9 October 2017
EMA/CHMP/662799/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 09-12 October 2017

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

09 October 2017, 13:00 – 19:30, room 2A

10 October 2017, 08:30 – 19:30, room 2A

11 October 2017, 08:30 – 19:30, room 2A

12 October 2017, 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).

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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 09-12 October 2017. See October 2017 CHMP minutes (to be published post November 2017 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 09-12 October 2017

1.3. Adoption of the minutes

CHMP minutes for 11-14 September 2017

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. - ocrelizumab - EMEA/H/C/004043

treatment of multiple sclerosis

Scope: Oral explanation/Opinion

Action: Oral explanation to be held on 10 October 2017 at time 09:00

List of Outstanding Issues adopted on 14.09.2017, Oral explanation held on 13.09.2017, 23.03.2017. List of Questions adopted on 15.09.2016.

2.1.2. - letermovir - Orphan - EMEA/H/C/004536

Accelerated assessment

Merck Sharp & Dohme Limited; prophylaxis of cytomegalovirus (CMV) reactivation and disease

Scope: Oral explanation

Action: Possible oral explanation to be held on 10 October 2017 at time 11:00

List of Outstanding Issues adopted on 12.09.2017. List of Questions adopted on 18.07.2017.

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

2.3.1. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0027

Merck Sharp & Dohme Limited; treatment of melanoma

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

Scope: "Extension of Indication to include 1st line treatment of metastatic non-squamous non-small cell lung cancer (NSCLC) in combination with platinum-pemetrexed chemotherapy based on the results from study KEYNOTE-021 (cohort G); a Phase 1/2, open-label trial of pembrolizumab in combination with chemotherapy or immunotherapy in patients with locally advanced or metastatic NSCLC.
As a consequence sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC have been updated and the Package Leaflet has been updated accordingly.
An updated RMP version 9.0 was provided as part of the application."

Scope: Oral explanation/Opinion

Action: Oral explanation to be held on 10 October 2017 at time 14:00

Request for Supplementary Information adopted on 14.09.2017, 22.06.2017.

2.4. Referral procedure oral explanations

2.4.1. Alcover 750 mg, 1250 mg, 1750 mg Granulat im Beutel – Sodium oxybate – EMEA/H/A-29(4)/1451

D&A Pharma

Initial assessment: Rapporteur: Andrea Laslop, Co-Rapporteur: Fatima Ventura,

Scope: SAG report/Oral explanation/Opinion

Action: Oral explanation to be held on 10 October 2017 at time 16:00

Decentralised Procedure number: AT/H/0552/01-03/DC, notification by the Austrian Agency dated 22 December 2016 notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC.

Opinion adopted on 22 June 2017, List of Outstanding issues adopted on 21.04.2017. List of Questions adopted on 26.01.2017.

See 10.7

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. - carmustine - EMEA/H/C/004326

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 20.07.2017. List of Questions adopted on 13.10.2016.

3.1.2. - ocrelizumab - EMEA/H/C/004043

treatment of multiple sclerosis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 14.09.2017, Oral explanation held on 13.09.2017, 23.03.2017. List of Questions adopted on 15.09.2016.

See 2.1

3.1.3. - tacrolimus - EMEA/H/C/004435

prophylaxis of transplant rejection and treatment of allograft rejection

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 20.07.2017. List of Questions adopted on 21.04.2017.

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

3.2.1. - rurioctocog alfa pegol - EMEA/H/C/004195

treatment of haemophilia A

Scope: 3rd Day 180 list of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 21.04.2017, 15.12.2016. List of Questions adopted on 21.07.2016.

3.2.2. - hydrocortisone - PUMA - EMEA/H/C/004416

treatment of adrenal insufficiency

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.04.2017.

3.2.3. - peramivir - EMEA/H/C/004299

treatment of influenza

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 18.05.2017.

3.2.4. - brigatinib - EMEA/H/C/004248

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

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 22.06.2017.

3.2.5. - betrixaban - EMEA/H/C/004309

treatment of prophylaxis of venous thromboembolism (VTE)

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.04.2017.

3.2.6. - burosumab - Orphan - EMEA/H/C/004275

Kyowa Kirin Limited; treatment of X-linked hypophosphataemia (XLH)

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.04.2017.

3.2.7. - enclomifene - EMEA/H/C/004198

treatment of hypogonadotrophic hypogonadism

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 26.01.2017.

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

AB Science; treatment of amyotrophic lateral sclerosis

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 26.01.2017.

3.2.9. - insulin glargine - EMEA/H/C/004280

treatment of diabetes mellitus

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 23.02.2017.

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

3.3.1. - erenumab - EMEA/H/C/004447

indicated for prophylaxis of migraine in adults

Scope: Day 120 list of questions

Action: For adoption

3.3.2. - emicizumab - EMEA/H/C/004406

Accelerated assessment

routine prophylaxis to prevent bleeding or reduce the frequency of bleeding episodes in patients with haemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors.

Scope: Day 120 list of questions

Action: For adoption

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

treatment of HIV

Scope: Day 120 list of questions

Action: For adoption

3.3.4. - pemetrexed - EMEA/H/C/003958

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

Scope: Day 120 list of questions

Action: For adoption

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

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

Scope: Day 120 list of questions

Action: For adoption

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

No items

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

No items

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

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. Humira - adalimumab - EMEA/H/C/000481/X/0164/G

AbbVie Limited

Rapporteur: Kristina Dunder

Scope: "Extension application to add a new strength/potency of 20 mg for adalimumab solution for injection in pre-filled syringe, grouped with a type II variation (C.I.4.z) to update of sections 4.2 of the SmPC in order to introduce new fixed dose regimen (posology) for the paediatric indications of JIA and Ps. The Package Leaflet and Labelling are updated accordingly.

In addition, the marketing authorisation holder took the opportunity to:
- introduce editorial changes to align wording and layout of the Product Information
- to amend the statement relating to anti-adalimumab antibody development in JIA patients, which will reside in section 5.1 of the Humira SmPCs (20 mg and 40 mg presentations)."

Action: For adoption

List of Questions adopted on 20.07.2017.

4.1.2. Oncaspar - pegaspargase - EMEA/H/C/003789/X/0008

Baxalta Innovations GmbH

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Patrick Batty

Scope: "Extension application to add a new pharmaceutical form, powder for solution for injection/infusion (750 U/ml)."

Action: For adoption

List of Questions adopted on 20.07.2017.

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

No items

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

No items

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

No items

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

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

5.1.1. Alecensa - alectinib - EMEA/H/C/004164/II/0001

Roche Registration Limited

Rapporteur: Filip Josephson, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Patrick Batty

Scope: "Extension of Indication to extend the indication of Alecensa (alectinib) to first line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC); as a consequence, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP are updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 22.06.2017.

5.1.2. 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

5.1.3. 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

5.1.4. Bydureon - exenatide - EMEA/H/C/002020/II/0045

AstraZeneca AB

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

Scope: "Extension of Indication to include treatment in combination with basal insulin for Bydureon; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated based on the study D5553C00002 (Duration 7 study) which evaluated safety and efficacy of exenatide once weekly therapy added to titrated basal insulin in patients with type 2 diabetes who have inadequate glycemic control on basal insulin with or without metformin. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor corrections in sections 4.8 and 5.1 of the SmPC. Furthermore, the updated RMP version 26 has been submitted.)"

Action: For adoption

Request for Supplementary Information adopted on 14.09.2017.

5.1.5. Cubicin - daptomycin - EMEA/H/C/000637/II/0061

Merck Sharp & Dohme Limited

Rapporteur: Greg Markey, Co-Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Julie Williams

Scope: "Extension of indication to extend the S. aureus bacteraemia indication to include paediatric patients 1 to 17 years of age; 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 and Labelling are updated accordingly.

In addition, the marketing authorisation holder (MAH) took the opportunity to bring the product information in line with the latest QRD template version 10 and to combine the SmPCs for both strengths (350 and 500 mg). The MAH also updated the RMP, from last approved version 9.1 to the current proposed version 10.0."

Action: For adoption

Request for Supplementary Information adopted on 21.04.2017.

5.1.6. Faslodex - fulvestrant - EMEA/H/C/000540/II/0059

AstraZeneca UK Ltd

Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of Indication to include the use of faslodex in combination with palbociclib for the treatment of hormone receptor (HR)-positive, human epidermal growth factor

receptor 2 (HER2)-negative locally advanced or metastatic breast cancer in women who have received prior endocrine therapy (see section 5.1). In pre- or perimenopausal women, the combination treatment with palbociclib should be combined with a luteinizing hormone releasing hormone (LHRH) agonist for Faslodex.

As a consequence, sections 4.1, 4.2, 4.4, 5.1, 5.3 and 6.6 of the SmPC are updated to update the safety and efficacy information.The Package Leaflet is updated in accordance. RMP version 11 was included in the application."

Action: For adoption

Request for Supplementary Information adopted on 22.06.2017.

5.1.7. Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0087

CSL Behring GmbH

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include immunomodulatory therapy for the treatment of patients with chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy to prevent relapse of neuromuscular disability and impairment. 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 is updated (v. 4.0)"

Action: For adoption

5.1.8. Pegasys - peginterferon alfa-2a - EMEA/H/C/000395/II/0091

Roche Registration Limited

Rapporteur: Filip Josephson, PRAC Rapporteur: Qun-Ying Yue

Scope: "Extension of Indication to include paediatric patients from 3 to less than 18 years of age with Chronic Hepatitis B in the immune-active phase for Pegasys.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add efficacy and safety information from study YV25718. The Package Leaflet is updated in accordance.
An updated EU RMP (version 8.0) is included in this application."

Action: For adoption

Request for Supplementary Information adopted on 20.07.2017, 23.02.2017.

5.1.9. Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0047

Janssen-Cilag International NV

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Eva A. Segovia

Scope: "Extension of indication to include the treatment of newly diagnosed high risk metastatic hormone sensitive prostate cancer and in combination with androgen deprivation therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 14.0) are updated accordingly. In addition, the

MAH took the opportunity to update the list of local representatives in the Package Leaflet"

Action: For adoption

Request for Supplementary Information adopted on 20.07.2017.

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. Raxone - idebenone - Orphan - EMEA/H/C/003834/II/0003

Santhera Pharmaceuticals (Deutschland) GmbH

Rapporteur: John Joseph Borg, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Carmela Macchiarulo

Scope: "Letter from the applicant dated 28 September 2017 requesting a re-examination of the Opinion adopted on 14 September 2017

Action: For adoption

Opinion adopted on 14.09.2017

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. - doravirine - H0004747

indicated in combination with other antiretroviral agents for the treatment of adults infected with HIV-1 without present or past evidence of viral resistance to doravirine

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

Action: For adoption

8.1.2. - doravirine, lamivudine, tenofovir disoproxil fumarate - H0004746

the fixed dose combination of doravirine/lamivudine/tenofovir disoproxil fumarate is indicated as a complete regimen for the treatment of adults infected with HIV-1 without past or present evidence of viral resistance to the regimen components

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

Action: For adoption

8.1.3. - inotersen – Orphan - H0004782

Ionis Pharmaceuticals Inc, Treatment of Transthyretin Amyloidosis

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. Prolia - denosumab - EMEA/H/C/001120/II/0068

MAH: Amgen Europe B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga

Scope: List of experts for ad hoc expert group meeting and CHMP list of questions to the ad hoc expert group

Action: For adoption

Request for Supplementary Information adopted on 22.06.2017.

9.1.2. Ebymect - dapagliflozin/metformin - EMEA/H/C/004162/WS1167/0021; Edistride – dapagliflozin - EMEA/H/C/004161/WS1167/0016; Forxiga – dapagliflozin - EMEA/H/C/002322/WS1167/0036; Xigduo - dapagliflozin/metformin - EMEA/H/C/002672/WS1167/0032

MAH: AstraZeneca AB

Lead Rapporteur: Kristina Dunder

Scope: "Update of sections 4.8 and 5.1 of the SmPC in order to add information regarding two initial combination studies (MB102021 and MB102034) in treatment-naïve patients of dapagliflozin 5 mg + metformin and dapagliflozin 10 mg + metformin, respectively, compared to each component separately.

In addition, the Worksharing applicant (WSA) took the opportunity to bring the PI in line with the latest QRD template version 10."

Action: For adoption

Request for Supplementary Information adopted on 20.07.2017.

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

Novartis Europharm Ltd

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 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

10.5.1. Scandonest and associated names – mepivacaine - EMEA/H/A-30/1455

Septodont group of companies and associated companies

Rapporteur: Romaldas Maciulaitis, Co-rapporteur: Fatima Ventura,

Scope: List of questions/Opinion

Action: For adoption

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

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

No items

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

10.7.1. Alcover 750 mg, 1250 mg, 1750 mg Granulat im Beutel – Sodium oxybate – EMEA/H/A-29(4)/1451

D&A Pharma

Initial assessment: Rapporteur: Andrea Laslop, Co-Rapporteur: Fatima Ventura,

Scope: SAG report/Opinion

Action: For adoption

Decentralised Procedure number: AT/H/0552/01-03/DC, notification by the Austrian Agency dated 22 December 2016 notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC.

Opinion adopted on 22 June 2017, List of Outstanding issues adopted on 21.04.2017. List of Questions adopted on 26.01.2017.

See 2.4

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

October 2017 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

No items

13.2. Innovation Task Force briefing meetings

Disclosure of information related to briefing meetings taking place with applicants cannot be released at present time as deemed to contain commercially confidential information

13.2.1. ITF Briefing Meeting

Meeting date: 24th October 2017

Action: For adoption

13.2.2. ITF Briefing Meeting

Meeting date: 27th October 2017

Action: For adoption

13.2.3. ITF Briefing Meeting

Meeting date: 8 November 2017

Action: For adoption

13.2.4. ITF Briefing Meeting

Meeting date: 27 November 2017

Action: For adoption

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

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

Area of expertise of co-opted member

The mandate of co-opted member (expertise in Quality and safety of biological medicinal products, including biotechnology derived medicines, cell therapies and gene therapies) will expire on 13 November 2017.

Timeline for appointment of the co-opted member:

Please send any proposals for areas of expertise

Agreement of area of expertise/Call for nomination for expert: October 2017

Election of co-opted member: November 2017

Action: For adoption

14.1.1. Abolition of sending an email with the EURD list to CHMP

Scope: It is proposed to abolish the sending of an email as the same list is always tabled in MMD for adoption.

Action: For information

14.1.2. Changes related to CHMP post-mail Annexes

Scope: The proposal is to stop tabling the individual documents on Article 61.3 notifications and Marketing Authorisation Transfers in MMD.

Action: For information

14.1.3. Update to the CHMP templates on initial Marketing Authorisation

Scope: Update to the Rapporteurs' D80 AR overview guidance document to add guidance specific to biosimilars (including a revised Benefit/Risk balance section).

The CHMP was requested to provide comments by 1 September 2017. Further to the CHMP comments received, the Rapporteurs' D80 AR overview guidance document was updated.

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 25-29 September 2017

Action: For information

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for October 2017

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 4-6 October 2017
Action: For information

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 18-19 September 2017

Action: For information

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at October 2017 PDCO

Action: For information

Report from the PDCO meeting held on 10-13 October 2017

Action: For information

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 3-5 October 2017
Action: For information

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

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 9-11 October 2017

Action: For information

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

14.3.1. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 25-28 September 2017. 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 20 September 2017

Action: For adoption

14.3.3. Infectious Disease Working Party (IDWP)

Vice Chair: María Jesús Fernández Cortizo

Call for nominations for Chair position: Nominations together with a brief resume in support of their candidature should be sent **by 23 October 2017**

Action: For information

14.3.4. Extrapolation Working Group (EWG)

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

CHMP: Robert James Hemmings

Action: For adoption

14.3.5. Quality Working Party (QWP)

Chair: Keith Pugh

PAT team comments on US FDA continuous manufacturing docket.

Presentation by Keith Pugh

Action: For information

14.3.6. Quality Working Party/Inspectors working group (QWP/IWG)

Chair: Keith Pugh (QWP) LoQ on Histamine levels in human and veterinary Gentamicin containing products/H/V to SWP

Action: For adoption

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

Co-chair: Kaisa Immonen

Minutes of PCWP/HCPWP joint meeting held on 27-28 June 2017 (EMA/355452/2017)

Action: For information

14.3.8. European Medicines Agency Human Scientific Committees' Working Party with Healthcare Professionals' Organisations (HCPWP)

Co-chair: Gonzalo Calvo

Minutes of PCWP/HCPWP joint meeting held on 27-28 June 2017 (EMA/355452/2017)

Action: For information

14.3.9. Blood Products Working Party (BPWP)

Chair: Jacqueline Kerr

BPWP/BWP response to CHMP LoQ on rurioctocog alfa pegol (EMEA/H/C/004195)

Action: For information

Guideline on the clinical investigation of recombinant and human plasma-derived factor VIII products (EMA/CHMP/BPWP/144533/2009 rev. 2)

Core SmPC for human plasma derived and recombinant coagulation factor VIII products (EMA/CHMP/BPWP/1619/1999 rev. 2)

Action: For adoption

Final minutes of the BPWP meeting held on 29-30 June 2017

Action: For information

Draft Minutes of EMA-FDA-HC TC Blood Cluster held on 13 July 2017

Action: For information

14.3.10. Biologicals Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

BWP report on the revision of the Ph. Eur. monograph on Human plasma (pooled and treated for virus inactivation) (1646) 'S/D plasma'

Action: For adoption

Quality support to accelerated access schemes

Action: For adoption

Nomination of new member to the BWP

Action: For adoption

Final minutes from meeting held on 10-12 July 2017 (EMA/CHMP/BWP/444271/2017)

Action: For information

Draft agenda for BWP meeting to be held on 30-31 October 2017 (EMA/CHMP/BWP/609436/2017)

Action: For information

14.3.11. Vaccines Working Party (VWP)

Chair: Mair Powell/Svein Rune Andersen

"Guideline on the clinical evaluation of medicinal products indicated for the prophylaxis or treatment of respiratory syncytial virus (RSV) disease"

Action: For adoption for 6 months public consultation

Minutes of VWP virtual meeting on 22 September 2017 (EMA/631333/2017)

Action: For information

14.3.12. Pharmacogenomics Working Party (PGWP)

Chair: Krishna Prasad/Markus Paulmichl

EMA expert meeting on genome editing technologies used in medicinal product development (EMA/359806/2017), taking place 18 October 2017.

Action: For information

14.3.13. Cardiovascular Working Party (CVSWP)

Chair: Pieter de Graeff/Kristina Dunder

Concept paper on the need for a paediatric addendum of the guideline on clinical investigation of medicinal products for the treatment and prophylaxis of venous thromboembolic disease

Action: For adoption for 3 months public consultation

14.3.14. Oncology Working Party (OWP)

Chair: Pierre Demolis/Paolo Foggi

Minutes of ONCWP virtual meeting on 6 September 2017 (EMA/591113/2017)

Action: For information

14.3.15. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink/Henrike Potthast

CMDh question to PKWP on Bioequivalence studies programme for multiple strengths product

Action: For adoption

CMDh question to PKWP on Bioequivalence studies for an oral solution of a BCS class II drug – Aripiprazole

Action: For adoption

CMDh Question to PKWP on Bioequivalence study requirements for generic applications for agomelatine co-crystals

Action: For adoption

Nomination of an observer Audrey Sultana (MT) to the PKWP

Action: For adoption

14.3.16. Biostatistics Working Party (BSWP)

Chair: Anja Schiel/Thomas Lang

Nomination of additional assessor to the BWSP

Action: For adoption

Minutes of BSWP face to face meeting on 6-7 July 2017 (EMA/432665/2017)

Action: For information

14.3.17. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus

Nomination of additional assessor to the RIWP

Action: For adoption

14.3.18. Radiopharmaceutical Drafting Group (RadDG)

Chair: Anabel Cortes

Guideline on core SmPC and Package Leaflet for technetium (99mTc) macrosalb

Action: For adoption for 3 months public consultation

Call for nomination for two new core members: Rad DG members have requested that one of the new core members would have expertise in clinical and another member would have expertise in quality aspects of radiopharmaceuticals.

Eligible experts, who wish to apply for the position as a member are requested to submit a brief letter in support of their candidature together with a brief CV, highlighting their expertise.

Applications should be sent **by 27th October 2017**.

Action: For information

14.3.19. Respiratory Drafting Group (RDG)

Chair: Karolina Törneke

Call for nomination for new core member. Eligible experts, who wish to apply for the member position are requested to submit a brief letter in support of their candidature together with a brief CV, highlighting their expertise.

Nominations should be sent **by 31st October 2017**.

Action: For information

14.4. Cooperation within the EU regulatory network

None

14.5. Cooperation with International Regulators

None

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

None

14.7. CHMP work plan

None

14.8. Planning and reporting

None

14.9. Others

None

15. Any other business

15.1. AOB topic

15.1.1. Preparedness of the system and capacity increase

Action: For information

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)*

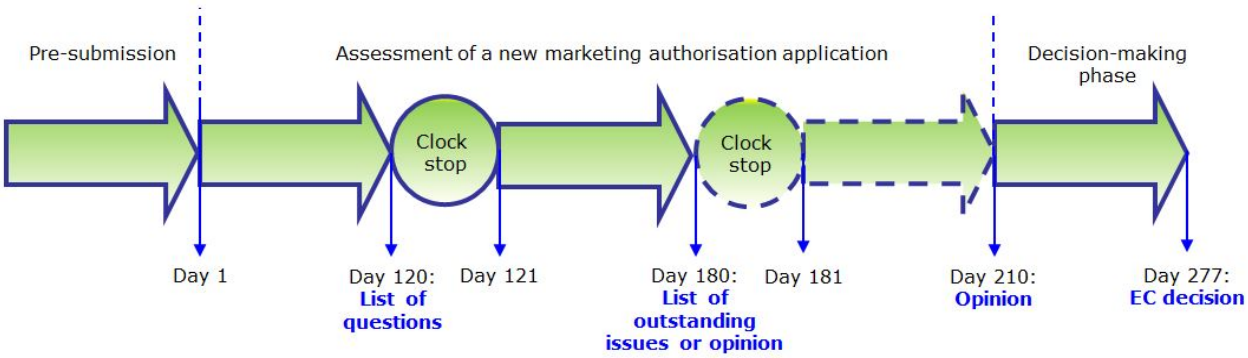
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

9 October 2017
EMA/655986/2017

Annex to 9-12 October 2017 CHMP Agenda

Pre submission and post authorisations issues

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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 October 2017: **For adoption**

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

Final Outcome of Rapporteurship allocation for October 2017: **For adoption**

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

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

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

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

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Jetrea - ocriplasmin -
EMEA/H/C/002381/R/0033
MAH: ThromboGenics NV, Rapporteur: Greg Markey, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Julie Williams
Request for Supplementary Information adopted on 14.09.2017.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Actelsar HCT - telmisartan / hydrochlorothiazide -
EMEA/H/C/002676/R/0015
MAH: Actavis Group PTC ehf, Generic, Generic of MicardisPlus, Rapporteur: Alar Irs, PRAC Rapporteur: Carmela Macchiarulo

Hexacima - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA),

poliomyelitis (inact.) and Haemophilus type B conjugate vaccine (adsorbed) - EMEA/H/C/002702/R/0068

MAH: Sanofi Pasteur SA, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Brigitte Keller-Stanislawski

Hexyon - 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/002796/R/0072

MAH: Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Brigitte Keller-Stanislawski

Imatinib Actavis - imatinib - EMEA/H/C/002594/R/0015

MAH: Actavis Group PTC ehf, Generic, Generic of Glivec, Rapporteur: Hrefna Gudmundsdottir, PRAC Rapporteur: Eva A. Segovia

Marixino - memantine - EMEA/H/C/002658/R/0012

MAH: Consilient Health Ltd., Generic, Generic of Ebixa, Rapporteur: Milena Stain, PRAC Rapporteur: Dolores Montero Corominas

Mycamine - micafungin - EMEA/H/C/000734/R/0034

MAH: Astellas Pharma Europe B.V., Rapporteur: Harald Enzmann, Co-Rapporteur: Koenraad Norga, PRAC Rapporteur: Martin Huber

Perjeta - pertuzumab - EMEA/H/C/002547/R/0031

MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Doris Stenver

Prepandrix - A/Indonesia/05/2005 (H5N1) like strain used (PR8-IBCDC-RG2) - EMEA/H/C/000822/R/0071

MAH: GlaxoSmithkline Biologicals SA, Rapporteur: Greg Markey, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Julie Williams

Privigen - human normal immunoglobulin - EMEA/H/C/000831/R/0122

MAH: CSL Behring GmbH, Rapporteur: Jan

Mueller-Berghaus, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Brigitte Keller-Stanislawski

Thalidomide Celgene - thalidomide - EMEA/H/C/000823/R/0054, Orphan
MAH: Celgene Europe Limited, Rapporteur: Alexandre Moreau, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Ghania Chamouni

Tolucombi - telmisartan / hydrochlorothiazide - EMEA/H/C/002549/R/0020
MAH: KRKA, d.d., Novo mesto, Generic, Generic of MicardisPlus, Rapporteur: Alar Irs, PRAC Rapporteur: Carmela Macchiarulo

B.2.3. Renewals of Conditional Marketing Authorisations

Alecensa - alectinib - EMEA/H/C/004164/R/0007
MAH: Roche Registration Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Patrick Batty

Holoclar - ex vivo expanded autologous human corneal epithelial cells containing stem cells - EMEA/H/C/002450/R/0015, Orphan, ATMP
MAH: Chiesi Farmaceutici S.p.A., Rapporteur: Egbert Flory, Co-Rapporteur: Paolo Gasparini, PRAC Rapporteur: Julie Williams

Ocaliva - obeticholic acid - EMEA/H/C/004093/R/0002, Orphan
MAH: Intercept Pharma Ltd, Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 14.09.2017.

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 25-29 September 2017 PRAC:

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its September 2017 meeting:

EMEA/H/C/PSUSA/00000871/201702
(collagenase clostridium histolyticum (treatment of Dupuytren's contracture and treatment of Peyronie's disease))
CAPS:
Xiapex (EMEA/H/C/002048) (collagenase clostridium histolyticum), MAH: Swedish Orphan Biovitrum AB (publ), Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, “28 August 2016 to 27 February 2017”

EMEA/H/C/PSUSA/00000998/201703
(dexmedetomidine)
CAPS:
Dexdor (EMEA/H/C/002268) (dexmedetomidine), MAH: Orion Corporation, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, “16/03/2016 - 15/03/2017”

EMEA/H/C/PSUSA/00001704/201702
(ibritumomab tiuxetan)
CAPS:
Zevalin (EMEA/H/C/000547) (ibritumomab tiuxetan), MAH: Spectrum Pharmaceuticals B.V., Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, “01 March 2014 – 28 February 2017”

EMEA/H/C/PSUSA/00002667/201702
(rotigotine)
CAPS:
Leganto (EMEA/H/C/002380) (rotigotine), MAH: UCB Manufacturing Ireland Limited, Rapporteur: Bruno Sepodes
Neupro (EMEA/H/C/000626) (rotigotine), MAH: UCB Pharma S.A., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ana Sofia Diniz Martins, “16 Feb 2014 to 15 Feb 2017”

EMEA/H/C/PSUSA/00009325/201702
(ulipristal acetate (treatment of moderate to severe symptoms of uterine fibroids))
CAPS:
Esmya (EMEA/H/C/002041) (ulipristal acetate), MAH: Gedeon Richter Plc., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “23/02/2016 - 22/02/2017”

EMEA/H/C/PSUSA/00010015/201702
(ruxolitinib)
CAPS:
Jakavi (EMEA/H/C/002464) (ruxolitinib), MAH: Novartis Europharm Ltd, Rapporteur: Filip

Josephson, PRAC Rapporteur: Ulla Wändel Liminga, “23 February 2016 to 22 February 2017”

EMEA/H/C/PSUSA/00010055/201703
(alemtuzumab)
CAPS:
Lemtrada (EMEA/H/C/003718) (alemtuzumab), MAH: Genzyme Therapeutics Ltd, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Doris Stenver, “13-Sep-2016 to 12-Mar-2017”

EMEA/H/C/PSUSA/00010094/201702
(florbetaben (18f))
CAPS:
Neuraceq (EMEA/H/C/002553) (florbetaben (18F)), MAH: Piramal Imaging Limited, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Patrick Batty, “21 August 2016 - 20 February 2017”

EMEA/H/C/PSUSA/00010120/201702
(nalmefene)
CAPS:
Selincro (EMEA/H/C/002583) (nalmefene), MAH: H. Lundbeck A/S, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, “25 Feb 2016 – 24 Feb 2017”

EMEA/H/C/PSUSA/00010317/201703
(naloxegol)
CAPS:
Moventig (EMEA/H/C/002810) (naloxegol), MAH: Kyowa Kirin Limited, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Almath Spooner, “16/09/2016 - 15/03/2017”

EMEA/H/C/PSUSA/00010366/201703
(naltrexone / bupropion)
CAPS:
Mysimba (EMEA/H/C/003687) (naltrexone hydrochloride / bupropion hydrochloride), MAH: Orexigen Therapeutics Ireland Limited, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Martin Huber, “27-Sep-2016 to 09-Mar-2017”

EMEA/H/C/PSUSA/00010403/201703
(pembrolizumab)
CAPS:
Keytruda (EMEA/H/C/003820) (pembrolizumab), MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, PRAC

Rapporteur: Sabine Straus, “4 September 2016 to 3 March 2017”

EMEA/H/C/PSUSA/00010493/201703
(ixekizumab)
CAPS:
Taltz (EMEA/H/C/003943) (ixekizumab), MAH: Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Brigitte Keller-Stanislawski, “23 September 2016 to 22 March 2017”

B.4. EPARs / WPARs

Adlumiz - anamorelin - EMEA/H/C/003847
Applicant: Helsinn Birex Pharmaceuticals Ltd, treatment of anorexia, cachexia or unintended weight loss in adult patients with non-small cell lung cancer (NSCLC), New active substance (Article 8(3) of Directive No 2001/83/EC)

Cyltezo - adalimumab - EMEA/H/C/004319
Applicant: Boehringer Ingelheim International GmbH, treatment of rheumatoid arthritis, axial spondyloarthritis, psoriasis, hidradenitis suppurativa (HS), Crohn’s disease, ulcerative colitis and uveitis., Similar biological application (Article 10(4) of Directive No 2001/83/EC)

Elebrato Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004781
Applicant: GlaxoSmithKline Trading Services Limited, treatment of adult patients with chronic obstructive pulmonary disease (COPD), Duplicate, Duplicate of Trelegy Ellipta, Fixed combination application (Article 10b of Directive No 2001/83/EC)

Human IGG1 monoclonal antibody specific for human interleukin-1 alpha XBiotech - human IgG1 monoclonal antibody specific for human interleukin-1 alpha - EMEA/H/C/004388
Applicant: XBiotech Germany GmbH, treatment of metastatic colorectal cancer, New active substance (Article 8(3) of Directive No 2001/83/EC)

Imatinib Teva B.V. - imatinib - EMEA/H/C/004748

Applicant: Teva B.V., treatment of newly diagnosed and chronic Philadelphia chromosome (bcr-abl) positive (Ph+) chronic myeloid leukaemia (CML), gastrointestinal stromal tumours (GIST), unresectable dermatofibrosarcoma protuberans (DFSP) and recurrent and/or metastatic DFSP, Generic, Generic of Glivec, Generic application (Article 10(1) of Directive No 2001/83/EC)

Masipro - masitinib - EMEA/H/C/004159, Orphan
Applicant: AB Science, treatment of mastocytosis , New active substance (Article 8(3) of Directive No 2001/83/EC)

Miglustat Gen.Orph - miglustat - EMEA/H/C/004366
Applicant: Gen.Orph, treatment of Gaucher disease, Generic, Generic of Zavesca, Generic application (Article 10(1) of Directive No 2001/83/EC)

Nyxoid - naloxone - EMEA/H/C/004325
Applicant: Mundipharma Corporation Limited, Nyxoid is intended for emergency use for known or suspected opioid overdose as manifested by respiratory and/or central nervous system depression, Hybrid application (Article 10(3) of Directive No 2001/83/EC)

Ontruzant - trastuzumab - EMEA/H/C/004323
Applicant: Samsung Bioepis UK Limited (SBUK), treatment of breast cancer and metastatic gastric cancer, Similar biological application (Article 10(4) of Directive No 2001/83/EC)

Ritonavir Mylan - ritonavir - EMEA/H/C/004549
Applicant: MYLAN S.A.S, treatment of HIV-1, Generic, Generic of Norvir, Generic application (Article 10(1) of Directive No 2001/83/EC)

Tookad - padeliporfin - EMEA/H/C/004182
Applicant: STEBA Biotech S.A, treatment of prostate cancer, New active substance (Article 8(3) of Directive No 2001/83/EC)

Trelegy Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004363
Applicant: GlaxoSmithKline Trading Services, treatment of adult patients with chronic

obstructive pulmonary disease (COPD), Fixed combination application (Article 10b of Directive No 2001/83/EC)	
Tremfya - guselkumab - EMEA/H/C/004271 Applicant: Janssen-Cilag International N.V., treatment of plaque psoriasis, New active substance (Article 8(3) of Directive No 2001/83/EC)	
VeraSeal - human fibrinogen / human thrombin - EMEA/H/C/004446 Applicant: Instituto Grifols, S.A., treatment of haemostasis, Known active substance (Article 8(3) of Directive No 2001/83/EC)	
Zejula - niraparib - EMEA/H/C/004249, Orphan Applicant: Tesaro UK Limited, treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer, New active substance (Article 8(3) of Directive No 2001/83/EC)	
Zubsolv - buprenorphine / naloxone - EMEA/H/C/004407 Applicant: Mundipharma Corporation Limited, treatment for opioid drug dependence, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Advate - octocog alfa - EMEA/H/C/000520/II/0082/G MAH: Baxter AG, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 20.07.2017, 23.02.2017.	Weekly start timetable.
Afstyla - lonoctocog alfa - EMEA/H/C/004075/II/0001 MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 20.07.2017, 21.04.2017.	Weekly start timetable.
Avastin - bevacizumab - EMEA/H/C/000582/II/0098	Weekly start timetable.

MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac	
Bortezomib Hospira - bortezomib - EMEA/H/C/004207/II/0006/G MAH: Hospira UK Limited, Generic, Generic of VELCADE, Rapporteur: Milena Stain Request for Supplementary Information adopted on 21.09.2017.	Weekly start timetable.
Brineura - cerliponase alfa - EMEA/H/C/004065/II/0001/G, Orphan MAH: BioMarin International Limited, Rapporteur: Martina Weise	Weekly start timetable.
Cetrotide - cetrorelix - EMEA/H/C/000233/II/0061 MAH: Merck Serono Europe Limited, Rapporteur: Martina Weise	Weekly start timetable.
Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0089 MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus	Weekly start timetable.
Imatinib Actavis - imatinib - EMEA/H/C/002594/II/0013 MAH: Actavis Group PTC ehf, Generic, Generic of Glivec, Rapporteur: Hrefna Gudmundsdottir Opinion adopted on 21.09.2017. Request for Supplementary Information adopted on 06.07.2017.	Positive Opinion adopted by consensus on 21.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Lartruvo - olaratumab - EMEA/H/C/004216/II/0006/G, Orphan MAH: Eli Lilly Nederland B.V., Rapporteur: Jorge Camarero Jiménez	Weekly start timetable.
Mircera - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/II/0062/G MAH: Roche Registration Limited, Rapporteur: Concepcion Prieto Yerro Opinion adopted on 28.09.2017.	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Praluent - alirocumab - EMEA/H/C/003882/II/0028/G MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 21.09.2017.	Weekly start timetable.
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0123/G MAH: CSL Behring GmbH, Rapporteur: Jan	Weekly start timetable.

Mueller-Berghaus	
Ranexa - ranolazine - EMEA/H/C/000805/II/0053 MAH: Menarini International Operations Luxembourg S.A., Rapporteur: Kristina Dunder	Weekly start timetable.
Ratiograstim - filgrastim - EMEA/H/C/000825/II/0054 MAH: ratiopharm GmbH, Rapporteur: Outi Mäki-Ikola	Weekly start timetable.
Remicade - infliximab - EMEA/H/C/000240/II/0205 MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder Opinion adopted on 21.09.2017. Request for Supplementary Information adopted on 20.07.2017.	Positive Opinion adopted by consensus on 21.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
RotaTeq - rotavirus vaccine (live, oral) - EMEA/H/C/000669/II/0069/G MAH: MSD Vaccins, Rapporteur: Greg Markey Request for Supplementary Information adopted on 21.04.2017.	Weekly start timetable.
TachoSil - human thrombin / human fibrinogen - EMEA/H/C/000505/II/0081 MAH: Takeda Austria GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 21.09.2017.	Weekly start timetable.
Tevagrastim - filgrastim - EMEA/H/C/000827/II/0064 MAH: TEVA GmbH, Duplicate, Duplicate of Biograstim, Rapporteur: Outi Mäki-Ikola	Weekly start timetable.
Vimizim - elosulfase alfa - EMEA/H/C/002779/II/0021/G, Orphan MAH: BioMarin Europe Ltd, Rapporteur: Johann Lodewijk Hillege	Weekly start timetable.
Xadago - safinamide - EMEA/H/C/002396/II/0019 MAH: Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege Opinion adopted on 21.09.2017.	Positive Opinion adopted by consensus on 21.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zaltrap - aflibercept - EMEA/H/C/002532/II/0038 MAH: sanofi-aventis groupe, Rapporteur: Filip Josephson Opinion adopted on 28.09.2017.	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1176/G **Nuwiq-EMEA/H/C/002813/WS1176/0019/G** **Vihuma-EMEA/H/C/004459/WS1176/0002/G** MAH: Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 28.09.2017.	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1243 **Rixathon-EMEA/H/C/003903/WS1243/0002** **Riximyo-EMEA/H/C/004729/WS1243/0002** MAH: Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 28.09.2017.	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Adempas - riociguat - EMEA/H/C/002737/II/0023, Orphan MAH: Bayer AG, Rapporteur: Johann Lodewijk Hillege, “Update of section 4.2 of the SmPC in order to add new information regarding posology for transitioning to and from riociguat based on results from study 16719: An open-label, international, multicentre, single-arm, uncontrolled, phase IIIb study of riociguat in patients with pulmonary arterial hypertension (PAH) who demonstrate an insufficient response to treatment with phosphodiesterase-5 inhibitors (PDE-5i). Section 5.1 of the SmPC was updated in parallel to reflect on the main study results. The Package Leaflet is updated accordingly.”	
Adempas - riociguat - EMEA/H/C/002737/II/0024/G, Orphan MAH: Bayer AG, Rapporteur: Johann Lodewijk Hillege, “II, C.I.4: Update of section 5.1 of the SmPC in order to reflect on results from study 12935 (PATENT-2): Long-term extension, multi-centre, multi-national study to evaluate the safety and tolerability of oral riociguat (1 mg, 1.5 mg, 2 mg, or 2.5 mg tid) in patients with symptomatic pulmonary arterial hypertension II, C.I.4: Update of section 5.1 of the SmPC in order to reflect on results from study 11349 (CHEST-2): Long-term extension, multi-centre, multi-national study to evaluate the safety and	

tolerability of oral riociguat (1 mg, 1.5 mg, 2 mg, or 2.5 mg tid) in patients with chronic thromboembolic pulmonary hypertension II, C.I.4: Update of section 5.1 of the SmPC in order to reflect on results from study 13605 (RISE-IIP): A randomized, double-blind, placebo-controlled phase II study to investigate the efficacy and safety of riociguat (0.5 mg, 1.0 mg, 1.5 mg, 2.0 mg and 2.5 mg tid) in patients with symptomatic pulmonary hypertension associated with idiopathic interstitial pneumonias”	
Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0027/G MAH: Biofrontera Bioscience GmbH, Rapporteur: Harald Enzmann, “C.I.4 Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the posology and method of administration of Ameluz for the treatment of actinic keratosis (AK) and field cancerization in combination with daylight and to update the safety information, based on the clinical study results from ALA-AK-CT009; this is a phase III, randomised, interventional, observer-blinded study aimed to compare the efficacy and safety of Ameluz in the treatment of mild to moderate AK with Metvix in combination with daylight photodynamic therapy. Section 5.2 of the SmPC has included a minor editorial change. 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. C.I.5.b Change in the legal status of Ameluz from “medicinal product subject to restricted medical prescription” to “medicinal product subject to medical prescription”.	
Bexsero - meningococcal group B vaccine (rDNA, component, adsorbed) - EMEA/H/C/002333/II/0059 MAH: GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, “Update of section 4.2 of the SmPC to update the dosing schedule for infants (2 months to 5 months of age) to allow for 2 primary doses plus 1 booster dose in the second year of life	

based on the results from study V72_28 and its extension V72_28E1 and to update the intervals between primary doses for children (2 years to 10 years of age) to not less than 1 month based on the results from the extension study V72_28E1. Update of section 4.8 of the SmPC to include the number of subjects exposed to at least 1 dose based on the results from the studies V72_28 and V72_28E1. Update of section 5.1 of the SmPC to update the information about immunogenicity in infants and children based on the results from the studies V72_28 and V72_28E1. The Package leaflet is updated accordingly. In addition, the MAH took the opportunity to make some editorial changes in the SmPC and labelling."	
Epivir - lamivudine - EMEA/H/C/000107/II/0104 MAH: ViiV Healthcare UK Limited, Rapporteur: Joseph Emmerich, "Update of section 4.5 of the SmPC of both Epivir tablets and oral solution, and section 4.4 of the SmPC for Epivir Oral solution only, to add information regarding the potential for interaction between lamivudine and sorbitol based on the results of Study 204857. Further, a minor amendment has been implemented throughout the SmPC to update the clinical terminology for 'Pneumocystis carinii pneumonia' to 'Pneumocystis jiroveci pneumonia'. In addition, the MAH has taken the opportunity to align the product information with the QRD template version 10, to make minor editorial changes in the annexes and to update the contact details of the local representative in Norway in the Package Leaflet." Request for Supplementary Information adopted on 21.09.2017, 05.05.2017.	Weekly start timetable.
Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0098 MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.8 of the SmPC in order to add membranous glomerulonephritis as a new Adverse event with a not known frequency following periodic cumulative review of adverse event data from the MAH adverse event (AE) database which resulted in the decision to update the company core data sheet. The Package Leaflet is updated accordingly. In addition, the Marketing	Negative Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

authorisation holder (MAH) took the opportunity to update the list of local representatives for Portugal in the Package Leaflet." Opinion adopted on 28.09.2017. Request for Supplementary Information adopted on 18.05.2017.	
Galafold - migalastat - EMEA/H/C/004059/II/0010, Orphan MAH: Amicus Therapeutics UK Ltd, Rapporteur: Johann Lodewijk Hillege, "Submission of the final report from study AT1001-041: A phase 3 open label extension study to assess the safety and efficacy of 150 mg migalastat HCl QOD in subjects with Fabry disease who have completed Studies AT1001-011, AT1001- 012 or FAB-CL-205, listed as a category 3 study in the RMP." Request for Supplementary Information adopted on 21.09.2017, 13.07.2017.	Weekly start timetable.
Humira - adalimumab - EMEA/H/C/000481/II/0169 MAH: AbbVie Limited, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to update the clinical data section based on interim data from the OLE Study M11-327 in non-infectious uveitis (A Multicenter Open-Label Study of the Long-term Safety and Efficacy of the Human Anti-TNF Monoclonal Antibody Adalimumab in Subjects with Non-infectious Intermediate, Posterior, or Panuveitis)" Request for Supplementary Information adopted on 20.07.2017.	Weekly start timetable.
Hycamtin - topotecan - EMEA/H/C/000123/II/0074 MAH: Novartis Europharm Ltd, Rapporteur: Filip Josephson, "To update the section 4.8 (Undesirable effects) of the SmPC in order to add two new identified ADRs: GI perforation and Mucosal inflammation, which have been identified for Hycamtin in the post-marketing experience. The package leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0, to update section 6.6 of the SmPC to remove the sentence "Liquid waste may be flushed with large amounts of water" as per EMA request on 25-May-2015 and to correct the renewal date in	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

the section 9 of the SmPC." Opinion adopted on 28.09.2017.	
Ibrance - palbociclib - **EMEA/H/C/003853/II/0006** MAH: Pfizer Limited, Rapporteur: Filip Josephson, "Update of sections 4.2, 4.8 and 5.1 in order to reflect the results of the study A5481008 (PALOMA-2) and of the Phase 2 portion of A5481010 single-arm study. The MAH took the opportunity to implement minor editorial changes to the PIL." Request for Supplementary Information adopted on 22.06.2017.	
Iclusig - ponatinib - **EMEA/H/C/002695/II/0041, Orphan** MAH: Incyte Biosciences UK Ltd, Rapporteur: Greg Markey, "Update of section 4.8 of the SmPC in order to update the safety information to include a paragraph in the SmPC section 4.8 on severe cutaneous reaction. The Package Leaflet is updated accordingly."	Weekly start timetable.
Izba - travoprost - **EMEA/H/C/002738/II/0008** MAH: Novartis Europharm Ltd, Rapporteur: Concepcion Prieto Yerro, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information in line with Travoprost 40 µg/mL Eye Drops PI, based on the review of clinical trial and post-marketing data along with literature references. The package leaflet section 4 is updated accordingly."	Weekly start timetable.
Kisplyx - lenvatinib - **EMEA/H/C/004224/II/0004** MAH: Eisai Europe Ltd., Rapporteur: Bart Van der Schueren, "Submission of full report regarding pharmacodynamic results (secondary endpoint) from Study E7080-G000-205." Opinion adopted on 28.09.2017. Request for Supplementary Information adopted on 18.05.2017.	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kyprolis - carfilzomib - **EMEA/H/C/003790/II/0018, Orphan** MAH: Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of section 4.4 of the SmPC to add a warning about increased incidence of fatal and serious adverse events of carfilzomib	

in combination with melphalan and prednisone in newly diagnosed transplant-ineligible multiple myeloma patients, with the aim to prevent use in this population. The update is based on CLARION study; a Randomized, Open-label Phase 3 Study of Carfilzomib, Melphalan, and Prednisone Versus Bortezomib, Melphalan, and Prednisone in Transplant-ineligible Patients With Newly Diagnosed Multiple Myeloma."	
Lenvima - lenvatinib - EMEA/H/C/003727/II/0008, Orphan MAH: Eisai Europe Ltd., Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of Clinical Study Report for Study E78080-J081-208" Request for Supplementary Information adopted on 20.07.2017, 06.04.2017.	Weekly start timetable.
Multaq - dronedarone - EMEA/H/C/001043/II/0038 MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Submission of the final results of a single historic prospective observational study to evaluate the efficacy of dronedarone in clinical practice (EFFECT-AF study). The product information and RMP remain unchanged." Request for Supplementary Information adopted on 01.06.2017.	Weekly start timetable.
Rapiscan - regadenoson - EMEA/H/C/001176/II/0026 MAH: Rapidscan Pharma Solutions EU Ltd., Rapporteur: Greg Markey, "Update of section 4.5 of the SmPC in order to add further information on molecular transporters based 5 non-clinical studies: Study-OPT-2016-045, Study-OPT-2016-046, Study-OPT-2016-099, Study-OPT-2016-100 and Study-OPT-2016-101."	Weekly start timetable.
Raxone - idebenone - EMEA/H/C/003834/II/0008, Orphan MAH: Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Carmela Macchiarulo, "Update of SmPC section 4.5 to include that CYP3A4 substrates known to have a narrow therapeutic index should be administered with caution in patients receiving idebenone, based on the final study report for study SNT-I-017: "An open-label study to assess the potential for pre-systemic inhibition of cytochrome P450 3A4 (CYP3A) by	Weekly start timetable.

idebenone in healthy male subjects using midazolam as a substrate". The Package Leafelt 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."	
Savene - dexrazoxane - EMEA/H/C/000682/II/0034/G MAH: Clinigen Healthcare Ltd, Rapporteur: Alexandre Moreau, "C.I.4 – Update of sections 4.2, 4.4, 5.2 of the SmPC in order to update the information on dose modification in patients with renal impairment based on PK modelling results from a study reported in the literature, the Package Leaflet is updated accordingly. C.I.4 – Update of section 4.5 of SmPC in order to update the information on PK interaction between dexrazoxane and doxorubicin and epirubicin, based on the literature review. C.I.4.z – Update of section 5.2 of SmPC in order to update the information on PK data in patients with extravasations based on study TT04. In addition, the MAH took the opportunity to update section 6.5 of the Savene SmPC, carton label and package insert to include reference to the bottle hangers and to bring the PI in line with the latest QRD template version 10."	
Sivextro - tedizolid phosphate - EMEA/H/C/002846/II/0021 MAH: Merck Sharp & Dohme Limited, Rapporteur: Bruno Sepodes, "Submission of the final report for the CANWARD 2016 study, a national population based surveillance system, assessing the prevalence of anti-microbial resistance in pathogens associated with respiratory, skin and soft tissue, urinary and bacteraemic infections in hospitalized patients in Canada, listed as a category 3 study in the RMP. This variation does not propose any changes to the product information." Opinion adopted on 21.09.2017.	Positive Opinion adopted by consensus on 21.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Spinraza - nusinersen - EMEA/H/C/004312/II/0001, Orphan MAH: Biogen Idec Ltd, Rapporteur: Bruno Sepodes, "Update of section 4.8 of the SmPC to include complications associated with lumbar puncture including serious infection. In addition,	Positive Opinion adopted by consensus on 21.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

the frequency on vomiting has been corrected to 'very common' in the list of adverse drug reactions (ADRs) in the same section. The package leaflet is updated accordingly." Opinion adopted on 21.09.2017.	
Tafinlar - dabrafenib - EMEA/H/C/002604/II/0025 MAH: Novartis Europharm Ltd, Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to include the results of a drug-drug interaction between dabrafenib and rosuvastatin (an OATP1B1/1B3 substrate) and between dabrafenib and midazolam (a CYP3A4 substrate) based on the final results of study 200919, a phase I open-label fixed sequence study to evaluate the effects of an OATP1B1/1B3 substrate (rosuvastatin) and of a CYP3A4 substrate (midazolam) on the repeat dose pharmacokinetics of dabrafenib in subjects with BRAFV60 mutation positive tumours, to fulfil MEA 001."	Weekly start timetable.
Telzir - fosamprenavir - EMEA/H/C/000534/II/0089 MAH: ViiV Healthcare UK Limited, Rapporteur: Joseph Emmerich, "Update of sections 4.6 and 5.2 of the SmPC in order to include new information on pregnancy based on data regarding placental transfer of amprenavir and a summary of the available data on fosamprenavir Antiviral Pregnancy Registry (APR). In addition, the MAH took this opportunity to make some QRD V10 updates in the labelling and some typographical corrections to the SmPC. The local representatives in the PL were updated."	Weekly start timetable.
Trobalt - retigabine - EMEA/H/C/001245/II/0047 MAH: Glaxo Group Ltd, Rapporteur: Hanne Lomholt Larsen, "Submission of amended clinical study report (CSR) for terminated post-authorisation efficacy study (PAES) RTG114855 "A randomised, double-blind, placebo-controlled, parallel-group, multicentre study to determine the efficacy and safety of 2 doses of retigabine immediate release (900 mg/day and 600 mg/day) used as adjunctive therapy in adult Asian subjects with drug-resistant partial-onset seizures"."	Weekly start timetable.
Visudyne - verteporfin -	

EMEA/H/C/000305/II/0095 MAH: Novartis Europharm Ltd, Rapporteur: Alexandre Moreau, “Update of sections 4.4 and 4.8 of the SmPC in order to add a warning to update the safety information to reflect current knowledge about the product based on new data from spontaneous reports on localised (skin) necrosis at the injection site following extravasation; 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 PI in line with the latest QRD template version 10.”	
Vyndaqel - tafamidis - EMEA/H/C/002294/II/0043, Orphan MAH: Pfizer Limited, Rapporteur: Joseph Emmerich, “Update of section 5.3 of the SmPC in order to include information on the completed 2-year carcinogenicity study in rats. In addition, the MAH took the opportunity to bring minor revisions to sections 2 and 4.6 of the SmPC, to correct a typographical error in Annex IIE and to align the PI with the latest QRD template version 10.0.”	Weekly start timetable.
Zeffix - lamivudine - EMEA/H/C/000242/II/0069 MAH: Glaxo Group Ltd, Duplicate, Duplicate of Epivir, Rapporteur: Joseph Emmerich, “Update of section 4.5 of the SmPC to add information regarding a potential interaction with sorbitol-containing medicines. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement a minor change in the labelling in line with the QRD template version 10.” Request for Supplementary Information adopted on 21.09.2017, 05.05.2017.	Weekly start timetable.
WS1156 **Combivir-EMEA/H/C/000190/WS1156/0090** **Kivexa-EMEA/H/C/000581/WS1156/0072** **Triumeq-EMEA/H/C/002754/WS1156/0042** **Trizivir-EMEA/H/C/000338/WS1156/0104** MAH: ViiV Healthcare UK Limited, Lead Rapporteur: Joseph Emmerich, “Update of section 4.5 of the SmPC to add information regarding the potential interaction between	Weekly start timetable.

lamivudine and sorbitol based on the results of Study 204857. The Package Leaflet has been updated accordingly. Further, a minor amendment has been implemented throughout the SmPC in order to update the clinical terminology of Pneumocystis carinii pneumonia to Pneumocystis jiroveci pneumonia. In addition, the MAH takes the opportunity to make minor editorial changes , to align the annexes with the QRD template version 10 and to update the contact details of the local representative in Norway in the Package Leaflet." Request for Supplementary Information adopted on 21.09.2017, 05.05.2017.	
WS1167 **Ebymect-EMEA/H/C/004162/WS1167/0021** **Edistride-EMEA/H/C/004161/WS1167/0016** **Forxiga-EMEA/H/C/002322/WS1167/0036** **Xigduo-EMEA/H/C/002672/WS1167/0032** MAH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder, "Update of sections 4.8 and 5.1 of the SmPC in order to add information regarding two initial combination studies (MB102021 and MB102034) in treatment-naïve patients of dapagliflozin 5 mg + metformin and dapagliflozin 10 mg + metformin, respectively, compared to each component separately. In addition, the Worksharing applicant (WSA) took the opportunity to bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 20.07.2017.	Weekly start timetable.
WS1193 **Evotaz-EMEA/H/C/003904/WS1193/0018** **Reyataz-EMEA/H/C/000494/WS1193/0113** MAH: Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Caroline Laborde, "To update sections 4.3 and 4.5 of the SmPC to include information on the contraindicated co-administration with grazoprevir-containing products, including elbasvir/grazoprevir fixed dose combination (used to treat chronic hepatitis C infection) reflecting the results of interaction studies. The Package Leaflets are updated accordingly. The RMP versions 13.0 and 5.0, for	Weekly start timetable.

Reyataz and Evotaz respectively have been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to make some editorial changes and typographical corrections in the REYATAZ and EVOTAZ Product Information." Request for Supplementary Information adopted on 28.09.2017.	
WS1210/G **Mekinist-EMEA/H/C/002643/WS1210/0021/G** **Tafinlar-EMEA/H/C/002604/WS1210/0026/G** MAH: Novartis Europharm Ltd, Lead Rapporteur: Paula Boudewina van Hennik, "Update of section 5.1 of the Mekinist (trametinib) and Tafinlar (dabrafenib) SmPC to include the 3-years overall survival (OS) results from study MEK115306 (COMBI-d), a phase III, randomised, double-blinded study comparing the combination of dabrafenib and trametinib to dabrafenib and placebo in first-line therapy for subjects with unresectable or metastatic BRAF V600/K mutation-positive cutaneous melanoma. Update of section 5.1 of the Mekinist (trametinib) and Tafinlar (dabrafenib) SmPC to include the 3-years overall survival (OS) results from study MEK116513 (COMBI-v), a phase III, open-label, 2 arm, randomised study comparing dabrafenib and trametinib combination therapy with vemurafenib monotherapy in BRAF V600 mutation-positive metastatic melanoma."	Weekly start timetable.
WS1222 **Ryzodeg-EMEA/H/C/002499/WS1222/0025** **Tresiba-EMEA/H/C/002498/WS1222/0029** **Xultophy-EMEA/H/C/002647/WS1222/0022** MAH: Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder, "Update of sections 4.2, 4.4 and 6.6 of the SmPC and relevant sections of the labelling and PL to minimise the potential risk of medication error as requested by PRAC (EPITT ref. No. 18893)."	

B.5.3. CHMP-PRAC assessed procedures

Defitelio - defibrotide - EMEA/H/C/002393/II/0026, Orphan	Weekly start timetable.

MAH: Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, "Update of sections 4.8 and 5.1 of the SmPC in order to update the frequencies of adverse reactions included in the tabulated list of adverse reactions and to update the clinical efficacy and safety information based on the results from study 2006-05 listed as category 3 in the RMP. This is a phase 3, open-label expanded access study designed to provide access to defibrotide as an investigational new drug to patients with severe hepatic veno-occlusive disease. The final study report is being submitted together with the revised risk management plan (version 3.0). The package leaflet is also being updated accordingly. In addition, the MAH took the opportunity to bring the SmPC in line with the latest QRD template (version 10), to update the list of local representatives in the package leaflet and to correct a translation error in the Polish, Finnish, Danish and Latvian languages." Request for Supplementary Information adopted on 28.09.2017.	
Galafold - migalastat - EMEA/H/C/004059/II/0011, Orphan MAH: Amicus Therapeutics UK Ltd, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Qun-Ying Yue, "Update of section 4.2 of the SmPC to provide further information on missing doses and to improve wording on the administration with food. No new data is submitted to support these changes. In addition, the MAH took this opportunity to include the ATC code and to update the local representatives in the Package Leaflet. Consequently changes are proposed in Annex I, IIIA and IIIB. The RMP version 2.0 has also been submitted" Request for Supplementary Information adopted on 28.09.2017.	Weekly start timetable.
Iclusig - ponatinib - EMEA/H/C/002695/II/0039/G, Orphan MAH: Incyte Biosciences UK Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, "Grouping of two variations to submit the final reports from two nonclinical studies (study RPT-03346 and study RPT-03342), performed to investigate the potential mechanism of action of ponatinib leading to vascular occlusion. Study RPT-03346 (Evaluation of the effects of	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

ponatinib on arterial remodeling and wall thickening in a murine model of stenosis) is listed in the agreed pharmacovigilance plan. The second study, RPT-03342 (Investigation of the Effects of Ponatinib on Photochemical-Induced Thrombosis in Mice and Rats) was conducted to further explore the potential relationship between ponatinib and thrombosis in a photochemical induced thrombosis model in mice and rats. An updated RMP (version 18) has been submitted, with the relevant amendments to reflect the submitted data. No update to the product information is triggered by these reports." Opinion adopted on 28.09.2017.	
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0033/G, Orphan MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, "C.I.4 (Type II) - Update of sections 4.4 and 5.1 of the SmPC in order to update the safety information related to bleeding related events based on final results from study PCYC-1132-NT listed as a category 3 (MEA 004.1) study in the RMP; this is an in-vitro study to evaluate the effect of ibrutinib on platelet aggregation; The Package Leaflet is updated accordingly. C.I.4 (Type II) - Update of section 4.4 and 4.5 of the SmPC in order to update the safety information based on final) results from study LYM1003 listed as a category 3 study in the RMP (MEA 009.1); this is a drug-drug interaction study to assess steady state PK of repeated oral doses of ibrutinib alone in patients with B-cell malignancies and when combined with a moderate and strong CYP3A inhibitor; The Package Leaflet is updated accordingly. C.I.4 (Type II) - Update of section 4.5 of the SmPC in order to update the safety information based on final results from study FK12024; this is a DDI study with CYP3A inhibitor posaconazole, in simulated subjects; The Package Leaflet is are updated accordingly. C.I.4 (Type II) - Update of section 4.4 of the SmPC in order to update the safety information	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on antimicrobial prophylaxis following routine pharmacovigilance activity.

C.I.11.z (Type IB) - Submission of an updated RMP in order to extend the closure date of study PCYC-1112-CA (ANX 003.2) to Q2 2019. Yearly updates will be submitted in Q2 2017 and Q2 2018. Annex II has been updated accordingly.

C.I.11.a (Type Iain) - To update the RMP to include an additional action for Study PCI-32765 CAN3001 (MEA017) to provide a “further interim report in 5 years’ from time from the cut-off date of the current report (12 November 2015)”. This change has been agreed by the CHMP in the outcome of EMA/H/C/ 003791/MEA/017.

The RMP version 6.8 has been submitted.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.”
Opinion adopted on 28.09.2017.
Request for Supplementary Information adopted on 09.06.2017.

INOmax - nitric oxide - EMEA/H/C/000337/II/0051
MAH: Linde Healthcare AB, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams

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Kyprolis - carfilzomib - EMEA/H/C/003790/II/0017/G, Orphan
MAH: Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Nikica Mirošević Skvrce, "C.I.4
Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information based on the second interim analysis of the overall survival data from study ENDEAVOR (study 20130398); this is a randomised, multicentre, open-label, phase 3 study of carfilzomib and dexamethasone compared to bortezomib with dexamethasone in patients with relapse multiple myeloma. The Package Leaflet is updated accordingly. The RMP version 9.0 has also been submitted.

C.I.4
Update of section 4.8 of the SmPC in order to revise the frequencies of certain adverse drug reactions based on the pooled data set including ENDEAVOR and 7 recently completed studies.

In addition, the Marketing authorisation holder (MAH) took the opportunity to add editorial changes in sections 4.2, 4.4, 6.3 and 6.6 of the SmPC. Editorial changes have also been included in the package leaflet and labelling."	
Lemtrada - alemtuzumab - EMEA/H/C/003718/II/0017 MAH: Genzyme Therapeutics Ltd, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Doris Stenver, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and long term use information in the posology following final results from study CAMMS03409 - An Extension Protocol For Multiple Sclerosis Patients Who Participated in Genzyme-Sponsored Studies of Alemtuzumab (ongoing at the time of the initial MAA) to evaluate the long term safety and efficacy of alemtuzumab in MS patients who received alemtuzumab during prior company-sponsored studies. The RMP version 3.0 has also been submitted. The PL has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0 and to introduce editorial corrections in the PI." Request for Supplementary Information adopted on 20.07.2017, 21.04.2017.	
Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0017 MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Almath Spooner, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect the long-term safety and efficacy data from Study VX12 809 105. Study VX12 809 105 is a Phase 3, rollover study to evaluate the safety and efficacy of long term treatment with LUM/IVA in subjects aged 12 years and older with cystic fibrosis, homozygous or heterozygous for the F508del CFTR mutation (MEA 001). A new version of the RMP (ver. 2.7) included in this submission has been updated to include the final data from Study 105. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted	

on 18.05.2017, 23.02.2017.	
Otezla - apremilast - EMEA/H/C/003746/II/0017 MAH: Celgene Europe Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Eva A. Segovia, , "Update of section 4.4 of the SmPC to include a warning on serious diarrhea, nausea, and vomiting following a safety cumulative review of all data source. The PL has been updated accordingly. RMP version 9.0 has been included to classify serious diarrhea, nausea, and vomiting as important potential risk. In addition the MAH took the opportunity to introduce editorial changes in Annex IIIA and to align the PI with QRD template 10.0."	
Rotarix - human rotavirus, live attenuated - EMEA/H/C/000639/II/0100 MAH: GlaxoSmithKline Biologicals S.A., Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Jean-Michel Dogné, "Submission of the final report from study ROTA-085-PMS (115927) listed as a category 3 study in the RMP. This is an observational prospective cohort study investigating the incidence of intussusception after vaccination for rotavirus gastroenteritis, conducted to determine the incidence of intussusception after vaccination with Rotarix in Japan." Opinion adopted on 28.09.2017.	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Sivextro - tedizolid phosphate - EMEA/H/C/002846/II/0019 MAH: Merck Sharp & Dohme Limited, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Dolores Montero Corominas, "Update of section 4.8 of the SmPC of the concentrate for solution for infusion formulation, in order to add information from BAY119-2631/16121, a Phase 3 randomized, double-blind, multi-centre study comparing the efficacy and safety of intravenous to oral 6-day tedizolid phosphate and intravenous to oral 10 day linezolid for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and change the reported expected frequency of the adverse reaction "infusion site phlebitis" from "uncommon" to "common". The Package Leaflet is updated accordingly. An updated RMP (version 3.0) has also been submitted, proposing to collect safety information regarding tedizolid phosphate by	Weekly start timetable.

conducting three investigator initiated studies and deleting the original proposed long term safety study. The MAH also took the opportunity to make minor editorial corrections throughout the product information." Request for Supplementary Information adopted on 06.07.2017.	
Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0117 MAH: GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to reflect the results from study10PN-PD-DIT-072, a phase III, open, controlled, multi-centric study to evaluate the immunogenicity, safety and reactogenicity of Synflorix in children at an increased risk of pneumococcal infection. The Package Leaflet is updated accordingly. An updated RMP version 16 has also been submitted. This submission fulfils the post-authorisation measure MEA 065." Request for Supplementary Information adopted on 06.07.2017.	Weekly start timetable.
Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0036/G MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "C.I.13: Submission of a Clinical Study Report for study 109HV321: A Randomized, Double-Blind, Phase 3b Study to Evaluate the Safety and Tolerability of BG00012 when Administered as 240 mg BID (twice daily) Dose Regimen with and without Aspirin Compared to Placebo or Following a Slow Titration (Category 3) C.I.13: Submission of a Clinical Study Report for study 109MS406 (ASSURE): A Phase 4, Randomized, Double-Blind Study with a Safety Extension Period to Evaluate the Effect of Aspirin on Flushing Events in Subjects with Relapsing-Remitting Multiple Sclerosis Treated with Tecfidera (Dimethyl Fumarate) Delayed-release Capsules (Category 4)" Request for Supplementary Information adopted on 28.09.2017, 05.05.2017.	Weekly start timetable.
Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0037 MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "C.I.4:	Weekly start timetable.

Submission of a Clinical Study Report for study 109MS307: An Open-Label Study to Assess the Immune Response to Vaccination in Tecfidera-Treated Versus Interferon-Treated Subjects With Relapsing Forms of Multiple Sclerosis (Category 3). Consequently, this variation includes an update to section 4.5 (Interaction with other medicinal products and other forms of interaction) of the Summary of Product Characteristics (SmPC) and section 2 of the package leaflet." Request for Supplementary Information adopted on 05.05.2017.	
Tresiba - insulin degludec - EMEA/H/C/002498/II/0028 MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "Update of section 5.1 of the SmPC based on new clinical data from a cardiovascular outcome trial EX1250-4080 (DEVOTE) conducted for Tresiba. DEVOTE was a randomised, double-blind and event-driven clinical trial with a median duration of 2 years comparing the cardiovascular safety of Tresiba versus insulin glargine (100 units/mL) in patients with type 2 diabetes mellitus at high risk of cardiovascular events. The RMP version 8.1 has consequently been agreed." Opinion adopted on 28.09.2017. Request for Supplementary Information adopted on 01.09.2017.	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xalkori - crizotinib - EMEA/H/C/002489/II/0050 MAH: Pfizer Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of sections 4.2, 4.3, 4.4, 4.8 and 5.2 of the SmPC in order to update the information about hepatic impairment based on the results of study (A8081012) which evaluated the effect of hepatic impairment on the pharmacokinetics and safety of crizotinib in advanced cancer patients. The package leaflet is updated accordingly. In addition, the final study report of study (A8081012) and an updated RMP version 7.4 are also being submitted."	
Xgeva - denosumab - EMEA/H/C/002173/II/0056 MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga,	

"Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to modify the special warnings and precautions for use and undesirable effects sections following the performance of a cumulative safety review of Multiple Vertebral Fractures (MVF) following treatment discontinuation from Xgeva clinical study database from 2 clinical trials 20060359 (ongoing randomized, placebo-controlled, blinded study of denosumab as adjuvant treatment for women with early-stage breast cancer at high risk of recurrence) and 20040113 (a completed phase 2 study comparing denosumab and intravenous (IV) bisphosphonate treatment, collected data on bone turnover markers during the 32-week post-treatment follow-up period) and post-marketing experience. The results of this analysis conclude that MVF may occur following discontinuation of XGEVA treatment; the Package Leaflet is updated accordingly. The RMP version 26.0 has also been submitted accordingly. A Direct Healthcare Professional Communication is also submitted in Module 1.8.2, to inform prescribers about the new identified risk of MVF following discontinuation of XGEVA. The proposed minor change to Section 5.1 (Pharmacodynamic Effects) to provide some further information to prescribers regarding the reversibility of the inhibition of bone turnover following cessation of treatment."	
Zelboraf - vemurafenib - EMEA/H/C/002409/II/0042/G MAH: Roche Registration Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from studies MO25515 (MEA006) [An Open-Label, Multicenter Study to Assess the Safety of RO5185426 (Vemurafenib) in Patients with Metastatic Melanoma] and GP28492 (MEA010) [ZeSS: A Prospective Observational Safety Study of Patients with BRAFV600 Mutationpositive Unresectable or Metastatic Melanoma Treated with Vemurafenib (Zelboraf®)]" Request for Supplementary Information adopted on 28.09.2017.	Weekly start timetable.
Zydelig - idelalisib - EMEA/H/C/003843/II/0035/G MAH: Gilead Sciences International Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, "Update of section 5.3 of the SmPC	Weekly start timetable.

in order to revise the carcinogenicity information for idelalisib based on final results from two long term carcinogenicity studies (TX-312-2017, TX-312-2019). The RMP version 2.3 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0." Request for Supplementary Information adopted on 28.09.2017.	
Zykadia - ceritinib - EMEA/H/C/003819/II/0015 MAH: Novartis Europharm Ltd, 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 information 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 22.06.2017.	See Agenda 9.1
WS1190/G **Enbrel-EMEA/H/C/000262/WS1190/0210/G** **Lifmior-EMEA/H/C/004167/WS1190/0009/G** MAH: Pfizer Limited, Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Patrick Batty Request for Supplementary Information adopted on 28.09.2017.	Weekly start timetable.

B.5.4. PRAC assessed procedures

PRAC Led **Herceptin - trastuzumab - EMEA/H/C/000278/II/0135** MAH: Roche Registration Limited, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from study BO20652 (OHERA), a non-interventional study aimed to determine the incidence of symptomatic congestive heart failure and cardiac death in patients with HER2-positive early breast cancer treated with Herceptin as per routine clinical practice. This study is listed as a	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

category 3 study in the RMP. The RMP version 18.0 has also been submitted." Opinion adopted on 28.09.2017.	
PRAC Led **Inflectra - infliximab -** **EMEA/H/C/002778/II/0054** MAH: Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "Submission of the final study report of the Post-Marketing Surveillance of Inflectra 100 mg (Infliximab) to Evaluate Its Safety and Efficacy in Korea. The study intended to identify any unexpected adverse event and serious adverse event and frequency and pattern of occurrence of adverse events under the condition of general clinical practice and determine any factor that may affect the safety and efficacy." Request for Supplementary Information adopted on 28.09.2017.	Weekly start timetable.
PRAC Led **Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) -** **EMEA/H/W/002300/II/0020** MAH: GlaxoSmithkline Biologicals SA, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Bart Van der Schueren, "Update of the RMP (version 3.0) in order to 1) add cerebral malaria as an important potential risk, 2) add mortality by gender as missing information, 3) add the WHO Pilot Implementation Programme as a category 3 study, 4) change the study dates for studies Malaria-073 (200596, Phase IIIb randomized, open, controlled study to evaluate the immunogenicity and safety of Mosquirix, when administered as primary vaccination at 6, 7.5 and 9 months of age with or without coadministration of measles and rubella and yellow fever vaccines to children living in sub-Saharan, Africa), EPI-MAL-002(115055, an observational cohort study to estimate the incidence of AESI, of meningitis and of other AE leading to hospitalisation or death, in children, prior to implementation of Mosquirix), EPI-MAL-003 (115056, a prospective surveillance study to evaluate the safety, the effectiveness and the impact of Mosquirix in infants and young	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

children in sub-Saharan Africa), EPI-MAL-005 (116682, an epidemiology study to assess Plasmodium falciparum parasite prevalence and malaria control measures in catchment areas of two interventional studies pre- and post-Mosquirix introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit-risk in children in sub-Saharan Africa), EPI-MAL-010 (205071, a longitudinal, cross-sectional ancillary study of the EPI-MAL-005 study to evaluate the genetic diversity in circumsporozoite sequences before and after the implementation of Mosquirix in malaria-positive subjects ranging from 6 months to less than 5 years of age), 5) amend the protocol of study EPI-MAL-002, 6) update the draft protocol of study EPI-MAL-003, 7) provide a new draft of the protocol of study EPI-MAL-010, 8) provide a new protocol for the Pilot Implementation Programme." Opinion adopted on 28.09.2017. Request for Supplementary Information adopted on 09.06.2017.	
PRAC Led **Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0062** MAH: Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Caroline Laborde, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final study report of non-interventional, non-imposed PASS study "Myozyme (alglucosidase alfa) Safety Information Packet effectiveness evaluation: a healthcare professional survey" (Myozyme SIP EU HCP Survey, ALGMYC08432). In addition, updated RMP version 8.0 has been submitted as part of this application." Opinion adopted on 28.09.2017. Request for Supplementary Information adopted on 09.06.2017.	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0020** MAH: Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an amended protocol for PASS study NN7008-3553, category 3 study in the RMP. Submission of an updated RMP version 3 to	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

update the timelines of the milestones in order to integrate the required additional pharmacovigilance activities, which include a change in the Last Patient Last Visit (LPLV) date and a change in the Clinical Trial Report (CTR) finalisation date. In addition, the duration of the trial has been amended from 4 to 7 years." Opinion adopted on 28.09.2017. Request for Supplementary Information adopted on 06.07.2017.	
PRAC Led **Remsima - infliximab - EMEA/H/C/002576/II/0045** MAH: Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "Submission of the final study report of the Post-Marketing Surveillance of REMSIMA 100 mg (Infliximab) to Evaluate Its Safety and Efficacy in Korea. The study intended to identify any unexpected adverse event and serious adverse event and frequency and pattern of occurrence of adverse events under the condition of general clinical practice and determine any factor that may affect the safety and efficacy." Request for Supplementary Information adopted on 28.09.2017.	Weekly start timetable.
PRAC Led **Revlimid - lenalidomide - EMEA/H/C/000717/II/0095, Orphan** MAH: Celgene Europe Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final results of the non-interventional, observational category 3 post-authorisation safety study (Study CC-5013-PASS-001) in subjects treated with lenalidomide to further characterise the safety profile of lenalidomide plus dexamethasone in the treatment of relapsed and/or refractory (R/R) MM in a real-world setting." Request for Supplementary Information adopted on 20.07.2017.	
PRAC Led **Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0045** MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission	Weekly start timetable.

of the final report from study 109MS419 listed as a category 3 study in the RMP. This is a retrospective, multicentre, observational study aimed to assess the effect of tecfidera delayed-release capsules on lymphocyte subsets in patients with relapsing forms of multiple sclerosis." Request for Supplementary Information adopted on 28.09.2017.	
PRAC Led **Xarelto - rivaroxaban - EMEA/H/C/000944/II/0055** MAH: Bayer AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final study report of a non-interventional PASS listed as a category 3 study in the RMP (MEA 019): An Observational Post-Authorization Safety Specialist Cohort Event Monitoring Study (SCEM) to Monitor the Safety and Utilization of Rivaroxaban (Xarelto) for the Prevention of Stroke in Patients with AF, Treatment of DVT and PE, and the Prevention of Recurrent DVT and PE in the Secondary Care Setting in England and Wales (The ROSE Study), study number 16171." Request for Supplementary Information adopted on 28.09.2017.	Weekly start timetable.
PRAC Led **Zavesca - miglustat - EMEA/H/C/000435/II/0057, Orphan** MAH: Actelion Registration Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, PRAC-CHMP liaison: Kristina Dunder, "Update of the RMP version 12.2 in order to remove the important identified risks of diarrhoea and other gastrointestinal (GI) events and tremor and the important potential risk of seizure in NP-C patients." Opinion adopted on 28.09.2017.	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1164** **Glyxambi-EMEA/H/C/003833/WS1164/0008** **Jardiance-EMEA/H/C/002677/WS1164/0033** **Synjardy-EMEA/H/C/003770/WS1164/0030** MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead	Weekly start timetable

PRAC Rapporteur: Dolores Montero Corominas, PRAC-CHMP liaison: Concepcion Prieto Yerro, "C.I.11: Submission of an updated RMP for Jardiance (v12.1), for Synjardy (9.2) and for Glyxambi (v3.0) in order to address the PRAC recommendation concluded in the Article 20 referral for SGLT2 inhibitors on the important potential risk for lower limb amputation. Additionally, the PRAC request to include pancreatitis as important potential risk for empagliflozin-containing medicines following the conclusion adopted by the PRAC after the review of PSUSA/00010077/201603 (canagliflozin) is discussed." Request for Supplementary Information adopted on 28.09.2017.	
PRAC Led **WS1207** **Bretaris Genuair-EMEA/H/C/002706/WS1207/0034** **Eklira Genuair-EMEA/H/C/002211/WS1207/0034** MAH: AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, Lead PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Robert James Hemmings, "Submission of the final report from study D6560R00005, (Aclidinium Bromide Drug Utilisation Post-Authorisation Safety Studies (DUS 1) in the United Kingdom, Denmark, and Germany) listed as a category 3 study in the RMP (MEA002). The updated RMP version 6.0 has also been submitted." Request for Supplementary Information adopted on 28.09.2017.	Weekly start timetable

B.5.5. CHMP-CAT assessed procedures

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/II/0005/G, Orphan, ATMP MAH: MolMed SpA, Rapporteur: Johannes Hendrikus Ovelgonne	

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

WS1183 **Ambirix-EMEA/H/C/000426/WS1183/0085** **Cervarix-EMEA/H/C/000721/WS1183/0090** **Infanrix hexa-EMEA/H/C/000296/WS1183/0223** **Synflorix-EMEA/H/C/000973/WS1183/0122** **Twinrix Adult-EMEA/H/C/000112/WS1183/0119** **Twinrix Paediatric-EMEA/H/C/000129/WS1183/0120** MAH: GlaxoSmithkline Biologicals SA, Lead Rapporteur: Kristina Dunder	Weekly start timetable.
WS1217 **Entresto-EMEA/H/C/004062/WS1217/0015** **Neparvis-EMEA/H/C/004343/WS1217/0013** MAH: Novartis Europharm Ltd, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 28.09.2017.	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1228/G **Silodyx-EMEA/H/C/001209/WS1228/0028/G** **Urorec-EMEA/H/C/001092/WS1228/0031/G** MAH: Recordati Ireland Ltd, Lead Rapporteur: Nithyanandan Nagercoil Opinion adopted on 28.09.2017.	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1238/G **Leganto-EMEA/H/C/002380/WS1238/0025/G** **Neupro-EMEA/H/C/000626/WS1238/0079/G** MAH: UCB Pharma S.A., Lead Rapporteur: Bruno Sepodes	Weekly start timetable.
WS1247/G **Enurev Breezhaler-EMEA/H/C/002691/WS1247/0022/G** **Seebri Breezhaler-EMEA/H/C/002430/WS1247/0022/G** **Tovanor Breezhaler-EMEA/H/C/002690/WS1247/0024/G** **Ultibro Breezhaler-EMEA/H/C/002679/WS1247/001**	Positive Opinion adopted by consensus on 28.09.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

6/G
Ulunar
Breezhaler-EMEA/H/C/003875/WS1247/001
6/G
Xoterna
Breezhaler-EMEA/H/C/003755/WS1247/001
9/G
MAH: Novartis Europharm Ltd, Lead Rapporteur: Hanne Lomholt Larsen
Opinion adopted on 28.09.2017.

WS1260
Blitzima-EMEA/H/C/004723/WS1260/0003
Ritemvia-EMEA/H/C/004725/WS1260/0003
Rituzena-EMEA/H/C/004724/WS1260/0004
MAH: Celltrion Healthcare Hungary Kft., Duplicate, Duplicate of Truxima, Lead Rapporteur: Sol Ruiz

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

Protopic - tacrolimus - EMEA/H/C/000374/II/0071/G
MAH: LEO Pharma A/S, Rapporteur: Peter Kiely
Withdrawal request submitted on 20.09.2017.

The MAH withdrew the procedure on 20.09.2017.

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

- buprenorphine - EMEA/H/C/004651
, treatment of opioid dependence within a framework of medical, social and psychological treatment

- durvalumab - EMEA/H/C/004771
, treatment of locally advanced, unresectable non-small cell lung cancer (NSCLC)

- damoctocog alfa pegol - EMEA/H/C/004054, Orphan
, Treatment and prophylaxis of haemophilia A

- pegfilgrastim - EMEA/H/C/004700
, treatment of neutropenia

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

- exenatide -

EMEA/H/C/002020/X/0048/G

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

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

- antithrombin alfa -
EMEA/H/C/000587/S/0030

- asfotase alfa -
EMEA/H/C/003794/S/0024, Orphan
MAH: Alexion Europe SAS

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

Iclusig - ponatinib -
EMEA/H/C/002695/R/0042, Orphan
MAH: Incyte Biosciences UK Ltd

Memantine ratiopharm - memantine -
EMEA/H/C/002671/R/0011
, Generic, Generic of Ebixa

Spedra - avanafil -
EMEA/H/C/002581/R/0029

Stribild - elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil -
EMEA/H/C/002574/R/0086

Voriconazole Accord - voriconazole -
EMEA/H/C/002669/R/0017
MAH: Accord Healthcare Limited, Generic, Generic of Vfend

Xtandi - enzalutamide -
EMEA/H/C/002639/R/0037
MAH: Astellas Pharma Europe B.V.

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

Cabometyx - cabozantinib -
EMEA/H/C/004163/II/0003
MAH: Ipsen Pharma, Rapporteur: Robert James Hemmings, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Sabine Straus, “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 ofthe 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.”	
Feraccru - ferric maltol - EMEA/H/C/002733/II/0010 MAH: Shield TX (UK) Ltd, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Harald Enzmann, PRAC Rapporteur: Adam Przybylkowski, “Extension of indication to widen the indication for Feraccru from the treatment “in adults with Iron deficiency anaemia in patients with IBD” to the treatment of “adults with Iron deficiency”; As a consequence, sections 4.1, 4, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.”	
Inovelon - rufinamide - EMEA/H/C/000660/II/0045, Orphan MAH: Eisai Ltd, Rapporteur: Alexandre Moreau, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Ghania Chamouni, “Extension of indication to include the treatment of seizures associated with Lennox Gastaut syndrome in patients 1 year of age and older as adjunctive therapy. As a consequence sections 4.1, 4.2, 4.5, 5.1 and 5.2. The Package Leaflet and the RMP (version 10.0) are updated accordingly. In addition the Marketing Authorisation Holder (MAH) took the opportunity to make small corrections with the Product Information and to update the name and contact details of the local representative in Belgium and Luxembourg. Furthermore, the Product Information is brought	

in line with the latest QRD template version 10."

Kalydeco - ivacaftor -
EMEA/H/C/002494/II/0063/G, Orphan
MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Dolores Montero Corominas, "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.II.e.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.II.e.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."

Opdivo - nivolumab -
EMEA/H/C/003985/II/0039
MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski,"Extension of Indication to include treatment of adult patients with advanced or recurrent gastric or gastroesophageal junction (GEJ) cancer after two or more prior systemic therapies, based on data from study ONO-4538-12. As a consequence, sections 4.1, 4.4, 4.8, and 5.1 of the SmPC are updated. The Annex II and Package Leaflet are updated in accordance. The RMP version version 11.0 has also been submitted."

Perjeta - pertuzumab -
EMEA/H/C/002547/II/0034
MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Doris Stenver, "Extension of Indication for Perjeta in combination with trastuzumab and chemotherapy for the adjuvant treatment of adult patients with HER2-positive early breast cancer. The submission is based on the primary analysis of efficacy and safety data from the pivotal Phase III study BIG-4-11/BO25126/TOC4939g (APHINITY). With

the submission of the APHINITY data, the MAH also aims to fulfil the Annex IID obligation from the approval of the neoadjuvant indication of Perjeta granted in 2015. Sections 4.2, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are. Annex II and the Package Leaflet have been updated accordingly. The RMP version 10.0 has also been submitted." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)	
Translarna - ataluren - EMEA/H/C/002720/II/0037, Orphan MAH: PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus, "Extension of Indication to include a new population (children from 2 to less than 5 years of age) for Translarna; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and RMP (version 7.1) is updated in accordance."	
Xeljanz - tofacitinib - EMEA/H/C/004214/II/0006 MAH: Pfizer Limited, Rapporteur: Robert James Hemmings, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus,"Extension of Indication to include treatment of adult patients with active psoriatic arthritis who have had an inadequate response or who have been intolerant to a prior disease-modifying anti-rheumatic drug (DMARD) therapy, based on data from studies A3921091, A3921092, A3921125. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the Annex II with minor editorial changes. The RMP version 3.0 has also been submitted."	

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

DuoTrav - travoprost / timolol - EMEA/H/C/000665/II/0051 MAH: Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro,	
Eliquis - apixaban - EMEA/H/C/002148/II/0049/G	

MAH: Bristol-Myers Squibb / Pfizer EEIG,
Rapporteur: Johann Lodewijk Hillege,

Kevzara - sarilumab -
EMEA/H/C/004254/II/0003/G
MAH: sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus,

Kineret - anakinra -
EMEA/H/C/000363/II/0058
MAH: Swedish Orphan Biovitrum AB (publ),
Rapporteur: Sinan B. Sarac,

Kyprolis - carfilzomib -
EMEA/H/C/003790/II/0020, Orphan
MAH: Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez,

Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine -
EMEA/H/C/002226/II/0069
MAH: Pfizer Limited, Rapporteur: Greg Markey,

Nucala - mepolizumab -
EMEA/H/C/003860/II/0011
MAH: GlaxoSmithKline Trading Services Limited,
Rapporteur: Nithyanandan Nagercoil,

NutropinAq - somatropin -
EMEA/H/C/000315/II/0068/G
MAH: Ipsen Pharma, Rapporteur: Hanne Lomholt Larsen,

Praluent - alirocumab -
EMEA/H/C/003882/II/0030
MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege,

Scenesse - afamelanotide -
EMEA/H/C/002548/II/0017, Orphan
MAH: Clinuvel (UK) Limited, Rapporteur: Harald Enzmann,

Strensiq - asfotase alfa -
EMEA/H/C/003794/II/0026/G, Orphan
MAH: Alexion Europe SAS, Rapporteur: Greg Markey,

Travatan - travoprost -
EMEA/H/C/000390/II/0057
MAH: Novartis Europharm Ltd, Rapporteur: Concepcion Prieto Yerro,

Xofigo - radium-223 -
EMEA/H/C/002653/II/0027

MAH: Bayer AG, Rapporteur: Harald Enzmann,

WS1233/G
Hexacima-EMEA/H/C/002702/WS1233/0070/G
Hexaxim-EMEA/H/W/002495/WS1233/0075/G
Hexyon-EMEA/H/C/002796/WS1233/0074/G
MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus

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

Buccolam - midazolam - EMEA/H/C/002267/II/0035
MAH: Shire Services BVBA, Rapporteur: Johann Lodewijk Hillege,"Update of SmPC sections 4.4 and 4.5 to strengthen the warning regarding concomitant administration of benzodiazepines and opioids following a recent review of the MAH's safety databases and literature. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to align the annexes with the latest QRD template and to update the contact details of the MAH in the Package Leaflet."

CellCept - mycophenolate mofetil - EMEA/H/C/000082/II/0136
MAH: Roche Registration Limited, Rapporteur: Greg Markey, "Update of sections 4.4 and 4.5 of the SmPC of all pharmaceutical forms, in order to update information regarding potential interactions with antibiotics and drugs interfering with glucuronidation pathway, based on a review of published literature. The Package Leaflet is updated accordingly. In addition, update of section 6.6 of the SmPC and section 3 of the package leaflet to improve the recommendations regarding safe handling of the powder for oral suspension formulation as well as other minor editorial changes."

Invirase - saquinavir - EMEA/H/C/000113/II/0122
MAH: Roche Registration Limited, Rapporteur: Milena Stain,"Update of sections 4.2, 4.3, and 4.5 of the SmPC following an update to the Company Core Data Sheet in order to include a cross-reference to a new contraindication against switching from rilpivirine to invirase/ritonavir

(section 4.2), to include lurasidone in the contraindications section (section 4.3) and to add information on additional interactions regarding lurasidone, rilpivirine, dasatinib, and sunitinib (section 4.5). The existing information regarding the interaction with alfuzosin has been updated to include a warning that co-administration may also cause potentially life-threatening cardiac arrhythmia. The existing information regarding interaction with medicines listed in the section 'neuroleptics' has been moved to the section 'antipsychotics' (section 4.5).
The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity the PI to correct formatting and minor typographical errors."

Natpar - parathyroid hormone - EMEA/H/C/003861/II/0005, Orphan
MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Bart Van der Schueren, "Update of section 5.1 of the SmPC in order to include the 60 months interim results of the long-term safety and efficacy study (PAR-C10-008); this is a long-term open-label study investigating the safety and tolerability of NPSP558, a recombinant human parathyroid hormone (rhPTH[1-84]), for the treatment of adults with hypoparathyroidism – a clinical extension study (RACE)."

Natpar - parathyroid hormone - EMEA/H/C/003861/II/0006, Orphan
MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Bart Van der Schueren, "Submission of the final report from studies (R7661M-SHP634 and R7673M-SHP634) listed as a category 3 studies in the RMP.

Study R7661M-SHP634 is a Comparison of the Effects of Once- versus Twice-Daily Dosing with NPSP558 (Recombinant Human Parathyroid Hormone (1-84)) on Osteoblast Proliferation and Bone
Formation in the Male Fischer 344 Rats.

Study R7673M-SHP634 is A 13-Week Subcutaneous Injection Study of NPSP558 (Recombinant Human PTH (1-84)) with an 8-Week Recovery Period in Juvenile Rats."

Roteas - edoxaban - EMEA/H/C/004339/II/0003
MAH: Daiichi Sankyo Europe GmbH, Rapporteur:

Concepcion Prieto Yerro,“Update of sections 4.2 and 5.1 of the SmPC in line with changes already introduce to Lixiana (EMEA/H/C/002629/II/0012) in order to add information deriving from clinical data for the use of edoxaban as anticoagulant therapy for patients with non-valvular atrial fibrillation undergoing cardioversion. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.8 of the SmPC as per the requirement of the finalised PSUSA/00010387/201610 procedure to include headache, abdominal pain and dizziness with a common frequency as new adverse drug reactions. The MAH took also the opportunity to bring the PI in line with the latest QRD template version 10.0. The MAH also took the occasion to introduce some editorial changes and minor corrections.”

Starlix - nateglinide - EMEA/H/C/000335/II/0033

MAH: Novartis Europharm Ltd, 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.”

Velphoro - mixture of polynuclear iron(III)-oxyhydroxide, sucrose and starches - EMEA/H/C/002705/II/0012

MAH: Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Johann Lodewijk Hillege, “Update of section 4.4 of the SmPC in order to remove a gluten warning for patients with allergy to gluten. The Package Leaflet has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor corrections in the SmPC in line with the Company Core Data Sheet (CCDS). Moreover, the MAH took the opportunity to bring the Annex IIIA in line with the latest QRD

template version 10."

Zostavax - shingles (herpes zoster) vaccine (live) - EMEA/H/C/000674/II/0115

MAH: MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.4 of the SmPC in order to include that fatal outcomes have been reported in individuals who are immunosuppressed or immunodeficient, based on post-marketing case reports. In addition, the MAH took the opportunity to make some editorial changes to the English product information and to following linguistic versions of the product information: NL, CZ, EL, ES, IT, NO, PL, PT, SV, SL, SK, HR, HU and FI."

B.6.10. CHMP-PRAC assessed procedures

Kuvan - sapropterin - EMEA/H/C/000943/II/0052, Orphan

MAH: BioMarin International LimitedRapporteur: Peter Kiely,"Based on a review of the post-marketing experience and in order to harmonize the safety information with the CCDS, update of section 4.4 of the Kuvan SmPC to add a warning regarding gastritis and update of section 4.8 to add the following adverse events regarding gastrointestinal tract and respiratory irritation: oropharyngeal pain, oesophageal pain, dyspepsia, nausea, gastritis and pharyngitis. The Package Leaflet is updated accordingly. The RMP version 13.0 has also been submitted."

Trulicity - dulaglutide - EMEA/H/C/002825/II/0022

MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey, PRAC Rapporteur: Carmela Macchiarulo, "Update of sections 4.2, 5.1 and 5.2 of the SmPC for Trulicity following completion of a Phase 3 study (H9X-MCGBDX (GBDX)) comparing the effect of once-weekly Trulicity with insulin glargine on glycaemic control over 52 weeks in patients with type 2 Diabetes Mellitus and moderate or severe chronic kidney disease.

In addition, an update to the ATC code and a correction to the "Instructions for use" in Section 6.6 of the SmPC to make it consistent with instructions on "How to store Trulicity" in the Package Insert Leaflet (PL) are proposed.

The RMP version 1.11 has also been submitted."

WS1248/G
Blitzima-EMEA/H/C/004723/WS1248/0002/G
Ritemvia-EMEA/H/C/004725/WS1248/0002/G
Rituzena-EMEA/H/C/004724/WS1248/0003/G
MAH: Celltrion Healthcare Hungary Kft., Duplicate, Duplicate of Truxima, Lead Rapporteur: Sol Ruiz, Lead PRAC Rapporteur: Doris Stenver,

B.6.11. PRAC assessed procedures

PRAC Led
Betaferon - interferon beta-1b - EMEA/H/C/000081/II/0118
MAH: Bayer AG, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg MarkeySubmission of the final report from study BETAPAEDIC, listed as a category 3 study in the RMP. This was a non-interventional study evaluating safety and tolerability of Betaferon in paediatric patients with multiple sclerosis.
The RMP version 3.2 has also been submitted."

PRAC Led
Eliquis - apixaban - EMEA/H/C/002148/II/0048
MAH: Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege"Submission of the final report from study (B0661073) listed as a category 4 study in the RMP. This is a non-interventional post-authorisation safety study (PASS) of the utilisation patterns of apixaban in Denmark. In addition, a revised RMP (version 18.0) is submitted."

PRAC Led
Eylea - aflibercept - EMEA/H/C/002392/II/0039
MAH: Bayer AG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau"Submission of the final report from the post authorisation safety study 16526, listed as a category 3 study in the RMP. This is an observational study to evaluate the physician and patient knowledge of safety and safe use

information for Aflibercept in Europe as stated in the EU Educational Material of Eylea."

PRAC Led

Nulojix - belatacept - EMEA/H/C/002098/II/0047/G

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson"Submission of the final report from studies IM103061 and IM103089, listed as a category 3 studies in the RMP.

IM103061 is an epidemiological study on pregnancy outcome among belatacept users in the US.

IM103089 evaluates data retrospectively to assess the association between belatacept and the risk of PTDL in renal transplant recipients in Europe.

An updated RMP, reflecting completion of the two above studies is being submitted as part of this variation (Version 15)."

PRAC Led

Sebivo - telbivudine - EMEA/H/C/000713/II/0048

MAH: Novartis Europharm Ltd, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Caroline Laborde, PRAC-CHMP liaison: Joseph Emmerich"Submission of an updated RMP version 11.0 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."

PRAC Led

WS1229

Ebymect-EMEA/H/C/004162/WS1229/0025

Edistride-EMEA/H/C/004161/WS1229/0019

Forxiga-EMEA/H/C/002322/WS1229/0039

Xigduo-EMEA/H/C/002672/WS1229/0036

AH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Qun-Ying Yue, PRAC-CHMP liaison: Kristina Dunder"Submission of the final report from study D1690R00013 listed

as a category 3 study in the RMP: Incidence of Diabetic Ketoacidosis among Patients with Type 2 Diabetes in the United States.
The RMP version 15 (Forxiga/Edistride) and version 10 (Xigduo/Ebymect) have been consequentially updated."

PRAC Led

WS1256

Harvoni-EMEA/H/C/003850/WS1256/0059

Sovaldi-EMEA/H/C/002798/WS1256/0044

MAH: Gilead Sciences International Limited, Lead PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey"Submission of the final report from study GS-EU-337-2030, listed as a category 3 study in the RMP. This is an observational, cross-sectional post-authorisation safety study to assess healthcare provider awareness of risks related to sofosbuvir and ledipasvir/sofosbuvir."

PRAC Led

WS1259

Ebymect-EMEA/H/C/004162/WS1259/0024

Edistride-EMEA/H/C/004161/WS1259/0018

Forxiga-EMEA/H/C/002322/WS1259/0038

Xigduo-EMEA/H/C/002672/WS1259/0035

AH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Qun-Ying Yue, PRAC-CHMP liaison: Kristina Dunder"Submission of the final report for the Drug Utilisation Study MB102-134 listed as a category 3 study in the RMP: Observational Single-cohort Data Base Study of Dapagliflozin Utilization in Europe.
The RMP version 15 (Forxiga/Edistride) and version 10 (Xigduo/Ebymect) have been consequentially updated."

PRAC Led

WS1264

Ariclaim-EMEA/H/C/000552/WS1264/0068

Cymbalta-EMEA/H/C/000572/WS1264/0072

Duloxetine Lilly-EMEA/H/C/004000/WS1264/0008

Xeristar-EMEA/H/C/000573/WS1264/0075

Yentreve-EMEA/H/C/000545/WS1264/0058

MAH: Eli Lilly Nederland B.V., Duplicate, Duplicate of Yentreve, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, PRAC-CHMP liaison: Concepcion Prieto Yerro"Submission of the final report from study F1J-MC-B056 listed as a category 3 study in the RMP. This is a non-interventional non-imposed study aimed to investigate the association between duloxetine exposure and suicide-related behaviours and ideation in women with stress urinary inconsistence (SUI). The RMP version 12.3 has also been submitted."

B.6.12. CHMP-CAT assessed procedures

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

WS1199/G
ProQuad-EMEA/H/C/000622/WS1199/0120/G
Zostavax-EMEA/H/C/000674/WS1199/0114/G

MAH: MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus

WS1245
Infanrix hexa-EMEA/H/C/000296/WS1245/0228

MAH: GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1246/G
Epclusa-EMEA/H/C/004210/WS1246/0017/G
Harvoni-EMEA/H/C/003850/WS1246/0060/G
Sovaldi-EMEA/H/C/002798/WS1246/0045/G
Vosevi-EMEA/H/C/004350/WS1246/0005/G

MAH: Gilead Sciences International Limited, Lead Rapporteur: Filip Josephson

WS1263/G
Avamys-EMEA/H/C/000770/WS1263/0035/G
Relvar Ellipta-EMEA/H/C/002673/WS1263/0034/G
Revinty Ellipta-EMEA/H/C/002745/WS1263/0030/G
MAH: Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro

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WS1279
Helixate NexGen-EMEA/H/C/000276/WS1279/0193
KOGENATE Bayer-EMEA/H/C/000275/WS1279/0201
MAH: Bayer AG, Lead Rapporteur: Jan Mueller-Berghaus

WS1280
Blitzima-EMEA/H/C/004723/WS1280/0005
Ritemvia-EMEA/H/C/004725/WS1280/0005
Rituzena-EMEA/H/C/004724/WS1280/0006
MAH: Celltrion Healthcare Hungary Kft., Duplicate, Duplicate of Truxima, Lead Rapporteur: Sol Ruiz

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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

Disclosure of information related to plasma master files cannot be released at 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):

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

Qualification of Biomarkers:

HTA:

Post-Scientific Advice Issues:

G.2. Ongoing procedures

G.3. PRIME

Disclosure of some information related to PRIME cannot be released at present time as these contain commercially confidential information.

G.3.1. List of procedures concluding at 09-12 October 2017 CHMP plenary:

G.3.2. List of procedures starting in October 2017 for November 2017 CHMP adoption of outcomes

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