMEA/H/C/002671/II/0012
ratiopharm GmbH, Generic, Generic of Ebixa, Rapporteur: Bart Van der Schueren
Request for Supplementary Information adopted on 18.01.2018.

NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0021/G

Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus
Request for Supplementary Information adopted on 14.12.2017.

Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0030/G
Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Nithyanandan Nagercoil

Pioglitazone Accord - pioglitazone - EMEA/H/C/002277/II/0015/G
Accord Healthcare Limited, Generic, Generic of Actos, Rapporteur: Peter Kiely

Plavix - clopidogrel - EMEA/H/C/000174/II/0127/G
Sanofi Clir SNC, Rapporteur: Bruno Sepodes
Request for Supplementary Information adopted on 26.10.2017, 20.07.2017.

Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0163
Pfizer Limited, Rapporteur: Kristina Dunder

Protopic - tacrolimus - EMEA/H/C/000374/II/0072/G
LEO Pharma A/S, Rapporteur: Peter Kiely
Request for Supplementary Information adopted on 15.02.2018.

Raplixa - human fibrinogen / human thrombin - EMEA/H/C/002807/II/0027/G
Mallinckrodt Pharmaceuticals Ireland Limited, Rapporteur: Nithyanandan Nagercoil

Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0020
CSL Behring GmbH, Rapporteur: Kristina Dunder
Request for Supplementary Information adopted on 08.02.2018.

Stelara - ustekinumab - EMEA/H/C/000958/II/0062/G
Janssen-Cilag International NV, Rapporteur: Greg Markey

Strensiq - asfotase alfa - EMEA/H/C/003794/II/0027/G, Orphan
Alexion Europe SAS, Rapporteur: Greg Markey

Taltz - ixekizumab -

EMEA/H/C/003943/II/0014 Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder	
Trulicity - dulaglutide - EMEA/H/C/002825/II/0026 Eli Lilly Nederland B.V., Rapporteur: Greg Markey	
Trulicity - dulaglutide - EMEA/H/C/002825/II/0027 Eli Lilly Nederland B.V., Rapporteur: Greg Markey	
Vaniqa - eflornithine - EMEA/H/C/000325/II/0051 Almirall S.A, Rapporteur: Peter Kiely Request for Supplementary Information adopted on 26.10.2017.	
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and Haemophilus type B conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0026 MCM Vaccine B.V., Rapporteur: Bart Van der Schueren	
Vpriv - velaglucerase alfa - EMEA/H/C/001249/II/0035, Orphan Shire Pharmaceuticals Ireland Ltd, Rapporteur: Harald Enzmann Request for Supplementary Information adopted on 18.01.2018.	
Xadago - safinamide - EMEA/H/C/002396/II/0020 Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 25.01.2018, 19.10.2017.	
XALKORI - crizotinib - EMEA/H/C/002489/II/0053/G Pfizer Limited, Rapporteur: Alexandre Moreau Opinion adopted on 08.03.2018.	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ziagen - abacavir - EMEA/H/C/000252/II/0101/G ViiV Healthcare UK Limited, Rapporteur: Joseph Emmerich Opinion adopted on 01.03.2018.	Positive Opinion adopted by consensus on 01.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1276/G **Incruse-**	

EMEA/H/C/002809/WS1276/0017/G **Rolufta-** **EMEA/H/C/004654/WS1276/0003/G** Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro Request for Supplementary Information adopted on 18.01.2018.	
WS1311/G **Aflunov-** **EMEA/H/C/002094/WS1311/0040/G** **Foclivia-** **EMEA/H/C/001208/WS1311/0034/G** Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri Opinion adopted on 08.03.2018. Request for Supplementary Information adopted on 01.02.2018.	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1339/G **Fertavid-** **EMEA/H/C/001042/WS1339/0038/G** **Puregon-** **EMEA/H/C/000086/WS1339/0096/G** Merck Sharp & Dohme Limited, Lead Rapporteur: Nithyanandan Nagercoil	
WS1347 **Blitzima-** **EMEA/H/C/004723/WS1347/0008** **Ritemvia-** **EMEA/H/C/004725/WS1347/0008** **Rituzena-** **EMEA/H/C/004724/WS1347/0009** **Truxima-** **EMEA/H/C/004112/WS1347/0009** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz	

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

Advate - octocog alfa - **EMEA/H/C/000520/II/0090** Baxter AG, Rapporteur: Jan Mueller-Berghaus, “Submission of the final clinical study report from study 060402. This was an interventional, randomised, controlled study aimed to compare the efficacy and safety of continuous infusion versus intermittent bolus infusion in patients with haemophilia A undergoing major orthopaedic surgery.” Opinion adopted on 08.03.2018.	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Request for Supplementary Information adopted on 18.01.2018.	
Bosulif - bosutinib - EMEA/H/C/002373/II/0028, Orphan Pfizer Limited, Rapporteur: Harald Enzmann, "Update of section 5.2 of the SmPC following further analyses of the pharmacokinetic (PK) data from Study B1871044 that has been already submitted to the EMA previously."	
Ceplene - histamine dihydrochloride - EMEA/H/C/000796/II/0034, Orphan Noventia Pharma Srl, Rapporteur: Jayne Crowe, "Submission of study report X-03064-3306- to fulfil SOB 002 - A cohort study to follow-up Minimal Residual Disease (MRD) in patients with Acute Myeloid Leukemia (AML) in First Complete Remission (CR1) - Comparison of patients who receive Ceplene/Interleukin-2 as remission maintenance therapy with matched controls."	
PRAC Led **Cetrotide - cetrorelix - EMEA/H/C/000233/II/0064** Merck Serono Europe Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Valerie Strassmann, PRAC-CHMP liaison: Martina Weise, "Update of the RMP (v5.1) to include ovarian hyper-stimulation syndrome (OHSS) as important identified risk and introduce other minor updates." Opinion adopted on 08.03.2018. Request for Supplementary Information adopted on 11.01.2018.	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Darzalex - daratumumab - EMEA/H/C/004077/II/0013, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, "Update of sections 4.4 and 4.8 of the SmPC in order to add the adverse reaction serious infusion-related reactions, including anaphylactic reactions with frequency unknown based on the cumulative review of clinical trial and post-marketing data. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to add a traceability statement to bring the product information in line with the guideline on good pharmacovigilance practices and to add specific text relating to the excipient sodium to align the product information with the updated published	

EMA EU excipient guideline."

Darzalex - daratumumab - EMEA/H/C/004077/II/0014, Orphan
Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, "Update of section 4.5 of the SmPC in order to add information relating to the daratumumab interference with Serum Protein Electrophoresis (SPE) and Immunofixation (IFE) assays and the daratumumab-specific immunofixation reflex assay (DIRA)."

Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0076
AstraZeneca AB, Rapporteur: Bart Van der Schueren, "Update of section 4.6 of the SmPC with regards to pregnancy and breast-feeding information based on the review and summary of pregnancy and lactation data from published literature and MAH pharmacovigilance database. The package leaflet has been updated accordingly."
Request for Supplementary Information adopted on 25.01.2018.

Glivec - imatinib - EMEA/H/C/000406/II/0109
Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, "Update of section 4.8 of the SmPC to add the new adverse drug reaction (ADR) 'pseudoporphyria' following a revision of the company's core data sheet (CDS). The package leaflet has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of the local representatives in Bulgaria, Hungary and Latvija in the Package Leaflet."
Request for Supplementary Information adopted on 18.01.2018.

Humira - adalimumab - EMEA/H/C/000481/II/0175
AbbVie Limited, Rapporteur: Kristina Dunder, "Update of sections 4.2 and 5.2 of the SmPC in order to include 80mg every other week (eow) as an alternative dosing option to the current approved 40 mg weekly dose in the following relevant indications; Rheumatoid arthritis (RA), Crohn's disease (CD), pediatric CD (patients ≥ 40 kg), psoriasis (Ps), ulcerative colitis (UC), hidradenitis suppurativa (HS), and adolescent

HS. As a consequence section 4.1 and 5.1 of the SmPC for the 80 Mg strength has been modified introducing relevant information on Rheumatoid Arthritis. The Package Leaflet is updated accordingly."

Invokana - canagliflozin - EMEA/H/C/002649/II/0033/G

Janssen-Cilag International NV, Rapporteur: Martina Weise, "Update of section 5.1 of the SmPC in order to update the safety information on 'Canagliflozin as initial combination therapy with metformin' based on final results from the DIA3011 study, which is Randomized, Double-Blind, 5-Arm, Parallel-Group, 26-Week, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin in Combination With Metformin as Initial Combination Therapy in the Treatment of Subjects With Type 2 Diabetes Mellitus With Inadequate Glycemic Control With Diet and Exercise.

Update of section 5.1 of the SmPC in order to update the safety information on 'Add-on combination therapy with Metformin and Dipeptidyl-peptidase-4 Inhibitor' based on final results from the DIA4004 study, which is a Randomized, Double-blind, Placebo Controlled, 2-arm, Parallel-group, 26-week, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin in the Treatment of Subjects with Type 2 Diabetes Mellitus with Inadequate Glycemic Control on Metformin and Sitagliptin Therapy."
Request for Supplementary Information adopted on 18.01.2018.

Kyprolis - carfilzomib - EMEA/H/C/003790/II/0025, Orphan

Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.4, 4.8 and 5.1 of the SmPC to update information based on the final analysis of overall survival data from study PX-171-009 (ASPIRE): A Randomized, Multicenter, Phase 3 Study Comparing Carfilzomib, Lenalidomide, and Dexamethasone (CRd) vs Lenalidomide and Dexamethasone (Rd) in Subjects with Relapsed Multiple Myeloma. This variation aims to fulfil the recommendation resulting from the initial MAA.

The Package Leaflet is updated accordingly.
In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10."

MabThera - rituximab - EMEA/H/C/000165/II/0143

Roche Registration Limited, Rapporteur: Sinan B. Sarac, "Submission of the final CSR of the PRIMA study (MO18264), a study in Patients with Advanced Follicular Lymphoma Evaluating the Benefit of Maintenance Therapy with Rituximab after Induction of Response with Chemotherapy plus Rituximab in Comparison with No Maintenance Therapy."

Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0071

Pfizer Limited, Rapporteur: Greg Markey, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the posology for infants from 6 weeks to less than 12 months of age and to remove the recommendation of a second dose in children above 12 months of age, and to add information regarding antibody persistence as measured by serum bactericidal assays 1 year after 1 or 2 doses of MenACWY-TT in toddlers. The posology update is based on results from Study 087 and antibody persistence update is based on results from Study 104 (assessed in procedure ANX 13.3). Study MenACWY-TT-087 is a phase IIIb, open, multi-country, controlled, randomised study to demonstrate the immunogenicity and safety of GSK Biologicals' meningococcal conjugate vaccine, MenACWY-TT in healthy infants, given on a 3+1 primary and booster (2, 4, 6 and 15-18 months of age), a 1+1 primary and booster (6 and 15-18 months of age) or as a single dose at 15-18 months of age.
The Package Leaflet is updated accordingly.
Annex II is also updated to take into account that the 1 year timeline was fulfilled in ANX 13.3."
Request for Supplementary Information adopted on 14.12.2017.

Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0074

Pfizer Limited, Rapporteur: Greg Markey,

"Update of sections 4.5 of the SmPC to include new information regarding co-administration of Nimenrix with Boostrix and Cervarix in individuals from the age of 9 to 25 years, based on data from Studies MenACWY-TT-098 (116705- Phase 3 study to demonstrate the non-inferiority of Nimenrix co-administered with Boostrix compared to Nimenrix administered alone) and MenACWY-TT-054 (113823- phase 3 study to demonstrate the non-inferiority of Nimenrix co-administered with Cervarix compared to Nimenrix alone). The Package Leaflet is updated accordingly. The MAH took also the opportunity to make editorial revision to section 4.8 of the SmPC."	
NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0023 Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to reflect data on untreated patients resulting from final results of the Guardian 2 (NN7008-3568) study and the Guardian 4 (NN7008-3809) study for NovoEight. The Package Leaflet was updated accordingly."	
Perjeta - pertuzumab - EMEA/H/C/002547/II/0035 Roche Registration Limited, Rapporteur: Sinan B. Sarac, "Update of section 4.2 of the SmPC to administer Perjeta with Herceptin SC as an alternative to the currently approved co-administration of Perjeta with Herceptin IV."	
Simponi - golimumab - EMEA/H/C/000992/II/0078/G Janssen Biologics B.V., Rapporteur: Kristina Dunder, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning on agranulocytosis and update neutropenia from uncommon to common based on new safety information in the Company Core Data Sheet (CCDS). The Marketing Authorisation Holder has taken the opportunity to include the safety data from the intravenous (IV) psoriatic arthritis (PsA), and IV ankylosing spondylitis (AS) studies that were recently included in the CCDS. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 14.12.2017.	

Sovaldi - sofosbuvir - EMEA/H/C/002798/II/0048 Gilead Sciences International Limited, Rapporteur: Filip Josephson, “Submission of the final report from study GS-US-334-1111, listed as a category 3 study in the RMP. This is a phase 1 relative bioavailability and food effect study of sofosbuvir (SOF) oral granules in healthy adult subjects.”	
Starlix - nateglinide - EMEA/H/C/000335/II/0033 Novartis Europharm Limited, Rapporteur: Greg Markey, “Update of section 5.2 of the SmPC to add information on the accumulation of M1 metabolite in diabetic patients with end-stage renal disease (ESRD), based on the review of the Core Data Sheet. This information is reflected in section 4.4 of the SmPC. The Package Leaflet and Labelling are updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with QRD template 10, combine the three SmPC into a single SmPC, align sections 1 and 2 of the package leaflet with the SmPC, and correct the name of the local representatives for Latvia and Bulgaria.” Request for Supplementary Information adopted on 07.12.2017.	
Stelara - ustekinumab - EMEA/H/C/000958/II/0063 Janssen-Cilag International NV, Rapporteur: Greg Markey, “Update of section 4.8 of the SmPC in order to revise the immunogenicity rate in patients with psoriasis from “less than 8%” to “up to 12.4 %” following based on new data generated from a Phase 3b study in psoriasis patients, CNTO1275PSO3009 (PSTELLAR) - A Study of Ustekinumab to Evaluate a "Subject-tailored" Maintenance Dosing Approach in Subjects With Moderate-to-Severe Plaque Psoriasis (PSTELLAR). In addition, the MAH took the opportunity to update section 4.4 of the SmPC and package leaflet with additional warning of the excipient sodium to align with the recent updates to the Annex of the EC guideline on excipients in labelling.”	
Tivicay - dolutegravir -	Positive Opinion adopted by consensus on

EMEA/H/C/002753/II/0031 ViiV Healthcare UK Limited, Rapporteur: Filip Josephson, “Update of section 4.8 of the SmPC to add the new ADR ‘anxiety’ based on post-marketing and clinical trial data. The Package Leaflet has been updated accordingly and minor editorial changes implemented.” Opinion adopted on 01.03.2018.	01.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/II/0047 ViiV Healthcare UK Limited, Rapporteur: Kristina Dunder, “Update of sections 4.5 and 5.2 of the SmPC based on new in vitro studies conducted for abacavir (ABC) and lamivudine (3TC). In addition, the MAH took the opportunity to implement minor corrections in section 5.1 of the SmPC and minor editorial changes in the SmPC.” Request for Supplementary Information adopted on 01.02.2018, 09.11.2017.	
Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/II/0049 ViiV Healthcare UK Limited, Rapporteur: Kristina Dunder, “Update of section 4.8 of the SmPC to add the new ADR ‘anxiety’ based on post-marketing and clinical trial data. The Package Leaflet has been updated accordingly.” Opinion adopted on 01.03.2018.	Positive Opinion adopted by consensus on 01.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Velcade - bortezomib - EMEA/H/C/000539/II/0088 Janssen-Cilag International NV, Rapporteur: Daniela Melchiorri, “Update of sections 4.2 and 5.1 of the SmPC in order to add a new dosing schedule for VELCADE (bortezomib) in combination with melphalan and prednisone (VMP) for the treatment of patients with newly diagnosed multiple myeloma who are not eligible for high-dose chemotherapy with hematopoetic stem cell transplant. The proposed new dosing schedule is supported by analyses comparing the current approved VcMP schedule (from 26866138MMY3002 [VISTA] study) with pooled modified less intensive ("once-weekly") VcMP schedules (from 54767414MMY3007 [ALCYONE], GIMENA MM-03-05 [GIMENA]). Additional supportive efficacy and safety data come from GEM2005MAS65 [PETHEMA].	

The PL (section 3) is amended accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the PL.”	
Venclyxto - venetoclax - EMEA/H/C/004106/II/0007/G, Orphan AbbVie Limited, Rapporteur: Filip Josephson, “Update of section 4.5 of the SmPC in order to update the drug-drug interaction between venetoclax and dogixin based on final results from study M16-042; this is study to assess the effect of venetoclax on the pharmacokinetics of digoxin in healthy female subjects. Update of section 4.5 of the SmPC in order to update the drug-drug interaction between venetoclax and ritonavir, based on final results from study M15-719; this is study to assess the effect of ritonavir on the pharmacokinetics of venetoclax in healthy female subjects of non-childbearing potential. Update of section 4.5 of the SmPC in order to update the drug-drug interaction between venetoclax and azithomycin, based on final results from study M16-068; this is study to assess effect of azithromycin on the pharmacokinetics of venetoclax in healthy female subjects. The MAH took the opportunity to update the Product Information with minor editorial and QRD updates.” Request for Supplementary Information adopted on 14.12.2017.	
Vibativ - telavancin - EMEA/H/C/001240/II/0033 Theravance Biopharma Ireland Ltd, Rapporteur: Greg Markey, “C.I.13. Submission of the final report ‘Telavancin Global Surveillance Report for 2016’ to monitor the activity of telavancin and the microbiological resistance as compared to other agents, through the longitudinal resistance surveillance program, in fulfilment of the condition ANX-002.3.”	
Vimpat - lacosamide - EMEA/H/C/000863/II/0070/G UCB Pharma S.A., Rapporteur: Filip Josephson, “C.I.4 - Update of sections 4.8, 5.1, and 5.2 of the SmPC in order to update clinical efficacy and	

safety data in the paediatric population with the results from study SP0969: a phase 3, multicentre, double-blind, randomized, placebo-controlled, parallel-group study to evaluate the efficacy and safety of lacosamide as adjunctive therapy in subjects with epilepsy ≥4 years to <17 years of age with uncontrolled partial-onset seizures; 3 new ADRs (nasopharyngitis, pharyngitis, and pyrexia) have been added based on the results of the above mentioned study; C.I.4 - Update of section 5.2 of the SmPC in order to update the pharmacokinetic data in the paediatric population based on results from the CL0430 population pharmacokinetic (PK) analyses; C.I.4 - Update of section 4.8 of the SmPC in order to update the incidence of decreased appetite, lethargy, and abnormal behaviour in the paediatric population based on results from the updated safety data for Pool SPX-1 with clinical cut-off date of 01 November 2016. The Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some editorial changes in the PI. The MAH also took the opportunity to revise Annex A as requested."	
Vokanamet - canagliflozin / metformin - EMEA/H/C/002656/II/0033/G Janssen-Cilag International NV, Rapporteur: Martina Weise, "Update of section 5.1 of the SmPC in order to update the safety information on 'Canagliflozin as initial combination therapy with metformin' based on final results from the DIA3011 study, which is Randomized, Double-Blind, 5-Arm, Parallel-Group, 26-Week, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin in Combination With Metformin as Initial Combination Therapy in the Treatment of Subjects With Type 2 Diabetes Mellitus With Inadequate Glycemic Control With Diet and Exercise. Update of section 5.1 of the SmPC in order to update the safety information on 'Add-on combination therapy with Metformin and Dipeptidyl-peptidase-4 Inhibitor' based on final results from the DIA4004 study, which is a	

Randomized, Double-blind, Placebo Controlled, 2-arm, Parallel-group, 26-week, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin in the Treatment of Subjects with Type 2 Diabetes Mellitus with Inadequate Glycemic Control on Metformin and Sitagliptin Therapy."
Request for Supplementary Information adopted on 18.01.2018.

Xeloda - capecitabine - EMEA/H/C/000316/II/0074
Roche Registration Limited, Rapporteur: Harald Enzmann, "Update of section 4.4 of the SmPC with regards to DPD deficiency genotyping, following a request from the PRAC after assessment of LEG-33.1."
Request for Supplementary Information adopted on 01.02.2018.

Xofigo - radium-223 - EMEA/H/C/002653/II/0029
Bayer AG, Rapporteur: Harald Enzmann, "Submission of Clinical Study Report for study 16506. This is an interventional re-treatment safety study of radium-223 dichloride in subjects with castration-resistant prostate cancer with bone metastases who received an initial course of six doses of radium-223 dichloride 50 kBq/kg every four weeks."

Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/II/0064
Bial - Portela & Cª, S.A., Rapporteur: Martina Weise, "Update of section 4.8 of the SmPC to add urticaria, angioedema and Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TEN) as adverse drug reactions with unknown frequency, based on recent safety signal evaluation information. The Package Leaflet is updated accordingly. In addition, revision of section 4.4 of the SmPC to align the information on the adverse event angioedema with the information already present in the Package Leaflet."

Zykadia - ceritinib - EMEA/H/C/003819/II/0016
Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.2, 4.4, 4.8 and 5.2 of the SmPC in order to include amendments to the posology in hepatically impaired patients and update the safety

information, respectively. The updates are based on the results from the hepatic function Study CLDK378A2110 which evaluated the PK, safety and tolerability of a single oral dose of ceritinib in subjects with varying degrees of impaired hepatic function and results from physiology-based pharmacokinetic (PBPK) modeling at steady-state.

Submission of the Report for Study A2110 fulfils MEA 001 for Zykadia."
Request for Supplementary Information adopted on 14.12.2017, 09.11.2017, 14.09.2017.

WS1273/G
Effentora-
EMEA/H/C/000833/WS1273/0047/G
Teva B.V., Lead Rapporteur: Martina Weise, "Update of sections 4.2 and 4.4 of the SmPC in order to add a warning on Hyperalgesia following an internal cumulative review. The Package Leaflet is updated accordingly.

Update of sections 4.4 and 4.45 of the SmPC in order to add a warning on the interaction of fentanyl with benzodiazepines or other CNS depressants including alcohol following an internal cumulative review. The Package Leaflet is updated accordingly.

In addition, the MAH took the opportunity to introduce editorial and format changes in the SmPC and PL."
Request for Supplementary Information adopted on 01.02.2018.

WS1295
Advagraf-
EMEA/H/C/000712/WS1295/0048
Modigraf-
EMEA/H/C/000954/WS1295/0026
Astellas Pharma Europe B.V., Lead Rapporteur: Jayne Crowe, "Update of section 4.8 of the SmPC in order to add pain in extremity reported as part of calcineurin-inhibitor induced pain syndrome (CIPS). In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor updates in sections 4.4 and 5.1 of the SmPC."

WS1308/G
Exviera-
EMEA/H/C/003837/WS1308/0033/G
Viekirax-

EMEA/H/C/003839/WS1308/0038/G AbbVie Limited, Lead Rapporteur: Filip Josephson, “Update of section 4.8 of the SmPC to add the adverse reactions anaphylactic reactions and erythema multiforme with unknown frequency following a safety review. The package leaflet is updated accordingly.” Request for Supplementary Information adopted on 25.01.2018.	
WS1310 **Descovy-** **EMEA/H/C/004094/WS1310/0026** **Genvoya-** **EMEA/H/C/004042/WS1310/0040** **Odefsey-** **EMEA/H/C/004156/WS1310/0026** **Vemlidy-** **EMEA/H/C/004169/WS1310/0008** Gilead Sciences International Limited, Lead Rapporteur: Robert James Hemmings, “Update of section 4.5 of the Descovy, Genvoya, Odefsey and Vemlidy SmPCs in order to include some information on the drug-drug interaction with sofosbuvir/velpatasvir/voxilaprevir fixed dose combination based on the results of study GS-US0367-1657, listed as a category 3 in the Vemlidy RMP, in order to fulfil MEA 006 for Vemlidy. Study GS-US0367 is a phase I multiple dose study to evaluate the drug-drug interaction potential between sofosbuvir/velpatasvir/voxilaprevir fixed dose combination and HIV anti-retrovirals in healthy subjects. In addition, the Worksharing applicant (WSA) took the opportunity to make some small corrections to section 4.5 of the SmPC for Descovy, Genvoya, Odefsey and Vemlidy and to make corrections to the DE, ES, HU, IS, IT, LV, NO, PT, SL and SV translations for Vemlidy.” Request for Supplementary Information adopted on 01.02.2018.	

B.5.3. CHMP-PRAC assessed procedures

Benlysta - belimumab - **EMEA/H/C/002015/II/0052** Glaxo Group Ltd, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “Submission of the final report from study HGS1006-C1074 (BEL112234) "A Multi-Center, Continuation Trial of Belimumab (HGS1006,	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

LymphoStat-B), a Fully Human Monoclonal Anti-BLyS Antibody, in Subjects with Systemic Lupus Erythematosus (SLE) who Completed the Phase 3 Protocol HGS1006-C1056 or HGS1006-C1057". The study is listed as a category 3 study in the RMP (MEA012). The RMP version 26.0 is updated accordingly. In addition the MAH has taken the occasion to update the RMP for the due date for final study report and to introduce protocol changes (reduced study sample size) already discussed and agreed in recent procedures EMEA/H/C/002015/MEA/006.4 and EMEA/H/C/002015/MEA/006.5 for study BEL116027." Opinion adopted on 08.03.2018. Request for Supplementary Information adopted on 11.01.2018.	
Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0085 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jean-Michel Dogné, "Submission of Study EPI-HPV-069, a meta-analysis assessing the risk of three autoimmune diseases following vaccination with Cervarix: autoimmune thyroiditis (AIT), Guillain-Barre Syndrome (GBS) and Inflammatory Bowel Disease (IBD). The EPI-HPV-069 study is a post-licensure commitment to the EMA (PASS register number EUPAS13332). As part of this submission, an updated RMP (version 18) is provided, including changes related to the EPI-HPV-069 meta-analysis submitted and minor updates related to other studies." Request for Supplementary Information adopted on 14.09.2017, 18.05.2017, 15.12.2016.	
Gilenya - fingolimod - EMEA/H/C/002202/II/0047 Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Submission of the CSR for Study D2399, a long-term safety and tolerability study of fingolimod 0.5 mg/day in approximately 5000 patients with relapsing multiple sclerosis." Request for Supplementary Information adopted	Request for supplementary information adopted

on 08.03.2018.	
Herceptin - trastuzumab - EMEA/H/C/000278/II/0140 Roche Registration Limited, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Update of sections 4.4 and 4.8 of the SmPC for Herceptin 150mg powder for concentrate for solution for infusion and sections 4.4, 4.8 and 5.1 of the SmPC for Herceptin 600mg solution for injection in vial, in order to update the safety information based on the final results from study BO22227 (Hannah) listed as a category 3 study in the RMP; this is a phase III, randomised, open-label study to compare pharmacokinetics, efficacy and safety of subcutaneous (SC) Herceptin with intravenous (IV) Herceptin administered in women with HER2 positive early breast cancer (EBC). The RMP version 19.0 has also been submitted.”	
Imnovid - pomalidomide - EMEA/H/C/002682/II/0027, Orphan Celgene Europe Limited, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Patrick Batty, “Update of sections 4.2, 4.4, and 4.8 of the SmPC in order to add new ADRs SJS, TEN and DRESS following a review of reports on severe skin reactions. The Package Leaflet is updated accordingly. The RMP version 12.0 has also been submitted.” Opinion adopted on 08.03.2018. Request for Supplementary Information adopted on 11.01.2018.	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
INOmax - nitric oxide - EMEA/H/C/000337/II/0051 Linde Healthcare AB, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams Request for Supplementary Information adopted on 14.12.2017, 12.10.2017.	
Keppra - levetiracetam - EMEA/H/C/000277/II/0169/G UCB Pharma S.A., Rapporteur: Koenraad Norga, PRAC Rapporteur: Laurence de Fays, “1) C.I.4 (type II): Update of section 4.8 of the SmPC to add the ADR Gait Disturbance, to address the CHMP recommendations from P46/085; 2) C.I.4 (type II): Update of section 4.2 of the SmPC to add Dysgeusia as a potential experience post administration and to section	

4.5 of the SmPC to remove drug interaction with Methotrexate, in accordance with the latest Levetiracetam Company Core Data Sheet); 3) C.I.4 (type II): Update of Section 4.6 to add information on 'Women of childbearing potential' and to update the Pregnancy section, to address PRAC recommendations from LEG-084.1; The Package Leaflet is updated accordingly. An updated to the Risk Management Plan (version 8) is included to address PRAC recommendations from LEG 84.1." Request for Supplementary Information adopted on 25.01.2018.	
Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0004 AbbVie Limited, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC in order to update information on the use of Maviret in liver or kidney transplant patients, based on new clinical data from study M13-596 (MAGELLAN-2), a post-registrational Phase 3 study listed as a category 3 study in the RMP, which evaluated the efficacy and safety of the glecaprevir/pibrentasvir regimen in adult subjects with chronic hepatitis C virus genotypes 1-6 infection, who have received a liver or renal transplant. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted." Request for Supplementary Information adopted on 25.01.2018.	
OFEV - nintedanib - EMEA/H/C/003821/II/0018/G, Orphan Boehringer Ingelheim International GmbH, Rapporteur: Jayne Crowe, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of section 4.4 in order to remove the current warning on co-administration with pirfenidone and update of section 5.1 to include the results of study 1199.222, a phase IV, 12 week, open label, randomised, parallel group study to evaluate the safety, tolerability and PK of oral nintedanib in combination with oral pirfenidone in comparison with nintedanib alone in patients with IPF. Update of section 5.2 of the SmPC in order to include the results of study 1199.229, a phase IV, open label, multi-dose, 2 groups study to investigate the DDI between nintedanib anfd	Request for supplementary information adopted

pirfenidone in patients with IPF, a category 3 study in the RMP.
The RMP version 5.0 has also been submitted.
In addition, the Marketing authorisation holder (MAH) took the opportunity to implement some corrections to the French and Swedish translations."
Request for Supplementary Information adopted on 08.03.2018, 11.01.2018.

Opdivo - nivolumab - EMEA/H/C/003985/II/0036/G

Bristol-Myers Squibb Pharma EEIG, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski, "C.I.4 (Type II) - Update of sections 4.2, 5.1, 5.2 and 6.6 of the SmPC in order to introduce new dosing regimens and schedule.

C.I.4 (Type II) - Update of sections 4.2, 5.1, 5.2 and 6.6 of the SmPC in order to introduce change the infusion time from 60 minutes to 30 minutes

These changes are based on interim results from study CA209153; this is a phase IIIb/IV safety trial of nivolumab in subjects with advanced or metastatic non-small cell Lung cancer who have progressed during or after receiving at least one prior systemic regimen;
The Package Leaflet is updated accordingly.
The RMP version 10.0 has also been submitted."
Request for Supplementary Information adopted on 22.02.2018, 14.09.2017.

Opdivo - nivolumab - EMEA/H/C/003985/II/0047

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning on the nivolumab use in patients who have previously undergone allogeneic HSCT and the increased risk of rapid onset and severe Graft versus Host Disease (GVHD) based on evidence from spontaneous case reports, literature case reports, and from 2 multicenter case series. Annex II.D and the Package Leaflet are updated accordingly.
The RMP version 7.8 has also been submitted to include the "risk of GVHD with nivolumab after allogeneic HSCT" as an "Important Potential Risk" based on the RMP template (Revision 2).

In addition, the Marketing authorisation holder (MAH) took the opportunity to make some minor editorial corrections to the PI."	
Raxone - idebenone - EMEA/H/C/003834/II/0008, Orphan Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Carmela Macchiarulo, "Update of SmPC section 4.5 to amend an existing warning in relation to CY3A4 substrates based on the final report of study SNT-I-017: An open-label study to assess the potential for pre-systemic inhibition of cytochrome P450 3A4 (CYP3A) by idebenone in healthy male subjects using midazolam as a substrate. The Package Leaflet was updated accordingly. An updated RMP version 1.5 was submitted as part of the application. The provision of the study report addresses the post-authorisation measure MEA 005.1." Opinion adopted on 08.03.2018. Request for Supplementary Information adopted on 11.01.2018.	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Rydapt - midostaurin - EMEA/H/C/004095/II/0002, Orphan Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of sections 4.5 and 5.2 of the SmPC in order to reflect the results from study R1600721 "Assessment of PKC412 and its metabolites (CGP052421 and CGP062221) as inhibitors of human bile salt export pump (BSEP) " and study R1701192 'In vitro assessment of cytochrome P450 3A4 and 3A5 enzyme inhibition by PKC412, CGP52421 and CGP62221', in fulfilment of the post-authorisation measures MEA 011 and REC 014. In addition, the MAH took the opportunity to update section 5.2 to correct figures as per Study A2107-Amendment 02 already assessed and to make editorial changes in the SmPC. The RMP (v 2.0) has also been updated to reflect the study results. In addition, the search criteria for the important identified risk pulmonary toxicity (including pleural effusion and interstitial lung disease) was updated to include the PT-pleural effusion."	
Symtuza - darunavir / cobicistat /	Positive Opinion adopted by consensus on

emtricitabine / tenofovir alafenamide - EMEA/H/C/004391/II/0002/G Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Julie Williams, "C.I.13 - type II to submit the results of the study GS-US-311-1089 "A Phase 3, Randomized, Double-Blind, Switch Study to Evaluate F/TAF in HIV 1 Positive Subjects who are Virologically Suppressed on Regimens containing FTC/TDF". The RMP version 1.3 has been updated to reflect the completion of the study. C.I.11.z - type II to update the RMP version .3 to remove pancreatitis, convulsion, and cardiac conduction abnormalities as risks in the RMP in alignment with the RMP for Prezista and Rezolsta." Opinion adopted on 08.03.2018. Request for Supplementary Information adopted on 11.01.2018.	08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Truberzi - eluxadoline - EMEA/H/C/004098/II/0005/G Allergan Pharmaceuticals International Ltd, Rapporteur: Harald Enzmann, PRAC Rapporteur: Adam Przybylkowski, "C.I.13: Submission of the final report from study ELX-PH-08 listed as a category 3 study. This is an in vitro evaluation study aimed to investigate the effects on treating primary cultures of cryopreserved human hepatocytes with eluxadoline on the expression of cytochrome P450 (CYP) enzymes C.I.13: Submission of the final report from study 3030-102-002 listed as a category 3 study. This is a randomised, open label study aimed to evaluate the effect of eluxadoline as a potential time dependent inhibitor of CYP3A4 with the substrate midazolam. C.I.11.a: To update the RMP for Truberzi to version v2.0 to update the important identified risk from "SO spasm" to "SO spasm (Sphincter of Oddi dysfunction, SOD)" and to include pancreatitis as an important identified risks. This change has been agreed by the CHMP/PRAC in the outcome of EMEA/H/C/PSUSA/00010528/201703." Request for Supplementary Information adopted on 08.03.2018.	Request for supplementary information adopted
XGEVA - denosumab -	Request for supplementary information adopted

EMEA/H/C/002173/II/0059 Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information and to revise the special warnings, precautions for use and undesirable effects based on cases of clinically significant hypercalcemia following discontinuation of denosumab in patients with growing skeletons (ie, adolescent subject with GCTB in Study 20062004) and in postmarketing reports of pediatric patients treated with denosumab for GCTB or for unapproved indications was previously determined to be an important identified risk; the Package Leaflet are updated accordingly. Consequently the RMP version 30 has also been submitted." Request for Supplementary Information adopted on 08.03.2018.	
Zelboraf - vemurafenib - EMEA/H/C/002409/II/0042/G Roche Registration Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the SmPC section 4.8 with information on radiation toxicity based on the data from study MO25515 (MEA 006) [An Open-Label, Multicenter Study to Assess the Safety of RO5185426 (Vemurafenib) in Patients with Metastatic Melanoma] Submission of study GP28492 (MEA 010) [ZeSS: A Prospective Observational Safety Study of Patients with BRAFV600 Mutation-positive Unresectable or Metastatic Melanoma Treated with Vemurafenib (Zelboraf)]. The RMP version 10.3 is also submitted." Opinion adopted on 01.03.2018. Request for Supplementary Information adopted on 18.01.2018, 28.09.2017.	Positive Opinion adopted by consensus on 01.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zykadia - ceritinib - EMEA/H/C/003819/II/0015 Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.2, 4.4, 4.5, 4.8 and 5.2 of the SmPC in order to update the safety informatio based on based on the primary PK and preliminary safety results of the food effect study CLDK378A2112. The Package Leaflet is updated accordingly. The RMP version 9.0 has also been submitted."	

Request for Supplementary Information adopted on 14.12.2017, 12.10.2017, 22.06.2017.	
WS1312 **Prezista-** **EMEA/H/C/000707/WS1312/0093** **Rezolsta-** **EMEA/H/C/002819/WS1312/0023** **Symtuza-** **EMEA/H/C/004391/WS1312/0005** Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.4, 4.6, 5.1 and 5.2 of the SmPCs for Prezista, Rezolsta and Symtuva to reflect the data of the category 3 study TMC114HIV3015 in HIV-1 infected pregnant women. The PL of Symtuza is also updated . Updated RMPs (version 25.3 for Prezista, 4.3 for Rezolsta and 2.1 for Symtuza) are proposed accordingly. In addition, the MAH took the opportunity to implement the template version 2 for the Prezista and Rezolsta RMPs, removal of the fulfilled category 4 DAD study from the Prezista and Rezolsta RMPs, removal of observational study on growth in children and 'growth abnormalities in the paediatric population' as important potential risk in the Prezista RMP and addition of the missing information 'Safety in patients with cardiac conduction disorders' in the Rezolsta RMP (alignement with Tybost RMP)."	See agenda 9.1
WS1333 **Blitzima-** **EMEA/H/C/004723/WS1333/0007** **Ritemvia-** **EMEA/H/C/004725/WS1333/0007** **Rituzena-** **EMEA/H/C/004724/WS1333/0008** **Truxima-** **EMEA/H/C/004112/WS1333/0008** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz, Lead PRAC Rapporteur: Doris Stenver, "Submission of the clinical study report (CSR) of final results (up to 76 weeks) of Study CT-P10 3.2. In addition, results up to Week 24 of Study CT-P10 3.3 (corresponding CSR submitted in D180 update [SN0004] are updated in this variation." Request for Supplementary Information adopted	Request for supplementary information adopted

on 08.03.2018.	

B.5.4. PRAC assessed procedures

PRAC Led **Ecalta - anidulafungin - EMEA/H/C/000788/II/0036** Pfizer Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "C.I.11: Submission of an updated RMP (version 12.1) in order to include new safety information, an update of incidence and prevalence of hepatotoxicity categorised as important identified risk and re-categorisation of convulsions from important potential risk to important identified risk based on ongoing study A8851008, PASS A8851030 study, the Global Antifungal Surveillance Program and the MAH's review and analysis of cumulative exposure data up to the DLP of 31 August 2017." Opinion adopted on 08.03.2018.	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Fiasp - insulin aspart - EMEA/H/C/004046/II/0003/G** Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "Update of the RMP to upgrade the risk of mix-up between basal and bolus insulin from a potential to an important identified risk (RMP version 2.1) Opinion adopted on 09.03.2018. Request for Supplementary Information adopted on 11.01.2018.	Positive Opinion adopted by consensus on 09.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Humira - adalimumab - EMEA/H/C/000481/II/0173** AbbVie Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from study BSRBR-RA (British Society for Rheumatology Biologics Registers Rheumatoid Arthritis). This is a registry in the UK, evaluating the influence of TNF inhibitor treatment on cancer incidence in RA patients with a history of malignancy. No changes to the PI are proposed." Request for Supplementary Information adopted on 08.03.2018.	Request for supplementary information adopted

PRAC Led **Imbruvica - ibrutinib - EMEA/H/C/003791/II/0040/G, Orphan** Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "C.I.11 (type II): Submission of an updated RMP version 9.1 in order to : - Include a feasibility assessment of experiments and/or studies to further understand the effect of ibrutinib on various components and functions of the adaptive and humoral immune system; - Include the completed non-clinical in vitro rabbit ventricular and atrial wedge study (under review in Procedure EMEA/H/C/003791/IB/0039) in the table of completed studies in the RMP annex; - Include a targeted follow-up questionnaire for cardiac arrhythmias as part of routine pharmacovigilance activities; - Update the text for clarification purposes, to modify the important potential risk of "Infections (excluding PML)" to "Infections (including viral reactivation)". PML is already listed as a separate important potential risk. C.I.11.z (type IB): To replace the 3 PAMs for Studies PCYC-1103-CA, PCI32765CAN3001 and PCYC-1116-CA related to long-term safety (> 2 years) of ibrutinib, with a single long-term safety PAM (Study 3038-1)." Opinion adopted on 08.03.2018.	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Otezla - apremilast - EMEA/H/C/003746/II/0018** Celgene Europe Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Concepcion Prieto Yerro, "Submission of an updated RMP version 10.0 in order to introduce changes on the pharmacovigilance activities related to the use of apremilast in pregnancy, to remove "use in patients of different racial origin" from the safety concerns." Opinion adopted on 08.03.2018.	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Saxenda - liraglutide - EMEA/H/C/003780/II/0016** Novo Nordisk A/S, Rapporteur: Johann Lodewijk	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report from study NN8022-4192, listed as a category 3 study in the RMP. This is a randomised, placebo-controlled trial on subjects with obesity or overweight who were otherwise healthy, to compare the effect of liraglutide 3.0 mg with placebo on postprandial gallbladder dynamics after 12 weeks of treatment. This variation fulfils post-authorisation measure MEA 009.2 for Saxenda. RMP version 29 was submitted, updated to reflect the completion of this additional pharmacovigilance activity. Opinion adopted on 08.03.2018."	
PRAC Led **SCENESSE - afamelanotide - EMEA/H/C/002548/II/0018, Orphan** Clinuvel (UK) Limited, PRAC Rapporteur: Valerie Strassmann, PRAC-CHMP liaison: Harald Enzmann, "Submission of an updated RMP version 8.1 which aims to address the comments made in procedure IB/14 and including: - Updates from pre-approval information to post-marketing information - Update of number of patients treated in clinical trials, special access schemes and commercial distribution - Change in development of the custom-made device - Postponement of pharmacokinetic study CUV052 - Update on timelines for safety extension study CUV037 from Q12013 to Q12018 - Update on timelines for on-going and planned PV studies - key elements of educational and training programme (annex 10) - Correction: replacement of pigmentary lesions by pigmentary expressions - General update of safety information" Opinion adopted on 08.03.2018. Request for Supplementary Information adopted on 11.01.2018.	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Sebivo - telbivudine - EMEA/H/C/000713/II/0048**	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Novartis Europharm Limited, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Caroline Laborde, PRAC-CHMP liaison: Joseph Emmerich, “Submission of RMP version 11.2 in order to upgrade the risk of lactic acidosis from an important potential to an important identified risk and to include a targeted questionnaire for fatal cases as additional risk minimisation measure as requested by the PRAC as part of the assessment of PSUSA/00002880/201608.” Opinion adopted on 08.03.2018. Request for Supplementary Information adopted on 11.01.2018, 30.11.2017.	recommendation.
PRAC Led **Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0124/G** GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, PRAC-CHMP liaison: Kristina Dunder, “Submission of the final study reports from two 5-year Invasive Pneumococcal Disease (IPD) post-marketing surveillance (PMS) studies “Monitoring the Population Effectiveness of Pneumococcal Conjugate Vaccination in the Finnish National Vaccination Programme” (MEA 019) and “Epidemiology of invasive pneumococcal disease in the Netherlands” (MEA 020), addressing the potential risks of "possible serotype replacement of disease isolates" and "possible breakthrough infections/vaccine failure". The MAH also submitted data from IPD surveillance in 5 other European countries (Austria, Bulgaria, Cyprus, Iceland and Sweden) and 6-year update results from a 5-year PMS in Kenya (Pneumococcal Conjugate Vaccine Impact Study (PCVIS), MEA 021). Submission of an updated RMP version 17 to reflect data from the PMS studies, close MEA 019 and MEA 020 and extend MEA 021. No changes to the Product Information are proposed with this submission.” Opinion adopted on 08.03.2018. Request for Supplementary Information adopted on 11.01.2018.	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Thymanax - agomelatine - EMEA/H/C/000916/II/0037** Servier (Ireland) Industries Ltd., Duplicate, Duplicate of Valdoxan, Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Kristin Thorseng	

Kvande, PRAC-CHMP liaison: Svein Rune Andersen, “Submission of the final report from the Post-Authorisation Safety Study (PASS) of Agromelatine and the Risk of Hospitalisation for Acute Liver Injury CLE-20098-094. This is a large, multinational, retrospective longitudinal cohort and nested case-control study to compares the risk of Acute Liver Injury (ACI) in patients initiating treatment with agomelatine and other antidepressants with the risk in patients initiating treatment with citalopram.”	
PRAC Led **Valdoxan - agomelatine - EMEA/H/C/000915/II/0038** Les Laboratoires Servier, Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Kristin Thorseng Kvande, PRAC-CHMP liaison: Svein Rune Andersen, “Submission of the final report from the Post-Authorisation Safety Study (PASS) of Agromelatine and the Risk of Hospitalisation for Acute Liver Injury CLE-20098-094. This is a large, multinational, retrospective longitudinal cohort and nested case-control study to compares the risk of Acute Liver Injury (ALI) in patients initiating treatment with agomelatine and other antidepressants with the risk in patients initiating treatment with citalopram.” Opinion adopted on 08.03.2018.	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0036** Pfizer Ireland Pharmaceuticals, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, “Update of the RMP (version 16) to implement changes from variations EMEA/H/C/002252/II/0029 and EMEA/H/C/002252/II/0022, as requested by PRAC following the latest PSUSA assessment. The update includes the addition of the new population (children from the age of 2 months) as approved in variation II/22; the amendment of the statement concerning additional monitoring following the renewal procedure in which the black triangle symbol was removed from the product information and the re-categorisation of the important identified risks hypersensitivity/anaphylaxis and C. difficile-associated diarrhea as not important. Other minor updates were also included in the revised	Positive Opinion adopted by consensus on 08.03.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

section. The MAH also took the opportunity to revise, reformat and update the content to align with the current RMP template." Opinion adopted on 08.03.2018.	
PRAC Led **WS1283** **Relvar Ellipta-** **EMEA/H/C/002673/WS1283/0035** **Revinty Ellipta-** **EMEA/H/C/002745/WS1283/0031** Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, PRAC-CHMP liaison: Concepcion Prieto Yerro, "Submission of the final report from study 205052 (PRJ2214). This is a drug utilization study to identify the extent of any off-label prescribing fluticasone furoate/vilanterol FF/VI in any dose in children less than 12 years of age; and prescribing of FF/VI 200/25 mcg in patients with a diagnosis of chronic obstructive pulmonary disease COPD, considering the presence of a concurrent diagnosis of asthma. The RMP version 9.1 has been updated accordingly." Request for Supplementary Information adopted on 08.03.2018, 11.01.2018.	Request for supplementary information adopted
PRAC Led **WS1326** **Truvada-** **EMEA/H/C/000594/WS1326/0145** **Viread-EMEA/H/C/000419/WS1326/0184** Gilead Sciences International Limited, Lead Rapporteur: Joseph Emmerich, Lead PRAC Rapporteur: Caroline Laborde, PRAC-CHMP liaison: Joseph Emmerich, "Submission of the final report from study GS-EU-104-0433, listed as a category 3 study in the RMP. This is an observational, drug utilisation study of Viread in children and adolescents with HIV-1 infection, in fulfilment of a post-authorisation measure (PAM) for Viread (MEA 46) and Truvada (MEA 276)." Request for Supplementary Information adopted on 08.03.2018.	Request for supplementary information adopted
PRAC Led **WS1355** **Prezista-** **EMEA/H/C/000707/WS1355/0094** **Rezolsta-**	

EMEA/H/C/002819/WS1355/0024
Janssen-Cilag International NV, Lead PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, “To amend the RMP with an amended due date for the final report for study GS-US-216-0128 from Q1 2022 to Q1 2024.”

B.5.5. CHMP-CAT assessed procedures

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

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

WS1291/G
Copalia-
EMEA/H/C/000774/WS1291/0095/G
Copalia HCT-
EMEA/H/C/001159/WS1291/0064/G
Dafiro-
EMEA/H/C/000776/WS1291/0097/G
Dafiro HCT-
EMEA/H/C/001160/WS1291/0065/G
Exforge-
EMEA/H/C/000716/WS1291/0094/G
Exforge HCT-
EMEA/H/C/001068/WS1291/0063/G
Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth

WS1336/G
Entresto-
EMEA/H/C/004062/WS1336/0017/G
Neparvis-
EMEA/H/C/004343/WS1336/0015/G
Novartis Europharm Limited, Lead Rapporteur: Johann Lodewijk Hillege

WS1360
Zutectra-
EMEA/H/C/001089/WS1360/0035
Biotest Pharma GmbH, Lead Rapporteur: Jan Mueller-Berghaus, “To rework and harmonise the section 4.8 of the SmPC following PRAC Rapporteur's recommendation provided during the assessment of procedure

EMEA/H/C/001089/II/0024. In addition, the MAH took the opportunity to update the labelling according with latest QRD template v 10.0. Finally, the contact details of the MAH in section 7 and of the SmPC and in the PL and the contact details for the HR local representative in the PL were updated.”	
Hexacima- **EMEA/H/C/002702/WS1306/0074** **Hexaxim-** **EMEA/H/W/002495/WS1306/0079** **Hexyon-** **EMEA/H/C/002796/WS1306/0078** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 25.01.2018.	

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

Aranesp - darbepoetin alfa - (EMEA/H/C/000332/II/0142) Amgen Europe B.V., Rapporteur: Martina Weise, Co-Rapporteur: Koenraad Norga Withdrawal request submitted on 21.02.2018.	The MAH withdrew the procedure on 21.02.2018.

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

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

bevacizumab - EMEA/H/C/004697, Treatment of adult patients with metastatic carcinoma of the colon or rectum, metastatic breast cancer, unresectable advanced, metastatic or recurrent non-small cell lung cancer, advanced and/or metastatic renal cell cancer, persistent, recurrent, or metastatic carcinoma of the cervix
pegfilgrastim - EMEA/H/C/005008, treatment of neutropenia,
trientine dihydrochloride - EMEA/H/C/004111, Orphan Univar BV, Treatment of Wilson's disease.

pegfilgrastim - EMEA/H/C/004789,
treatment of neutropenia

apalutamide - EMEA/H/C/004452,
treatment of non metastatic castration resistant prostate cancer (NM CRPC)

hydroxycarbamide - EMEA/H/C/004837,
prevention of complications of Sickle Cell disease

dacomitinib - EMEA/H/C/004779, first-line treatment of adults with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR)-activating mutations.

glutamine - EMEA/H/C/004734, treatment of sickle cell disease

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

Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/X/0034/G
Vertex Pharmaceuticals (Europe) Ltd.,
Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Daniela Melchiorri, PRAC
Rapporteur: Almath Spooner

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

Bydureon - exenatide - EMEA/H/C/002020/X/0048/G
AstraZeneca AB, Rapporteur: Kristina Dunder,
PRAC Rapporteur: Qun-Ying Yue
List of Questions adopted on 25.01.2018.

lesinurad / allopurinol - EMEA/H/C/004412, gout
List of Questions adopted on 09.11.2017.

adalimumab - EMEA/H/C/004429
, treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis
List of Questions adopted on 14.09.2017.

Imbruvica - ibrutinib - EMEA/H/C/003791/X/0037, Orphan
Janssen-Cilag International NV, Rapporteur:
Filip Josephson, PRAC Rapporteur: Patrick Batty,
“Extension application to introduce a new pharmaceutical form (film-coated tablets)

associated with new strengths (140 mg, 280 mg, 420 mg and 560 mg)."
List of Questions adopted on 22.02.2018.

vigabatrin - EMEA/H/C/004534, PUMA
, Treatment in monotherapy of infantile spasms (West's syndrome) and resistant partial epilepsy in infants and children
List of Questions adopted on 14.12.2017.

trastuzumab - EMEA/H/C/004463
, treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)
List of Questions adopted on 09.11.2017.

abemaciclib - EMEA/H/C/004302
, treatment of hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer
List of Questions adopted on 14.12.2017.

volanesorsen - EMEA/H/C/004538, Orphan, Akcea Therapeutics UK Ltd., indicated as an adjunct to diet for the treatment of patients with familial chylomicronemia syndrome (FCS).
List of Questions adopted on 14.12.2017.

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

histamine dihydrochloride - EMEA/H/C/000796/S/0035, Orphan
Noventia Pharma Srl

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

Abilify Maintena - aripiprazole - EMEA/H/C/002755/R/0025
Otsuka Pharmaceutical Europe Ltd, Rapporteur: Bruno Sepodes, Co-Rapporteur: Eleftheria Nikolaidi,PRAC Rapporteur: Qun-Ying Yue

Ceplene - histamine dihydrochloride - EMEA/H/C/000796/R/0036, Orphan
Noventia Pharma Srl, Rapporteur: Jayne Crowe, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Almath Spooner

Fortacin - lidocaine / prilocaine - EMEA/H/C/002693/R/0023
Recordati Ireland Ltd, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Dolores Montero Corominas

Invokana - canagliflozin - EMEA/H/C/002649/R/0037
Janssen-Cilag International NV, Rapporteur: Martina Weise, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Valerie Strassmann

Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/R/0039
Roche Registration Limited, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Doris Stenver

Oprymea - pramipexole - EMEA/H/C/000941/R/0029
KRKA, d.d., Novo mesto, Generic, Generic of Sifrol, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Doris Stenver

Opsumit - macitentan - EMEA/H/C/002697/R/0027, Orphan
Actelion Registration Limited, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Dolores Montero Corominas

Rasilez HCT - aliskiren / hydrochlorothiazide - EMEA/H/C/000964/R/0087
Noden Pharma DAC, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Melinda Sobor, PRAC Rapporteur: Carmela Macchiarulo

Relvar Ellipta - fluticasone furoate / vilanterol - EMEA/H/C/002673/R/0037
Glaxo Group Ltd, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Dolores Montero Corominas

Revinty Ellipta - fluticasone furoate / vilanterol - EMEA/H/C/002745/R/0033
Glaxo Group Ltd, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Dolores Montero Corominas

Translarna - ataluren - EMEA/H/C/002720/R/0041, Orphan
PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, Co-

Rapporteur: Concepcion Prieto Yerro, PRAC
Rapporteur: Sabine Straus

Zalmoxis - allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - EMEA/H/C/002801/R/0010, Orphan, ATMP
MolMed SpA, Rapporteur: Johannes Hendrikus Ovelgonne, PRAC Rapporteur: Brigitte Keller-Stanislawski

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

Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0055, Orphan
Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus, “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.”

Mozobil - plerixafor - EMEA/H/C/001030/II/0034, Orphan
Genzyme Europe BV, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, “Extension of Indication to include paediatric patients aged 1 to 18 years for Mozobil, as a consequence, sections 4.1, 4.2,

4.8, 5.1, 5.2 and 5.3 of the SmPC are updated.
The Package Leaflet is updated in accordance."

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, "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."

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, "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)

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, "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 update RMP version 12.1 was submitted in order to include the changes related to the extension of indication."	
Yervoy - ipilimumab - EMEA/H/C/002213/II/0055 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "Extension of indication to include the treatment of advanced (unresectable or metastatic) melanoma in adults in combination with nivolumab for Yervoy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package	

Leaflet and the RMP (version 20.0) are updated in accordance. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the contact details of the Irish local representative in the Package Leaflet."

WS1344
Edistride-
EMEA/H/C/004161/WS1344/0025
Forxiga-
EMEA/H/C/002322/WS1344/0044
AstraZeneca AB, Lead Rapporteur: Kristina Dunder, Lead Co-Rapporteur: Martina Weise, Lead PRAC Rapporteur: Qun-Ying Yue, "Extension of Indication to include new indication for the treatment of insufficiently controlled type 1 diabetes mellitus as an adjunct to insulin, when insulin does not provide adequate glycaemic control, for Forxiga and Edistride; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The updated RMP version 16 has also been submitted.
In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor editorial changes to SmPC and Package Leaflet."

WS1369
Elebrato Ellipta-
EMEA/H/C/004781/WS1369/0001
Trelegy Ellipta-
EMEA/H/C/004363/WS1369/0001
GlaxoSmithKline Trading Services, Lead Rapporteur: Peter Kiely, Lead Co-Rapporteur: Harald Enzmann, Lead PRAC Rapporteur: Qun-Ying Yue, "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."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0094
GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren

Cyramza - ramucirumab - EMEA/H/C/002829/II/0022
Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik

Flixabi - infliximab - EMEA/H/C/004020/II/0025
Samsung Bioepis UK Limited, Rapporteur: Jan Mueller-Berghaus

Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0078/G
AstraZeneca AB, Rapporteur: Bart Van der Schueren

Granupas - para-aminosalicylic acid - EMEA/H/C/002709/II/0024, Orphan
Lucane Pharma, Rapporteur: Greg Markey

Hemoblast - thrombin - EMEA/H/D/002769/II/0003/G
BSI Group, Rapporteur: Daniela Melchiorri

Imatinib Teva - imatinib - EMEA/H/C/002585/II/0033
Teva B.V., Generic, Generic of Glivec, Rapporteur: Jorge Camarero Jiménez

Imraldi - adalimumab - EMEA/H/C/004279/II/0007/G
Samsung Bioepis UK Limited (SBUK), Rapporteur: Outi Mäki-Ikola

Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0006/G
AbbVie Limited, Rapporteur: Joseph Emmerich

Ongentys - opicapone - EMEA/H/C/002790/II/0009
Bial - Portela & Cª, S.A., Rapporteur: Greg Markey

OPDIVO - nivolumab -
EMEA/H/C/003985/II/0051/G
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez

Xolair - omalizumab -
EMEA/H/C/000606/II/0084
Novartis Europharm Limited, Rapporteur: Kristina Dunder

Zerbaxa - ceftolozane / tazobactam -
EMEA/H/C/003772/II/0015/G
Merck Sharp & Dohme Limited, Rapporteur: Robert James Hemmings

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

Brilique - ticagrelor -
EMEA/H/C/001241/II/0038
AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.5 of the SmPC in order to include interaction information between morphine and ticagrelor based on the Conclusion of the legally binding measure LEG 022; the Package Leaflet is updated accordingly."

Dynastat - parecoxib -
EMEA/H/C/000381/II/0072
Pfizer Limited, Rapporteur: Jayne Crowe, "Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to update the information on the use of parecoxib beyond 3 days based on a recent publication on the 'Safety of parecoxib when used for more than 3 days for the management of postoperative pain'; this is an observatory study of the Pfizer clinical trial database to identify randomized, double-blind, placebo controlled trials in which patients could have, potentially, received parecoxib for longer than 3 days for the management of postoperative pain. The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the Package Leaflet in line with the SmPC with the inclusion of diazepam and omeprazole in section 2 of the Package Leaflet."

IBRANCE - palbociclib -
EMEA/H/C/003853/II/0011
Pfizer Limited, Rapporteur: Filip Josephson,

"Update of section 5.1 of the SmPC to update the clinical efficacy data from pivotal Phase 3 Study A5481008 (PALOMA-2), a study of IBRANCE in combination with letrozoleto, to include the results from recent analyses of the study with a data cutoff date of 31 May 2017. In addition, the MAH took the oportunity to update section 4.2 to include that when coadministered with an aromatase inhibitor, the later should be administered according to the dose schedule reported in the Summary of Product Characteristics."	
Inflectra - infliximab - EMEA/H/C/002778/II/0061 Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey, "To submit the final report from study CT-P13 3.4, listed as a category 3 study in the RMP. A Randomized, Double-Blind, Parallel-Group, Phase 3 Study to Demonstrate Noninferiority in Efficacy and to Assess Safety of CT-P13 Compared to Remicade in Patients with Active Crohn's Disease."	
Lumigan - bimatoprost - EMEA/H/C/000391/II/0055 Allergan Pharmaceuticals Ireland, Rapporteur: Mark Ainsworth, "Submission of the final report of the Phase 4 clinical safety study P-192024-054 listed as a category 3 study in the RMP."	
Mirvaso - brimonidine - EMEA/H/C/002642/II/0017 Galderma International, Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to update the frequency of the adverse drug reaction (ADR) rosacea from "uncommon" to "common" following a re-examination of the frequency of ADRs in pertinent studies. The package leaflet is updated accordingly."	
NovoRapid - insulin aspart - EMEA/H/C/000258/II/0121 Novo Nordisk A/S, Rapporteur: Kristina Dunder, "Update of section 4.2 of the SmPC to include a passive discouragement of withdrawing insulin with a syringe from cartridges and pre-filled pens; update of section 6.6 of the SmPC to allow the withdrawal of insulin with a syringe from cartridges and pre-filled pens in emergency situations. This variation was	

submitted following a recommendation by the PRAC in November 2017, subsequent the evaluation of the signal on potential increased risk of medication error associated with withdrawing insulin from pre-filled pens and cartridges, leading to dysglycaemia. The PIL is updated accordingly. In addition, the MAH took the opportunity to reinsert and clarify information in the SmPC regarding mixing of NovoRapid with NPH insulin (sections 4.2 and 6.2), which has previously been deleted from the SmPC by mistake. Other editorial changes are also proposed within this variation."	
Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0111 Boehringer Ingelheim International GmbH, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Doris Stenver, "Update of section 5.1 of the SmPC to reflect the phase II outcome results from the Global Registry on Long-Term Oral Antithrombotic TReatment In PAtients with Atrial Fibrillation (GLORIA-AF) including the main objective "to collect real-world data on important outcome events of antithrombotic treatments for the prevention of stroke" for patients taking pradaxa. In addition, the results of the Medicare study (P14-15648) are proposed to be included also in section 5.1 with further information on the effectiveness and safety of pradaxa in patients with NVAF (non-valvular atrial fibrillation) in a real-world setting. The RMP (version 35.0) has also been updated to reflect the study results."	
Praluent - alirocumab - EMEA/H/C/003882/II/0037 sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Submission of the second step analysis report of the clinical study EFC13786 (study title: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study Evaluating the Efficacy and Safety of Alirocumab in Patients with Primary Hypercholesterolemia not treated with a statin) as per MEA014."	
Remicade - infliximab - EMEA/H/C/000240/II/0212 Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.4 to include a warning	

recommending adult patients to be brought up to date with all vaccinations if possible prior to initiating Remicade therapy (in line with the current warning for children) and to clarify that patients on infliximab may receive concurrent vaccinations, except for live vaccines. Relevant sections of the PL and the RMP (v 15.1) were updated accordingly.
The MAH took the opportunity the include minor editorial changes in the PI."

Remicade - infliximab - EMEA/H/C/000240/II/0213/G
Janssen Biologics B.V., Rapporteur: Kristina Dunder, "Update of section of 4.8 of the SmPC in order to add the following adverse reactions: 'Hemophagocytic Lymphohistiocytosis (HLH)' with a frequency 'very rare' and 'Linear IgA Bullous Dermatosis (LABD)' with a 'rare' frequency. In addition, the Marketing authorisation holder (MAH) took the opportunity to add additional instructions for obese Adult patients in section 6.6 of the SmPC; relevant sections of the PL have been updated accordingly. The MAH also took the opportunity to introduce some editorial changes in the Product Information."

Remsima - infliximab - EMEA/H/C/002576/II/0052
Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey, "To submit the final report from study CT-P13 3.4, listed as a category 3 study in the RMP. A Randomized, Double-Blind, Parallel-Group, Phase 3 Study to Demonstrate Noninferiority in
Efficacy and to Assess Safety of CT-P13 Compared to Remicade in Patients with Active Crohn's Disease."

Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0046
Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, "Update of the PI to align with the company's Core Safety Data Sheet:
Update of information related to liver function tests, thrombotic and thromboembolic complications, MDS in the section 4.4;
Update of DDI and food interaction information in the sections 4.5 and 5.2;
Update of the section 4.8 by: inclusion and

removal of ADRs, changes in some ADRs frequencies following pooling of safety data; Reorganisation of the section 5.1 in relation to severe aplastic anaemia;
Update of the section 5.3 with information related to Juvenile animal studies.
The MAH took the opportunity to make some editorial changes throughout the PI. The Package leaflet is updated accordingly."

TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0051/G

Biogen Idec Ltd, Rapporteur: Martina Weise, "C.I.13: Submission of the final report from study 109HV114. This is a randomised, open-label, single-dose, crossover study in healthy volunteers to assess the pharmacokinetics of 4 new formulations compared to Tecfidera 240mg capsules.

C.I.13: Submission of the final report from study 109MS201 listed as a category 3 study in the RMP. This is an open-label, multicentre study in patients with Relapsing-Remitting Multiple Sclerosis to evaluate the safety and tolerability of 240 mg Tecfidera three times daily administered as add-on therapy to beta interferons (IFNβ) or Glatiramer Acetate (GA).

C.I.13: Submission of the synopsis report from study 109MS308. This is a randomised, multicentre, double-blind, placebo-controlled study of the efficacy and safety of Tecfidera in delaying disability progression in patients with secondary progressive multiple sclerosis.

C.I.13: Submission of the final report (abbreviated) from study 109MS416. This is a randomised, multicentre, treatment-blinded, parallel group Phase IIIb study aimed to evaluate the effect of 6-week up-titration of Tecfidera treatment on the severity of gastrointestinal adverse effects in patients with multiple sclerosis."

Tivicay - dolutegravir - EMEA/H/C/002753/II/0034

ViiV Healthcare UK Limited, Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC to add the new ADRs 'acute hepatic failure' and 'weight increased' based on post-marketing and clinical trial data. The Package Leaflet has been updated accordingly."

Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/II/0053

ViiV Healthcare UK Limited, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC to add the new ADRs 'acute hepatic failure' and 'weight increased' based on post-marketing and clinical trial data. The Package Leaflet has been updated accordingly."

WS1363
Kisplyx-EMEA/H/C/004224/WS1363/0010
Lenvima-EMEA/H/C/003727/WS1363/0013

Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren, "Update of sections 4.4 and 4.8 of the SmPC to add wound healing and aortic dissection. The PIL is updated accordingly."

B.6.10. CHMP-PRAC assessed procedures

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)."

Eylea - aflibercept - EMEA/H/C/002392/II/0045

Bayer AG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of sections 4.2 and 5.1 of the SmPC in order to add information for the Health Care Professional related to earlier treatment extension and related increments intervals based on final results from phase 4 study ALTAIR. This is an interventional study evaluating the efficacy and safety of repeated doses of intravitreal (IVT) aflibercept with variable treatment intervals in Japanese subjects with neovascular AMD. The Package Leaflet is updated accordingly. The RMP version 24.1 has also been submitted."

Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0023, Orphan

Roche Registration Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Patrick Batty, "Update of section 5.1 of the SmPC in order to update the overall survival data based on final results from study BO21004/CLL11 listed as a category 3 study in the RMP; this is the pivotal study that evaluated the efficacy and safety of obinutuzumab as therapy for patients with previously untreated CLL with comorbidities; The RMP version 4.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity format the listing of "other side effects" and correct the term heart attack to heart failure in section 4 of the Package Leaflet."

B.6.11. PRAC assessed procedures

PRAC Led

Inflectra - infliximab - EMEA/H/C/002778/II/0060

Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "To update the RMP for Inflectra to version 8.0 to introduce the new RMP template, update some milestones of the Pharmacovigilance plan and delete some safety concerns form the educational material to Health Care Profesionals."

PRAC Led

Remsima - infliximab -
EMEA/H/C/002576/II/0051
Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "To update the RMP for Remsima to version 8.0 to introduce the new RMP template, update some milestones of the Pharmacovigilance plan and delete some safety concerns form the educational material to HCP."

PRAC Led
Renvela - sevelamer carbonate -
EMEA/H/C/000993/II/0043
Genzyme Europe BV, PRAC Rapporteur: Laurence de Fays, PRAC-CHMP liaison: Bart Van der Schueren, "Submission of the final report from study SEVELC08371. This was a historical cohort study of adult patients with severe chronic kidney disease assessing the risk of bladder cancer by sevelamer exposure."

PRAC Led
Suboxone - buprenorphine / naloxone -
EMEA/H/C/000697/II/0037
Indivior UK Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "C.I.13: Submission of the final report for study PEUS005" SUBOXONE mortality study in the UK with The Health Improvement Network Database (THIN)". This is a PASS to estimate the all-cause mortality among patients exposed to SUBOXONE in comparison to buprenorphine and methadone. RMP version 13.0 has been submitted."

PRAC Led
Sycrest - asenapine -
EMEA/H/C/001177/II/0031/G
N.V. Organon, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "Submission of the final reports from studies P08307 (EP04026.001), P08308 (EP04026.003), P08309 (EP04026.002) and P08310 (EP04026.004) listed as a category 3 studies in the RMP. They are observational studies to study different safety aspects. No changes in the PI are proposed. The RMP (version 5.1) is updated accordingly."

PRAC Led
WS1364
Lyrica-EMEA/H/C/000546/WS1364/0092

Pregabalin Pfizer-
EMEA/H/C/003880/WS1364/0021

Pfizer Limited, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Sabine Straus, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 12.0 in order to include the changes proposed by EMEA/H/C/PSUSA/00002511/201701, updating the safety specifications and risk minimisation measures. The pharmacovigilance plan has also been updated. The draft protocol for non-interventional non-imposed PASS (A0081359) titled "A population-based cohort study of Pregabalin to characterize pregnancy outcomes" has been submitted.

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

B.6.12. CHMP-CAT assessed procedures

spheroids of human autologous matrix-associated chondrocytes -
EMEA/H/C/002736/II/0001, ATMP

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

, "Update of sections 4.2, 4.7, 4.8 and 5.1, of the SmPC in order to revise the wording and to update the safety and efficacy information based on the interim results from studies 16 HS 13 (24-month follow-up data) and 16 HS 14 (48-month follow-up data); the Package leaflet is updated accordingly.

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

Study 16 HS 14 is listed as a category 3 study in the RMP. It is a phase II, randomised, open label study, aimed to evaluate the efficacy and safety of the treatment of large defects (4-10 cm^2) with 3 different doses of Spherox (ACT3D-CS) in subjects with cartilage defects of the knee."

allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) -
EMEA/H/C/002801/II/0009/G, Orphan, ATMP
MolMed SpA,

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

WS1320/G
Tivicay-
EMEA/H/C/002753/WS1320/0035/G
Triumeq-
EMEA/H/C/002754/WS1320/0054/G
ViiV Healthcare UK Limited, Lead Rapporteur: Filip Josephson

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

WS1350
Hexacima-
EMEA/H/C/002702/WS1350/0078
Hexaxim-
EMEA/H/W/002495/WS1350/0083
Hexyon-
EMEA/H/C/002796/WS1350/0082
Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus

WS1352/G
Corlentor-
EMEA/H/C/000598/WS1352/0049/G
Ivabradine Anpharm-
EMEA/H/C/004187/WS1352/0008/G
Procoralan-

EMEA/H/C/000597/WS1352/0048/G
Les Laboratoires Servier, Lead Rapporteur: Johann Lodewijk Hillege

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

WS1373/G
AMGEVITA-
EMEA/H/C/004212/WS1373/0005/G
SOLYMBIC-
EMEA/H/C/004373/WS1373/0005/G
Amgen Europe B.V., Lead Rapporteur: Kristina Dunder

WS1378
Blitzima-
EMEA/H/C/004723/WS1378/0011
Ritemvia-
EMEA/H/C/004725/WS1378/0011
Rituzena-
EMEA/H/C/004724/WS1378/0012
Truxima-
EMEA/H/C/004112/WS1378/0012
Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz

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:

No items

HTA:

G.2. Ongoing procedures

G.3.

G.4. PRIME

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

G.4.1. List of procedures concluding at 19-22 March 2018 CHMP plenary:

G.4.2. List of procedures starting in March 2018 for April 2018 CHMP adoption of outcomes

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