23 January 2017
EMA/41689/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Draft agenda of the meeting on 23-26 January 2017

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann
23 January 2017, 13:00 – 19:30, room 2A

24 January 2017, 08:30 – 19:30, room 2A

25 January 2017, 08:30 – 19:30, room 2A

26 January 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 23-26 January 2017. See January 2017 CHMP minutes (to be published post February 2017 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 23-26 January 2017

1.3. Adoption of the minutes

CHMP minutes for 12-16 December 2016

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. - adalimumab - EMEA/H/C/004212

treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn's disease, paediatri Crohn's disease and Ulcerative colitis

Scope: Possible oral explanation

Action: Possible oral explanation to be held on 25 January 2017 at time 11:00

List of Outstanding Issues adopted on 15.09.2016. List of Questions adopted on 28.04.2016.

2.1.2. - brodalumab - EMEA/H/C/003959

moderate to severe plaque psoriasis

Scope: Oral explanation

Action: Oral explanation to be held on 24 January 2017 at time 14:00

List of Outstanding Issues adopted on 10.11.2016, 15.09.2016. List of Questions adopted on 01.04.2016.

2.1.3. - adalimumab - EMEA/H/C/004373

treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn's disease, paediatri Crohn's disease and Ulcerative colitis

Scope: Possible oral explanation

Action: Possible oral explanation to be held on 25 January 2017 at time 11:00

List of Outstanding Issues adopted on 15.09.2016. List of Questions adopted on 28.04.2016.

2.2. Re-examination procedure oral explanations

2.2.1. Helicobacter Test INFAI - 13C-urea - EMEA/H/C/000140/II/0019

INFAI GmbH

Scope: “Update of the SmPC section 4.2, 4.3, 5.1 and 6.5 in order to add information on use of Refex test meal prior to the Helicobacter Test INFAI administration. The Package leaflet has been updated accordingly. Additionally, the MAH has taken the opportunity to align the PI with the latest QRD template version 9.1.”

Action: Oral explanation to be held on 24 January 2017 at 11:00

Opinion adopted on 13.10.2016.

2.3. Post-authorisation procedure oral explanations

2.3.1. Synjardy - empagliflozin / metformin - EMEA/H/C/003770/II/0015

Boehringer Ingelheim GmbH

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Dolores Montero Corominas

Scope: “Extension of Indication to include treatment with Synjardy as adjunct to standard care therapy in adult patients with type 2 diabetes mellitus and high cardiovascular risk when treatment with empagliflozin and metformin is appropriate and empagliflozin is needed to reduce the risk of all-cause mortality by reducing cardiovascular death and cardiovascular death or hospitalization for heart failure. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated based on the final CSR of study EMPA-REG OUTCOME. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes/corrections in the SmPC. Moreover, the updated RMP version 5.0 has been submitted.”

Action: Possible oral explanation to be held on 24 January 2017 at 09:00

Request for Supplementary Information adopted on 15.09.2016, 26.05.2016.

2.4. Referral procedure oral explanations

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. - daptomycin - EMEA/H/C/004310

treatment of complicated skin and soft-tissue infections

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 10.11.2016. List of Questions adopted on 23.06.2016.

3.1.2. - methotrexate - EMEA/H/C/003756

treatment of rheumatological and dermatological diseases

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 10.11.2016. List of Questions adopted on 23.07.2015.

3.1.3. - sodium zirconium cyclosilicate - EMEA/H/C/004029

for the treatment of hyperkalaemia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 10.11.2016. List of Questions adopted on 28.04.2016.

3.1.4. - umeclidinium - EMEA/H/C/004654

treatment of chronic obstructive pulmonary disease (COPD)

Scope: Opinion

Action: For adoption

3.1.5. - tadalafil - EMEA/H/C/004666

Treatment of erectile dysfunction in adult males

Scope: Opinion

Action: For adoption

3.1.6. - miglustat - EMEA/H/C/004016

treatment of Gaucher disease

Scope: Opinion

Action: For adoption

Oral explanation held on 21.06.2016. List of Outstanding Issues adopted on 23.06.2016, 01.04.2016. List of Questions adopted on 23.07.2015.

3.1.7. - tofacitinib - EMEA/H/C/004214

treatment of active rheumatoid arthritis

Scope: Opinion

Action: For adoption

List of Questions adopted on 15.12.2016, 21.07.2016.

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

3.2.1. - tivozanib hydrochloride monohydrate - Orphan - EMEA/H/C/004131

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

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.07.2016.

3.2.1. - prasterone - EMEA/H/C/004138

treatment of vulvovaginal atrophy

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 13.10.2016. List of Questions adopted on 26.05.2016.

3.2.2. - meningococcal group B vaccine (recombinant, component, adsorbed) - EMEA/H/C/004051

prevent invasive meningococcal disease caused by Neisseria meningitidis serogroup B

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 15.09.2016.

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

3.3.1. - insulin lispro - EMEA/H/C/004303

treatment of diabetes mellitus

Scope: Day 120 list of questions

Action: For adoption

3.3.2. - caffeine citrate - Orphan - EMEA/H/C/004100

Viridian Pharma Ltd; indicated in preterm neonates for the prevention of bronchopulmonary dysplasia

Scope: Day 120 list of questions

Action: For adoption

3.3.3. - darunavir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004391

treatment of human immunodeficiency virus type 1 (HIV-1)

Scope: Day 120 list of questions

Action: For adoption

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

treatment of hypogonadotrophic hypogonadism

Scope: Day 120 list of questions

Action: For adoption

3.3.5. - glibenclamide - Orphan - EMEA/H/C/004379

Accelerated assessment

Pharma Services; treatment of neonatal diabetes

Scope: Day 90 list of questions, request for extension of clock-stop.

Action: For adoption

3.3.6. - ribociclib - EMEA/H/C/004213

treatment of breast cancer

Scope: Day 120 list of questions

Action: For adoption

3.3.7. - lacosamide - EMEA/H/C/004443

treatment of epilepsy

Scope: Day 120 list of questions

Action: For adoption

3.3.8. - velmanase alfa - Orphan - EMEA/H/C/003922

Chiesi Farmaceutici S.p.A.; for long-term enzyme replacement therapy in patients with alpha-mannosidosis

Scope: Day 120 list of questions

Action: For adoption

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

AB Science; treatment of amyotrophic lateral sclerosis

Scope: Day 120 list of questions

Action: For adoption

3.3.10. - binimetinib - EMEA/H/C/004052

treatment of unresectable or metastatic melanoma
Treatment of unresectable melanoma, with NRA Q61 mutation.

Scope: Day 120 list of questions

Action: For adoption

3.3.11. - trastuzumab - EMEA/H/C/004323

treatment of breast cancer and metastatic gastric cancer

Scope: Day 120 list of questions

Action: For adoption

3.3.12. - sirukumab - EMEA/H/C/004165

treatment of rheumatoid arthritis

Scope: Day 120 list of questions

Action: For adoption

3.3.13. - nusinersen - Orphan - EMEA/H/C/004312

Accelerated assessment

Biogen Idec Ltd; for the treatment of Spinal Muscular Atrophy (SMA).

Scope: Day 90 list of questions

Action: For adoption

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

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

treatment of haemophilia A

Scope: Letter from the applicant dated 22 December 2016 requesting an extension of clock stop to respond to the List of Outstanding Issues adopted on 15 December 2016

Action: For adoption

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

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

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

Scope: Letter from the applicant dated 3 January 2017 requesting an extension of clock stop to respond to the List of Questions adopted on 15 December 2016

Action: For adoption

List of Questions adopted on 15.12.2016.

3.4.3. - pentosan polysulfate sodium - Orphan - EMEA/H/C/004246

bene-Arzneimittel GmbH; treatment of Interstitial Cystitis

Scope: List of experts for ad hoc expert group meeting

Action: For adoption

List of Outstanding Issues adopted on 10.11.2016. List of Questions adopted on 23.06.2016.

3.4.4. - padeliporfin - EMEA/H/C/004182

treatment of prostate cancer

Scope: Adoption of a list of questions for the SAG

Action: For adoption

List of Questions adopted on 26.05.2016. List of Outstanding Issue adopted on 15.12.2016.

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

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

Scope: Letter from the applicant dated 6 January 2017 requesting an extension of clock stop to respond to the List of Questions adopted on 13 October 2016

Action: For adoption

List of Questions adopted on 13.10.2016.

3.4.6. - gemtuzumab ozogamicin - Orphan - EMEA/H/C/004204

Pfizer Limited; combination therapy with daunorubicin (DNR) and cytarabine (AraC) for the treatment of adult patients with previously untreated, de novo acute myeloid leukaemia (AML).

Scope: Similarity assessment

Action: For adoption

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

3.6. Initial applications in the decision-making phase

3.7. Withdrawals of initial marketing authorisation application

3.7.1. pegfilgrastim - EMEA/H/C/004211

treatment of neutropenia

Scope: Withdrawal of initial marketing authorisation application

Action: For information

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

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

4.1.1. BeneFIX - nonacog alfa - EMEA/H/C/000139/X/0139

Pfizer Limited

Rapporteur: Jan Mueller-Berghaus

Scope: "Extension application to add a new strength of 1500 IU."

Action: For adoption

4.1.2. Brilique - ticagrelor - EMEA/H/C/001241/X/0034

AstraZeneca AB

Rapporteur: Johann Lodewijk Hillege

Scope: "To add new pharmaceutical form (orodispersible tablets 90 mg) to the currently approved presentations for Brilique."

Action: For adoption

List of Questions adopted on 15.09.2016.

4.1.3. Humira - adalimumab - EMEA/H/C/000481/X/0157

AbbVie Ltd.

Rapporteur: Kristina Dunder

Scope: "Extension application to add a new strength of 80 mg (80 mg/0.8 ml) for adalimumab solution for injection in single-use pre-filled syringe, for subcutaneous injection."

Action: For adoption

List of Questions adopted on 13.10.2016.

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

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

4.3.1. Prolia - denosumab - EMEA/H/C/001120/X/0059/G

Amgen Europe B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: “Extension application”

Action: For adoption

4.3.2. SonoVue - sulphur hexafluoride - EMEA/H/C/000303/X/0034/G

Bracco International B.V.

Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard

Scope: “Extension application to introduce a new route of administration (intravesical use) grouped with a type II variation (C.I.6.a) to add a new indication (to include use in ultrasonography of the excretory urinary tract in paediatric patients to detect or exclude vesicoureteral reflux).
As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 6 of the SmPC are updated. The Package Leaflet is updated accordingly.
In addition, the Marketing Authorisation Holder (MAH) took the opportunity to bring Annex IIIA in line with the latest QRD template version 10.
Moreover, the updated RMP version 9.1 has been submitted as part of this application.”

Action: For adoption

4.3.3. Xgeva - denosumab - EMEA/H/C/002173/X/0048/G

Amgen Europe B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: “Line extension”

Action: For adoption

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

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

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. Gazyvaro - obinutuzumab - Orphan - EMEA/H/C/002799/II/0016

Roche Registration Limited

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Pierre Demolis, PRAC Rapporteur: Julie Williams

Scope: "Extension of Indication to include a new indication for Gazyvaro in combination with chemotherapy, followed by Gazyvaro maintenance therapy in patients achieving a response, for the treatment of patients with previously untreated advanced follicular lymphoma.
As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and the RMP are updated in accordance. In addition, the due date for provision of the final clinical study report of study BO21223/GALLIUM listed in the Gazyvaro RMP as Category 3 has been updated.
Furthermore, the PI is brought in line with the missing information of QRD template version 9.1 regarding annex II C. In addition, clarification or editorial changes to the SmPC are proposed for accuracy and clarity.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

5.1.2. Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/II/0039

Gilead Sciences International Ltd

Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "Extension of indication to add treatment of chronic hepatitis C in adolescents aged 12 to < 18 years.
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 information on posology, warnings, safety, efficacy and pharmacokinetics.
The Package Leaflet and Risk Management Plan (RMP version 2) are updated in accordance."

Action: For adoption

5.1.3. Humira - adalimumab - EMEA/H/C/000481/II/0158

AbbVie Ltd.

Rapporteur: Kristina Dunder

Scope: "Extension of Indication to include new indication for moderate to severe nail psoriasis in adult patients who are candidates for systemic therapy for Humira.
As a consequence, sections 4.1 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Furthermore, the PI is brought in line with the latest QRD template version 9.1."

Action: For adoption

Request for Supplementary Information adopted on 13.10.2016.

5.1.4. Kaletra - lopinavir / ritonavir - EMEA/H/C/000368/II/0161/G

AbbVie Ltd.

Rapporteur: Joseph Emmerich, PRAC Rapporteur: Claire Ferard

Scope: "Extension of Indication to include children aged 14 days and older in the treatment of HIV-1.
As a consequence, sections 4.1, 4.2, 4.3, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. The studies provided in support of the paediatric indication are part of the agreed PIP decision P/0144/2012.

In addition, the Marketing authorisation holder (MAH) further updated section 4.4 to add information regarding the use of Kaletra oral solution with feeding tubes.
The updated RMP v.8 is provided accordingly.

IB-B.II.e.5.a.2-To add a new pack size of 120 ml in (2X 60ml bottles) for Kaletra 80mg/ml/20 mg/ml oral solution (EU/1/01/172/003).

IA-B.IV.1.a.1-To add a new 2 ml oral dose syringe for the 120ml presentation."

Action: For adoption

5.1.5. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0014

Merck Sharp & Dohme Limited

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

Scope: "Extension of Indication to include the treatment of classical Hodgkin Lymphoma (cHL) in adults who have refractory disease, or who have relapsed after greater than 3 prior lines of therapy, based on the results from study KEYNOTE-087, an open-label Phase II trial of pembrolizumab in subjects with relapsed or refractory cHL and study KEYNOTE-013, a Phase Ib multi-cohort trial of pembrolizumab in subjects with hematologic malignancies.
As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated and the Package Leaflet is updated accordingly. An updated RMP version 5.0 was provided as part of the application."

Action: For adoption

5.1.6. Opdivo - nivolumab - EMEA/H/C/003985/II/0017

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of Indication to include treatment of recurrent or metastatic squamous cell cancer of the head and neck (SCCHN) after platinum-based therapy in adults for OPDIVO.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, of the SmPC are updated in order to add the proposed new indication, add a warning that patients with a baseline performance score ≥ 2, untreated brain metastasis, active autoimmune disease, or medical conditions requiring systemic immunosuppression were excluded from the SCCHN clinical trial and update the undesirable effect and safety information. Labelling is updated in accordance. Moreover, the updated RMP version 6.0 has been submitted"

Action: For adoption

Request for Supplementary Information adopted on 13.10.2016.

5.1.7. Orencia - abatacept - EMEA/H/C/000701/II/0105

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Kirsti Villikka

Scope: "Extension of Indication to include a new indication for Orencia: treatment of psoriatic arthritis in adults.

As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are proposed to be updated. The Package Leaflet is updated in accordance.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.

A revised RMP was included in this submission (version 21)."

Action: For adoption

5.1.8. Revlimid - lenalidomide - Orphan - EMEA/H/C/000717/II/0089/G

Celgene Europe Limited

Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard

Scope: "Extension of indication to add treatment of adult patients with newly diagnosed multiple myeloma (NDMM) who have undergone autologous stem cell transplantation (ASCT). Consequently SmPC sections 4.1, 4.2, 4.4, 4.8 and 5.1 have been updated with the efficacy and safety data. The Package Leaflet and the RMP have been updated accordingly. Furthermore, the MAH introduced 7-day pack sizes for the 10 mg and 15 mg strengths with subsequent changes to the Product Information."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2016.

5.1.9. Renvela Sevelamer carbonate Zentiva - sevelamer sevelamer - EMEA/H/C/WS0965

Genzyme Europe BV

Lead Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Laurence de Fays

Scope: "Extension of indication for Renvela and Sevelamer carbonate Zentiva to include the control of hyperphosphataemia in paediatric patients (>6 years of age and a Body Surface Area (BSA) of >0.75 m2) with chronic kidney disease.

As a consequence, section 4.2 of the SmPC is updated to detail posology in the paediatric patients.

The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2016.

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

5.2.1. Xgeva - denosumab - EMEA/H/C/002173/II/0045

Amgen Europe B.V.

Rapporteur: Kristina Dunder

Scope: Withdrawal of procedure of type II variation on extension of indication to include "Treatment of Hypercalcemia of Malignancy refractory to intravenous bisphosphonate".

Action: For information

Request for supplementary information adopted on 16.10.2016.

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

6. Ancillary medicinal substances in medical devices

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

6.1.1. - human serum albumin - EMEA/H/D/004287

Human serum albumin ancillary action prevents adsorption to the container of various amino acids, vitamins which may be present in trace quantities and acts as a carrier of these substances to support growth and maintenance of gametes and/or embryos. Scavenges embryotoxic components generated prevents adsorption to the container of various amino acids and vitamins, acts as a carrier of these substances to support growth

and maintenance of gametes and/or embryos, Scavenges embryotoxic components generated during embryo's metabolism in vitro

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 13.10.2016. List of Questions adopted on 28.01.2016.

6.2. Update of Ancillary medicinal substances in medical devices

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

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

8. Pre-submission issues

8.1. Pre-submission issue

8.2. 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

Note: Products requesting eligibility under PRIME scheme are listed in the Annex G.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

Note: Recommendation for PRIME are listed in the Annex G.

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Budesonide/Formoterol Teva - budesonide/formoterol - EMEA/H/C/003951

Teva Pharma B.V.; treatment of asthma and chronic obstructive pulmonary disease (COPD)

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: David Lyons, PRAC Rapporteur: Torbjorn Callreus

Scope: Withdrawal

Action: For information

Hybrid application (Article 10(3) of Directive No 2001/83/EC)

9.1.2. Vylaer Spiromax - budesonide/formoterol - EMEA/H/C/003952

Teva Pharma B.V.; treatment of asthma and chronic obstructive pulmonary disease (COPD)

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: David Lyons, PRAC Rapporteur: Torbjorn Callreus

Scope: Withdrawal

Action: For information

Hybrid application (Article 10(3) of Directive No 2001/83/EC)

9.1.3. Budesonide/Formoterol Teva Pharma B.V. - budesonide/formoterol - EMEA/H/C/003953

Teva Pharma B.V.; treatment of asthma

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: David Lyons, PRAC Rapporteur: Greg Markey

Scope: Withdrawal

Action: For information

Hybrid application (Article 10(3) of Directive No 2001/83/EC)

9.1.4. Fampyra - fampridine - EMEA/H/C/002097/II/0036/G

MAH: Biogen Idec Ltd

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus,

Scope: “This is a grouped variation proposing updates:- to the SmPC sections 4.2, 5.1, Annex II and Package Leaflet based on the clinical study Enhance,

- to the SmPC section 4.6 based on the data from pregnancy registry.

- Further changes to the PI, section 4.2 and 5.2 of the SmPC have been introduced based

on the Core Data Sheet (CDS) and PRAC review of the Fampyra PSUR 03.

The RMP (version 11) 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.

With this application the MAH requests to switch the marketing authorisation from conditional to standard."

Opinion

Action: For adoption

See also B.5.3

9.1.5. Ilaris - canakinumab - EMEA/H/C/001109/S/0047

Novartis Europharm Ltd, treatment of cryopyrin-associated periodic syndromes (CAPS), including Muckle-Wells Syndrome (MWS), Neonatal-Onset Multisystem Inflammatory Disease (NOMID) / Chronic Infantile Neurological, Cutaneous, Articular Syndrome (CINCA) and severe forms of Familial Cold Autoinflammatory Syndrome (FCAS) / Familial Cold Urticaria (FCU); Still's Disease and Gouty arthritis

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

Scope: 7th annual re-assessment with a proposal to change to the Marketing Authorisation status

Action: For adoption

9.1.6. Update of Fluoropyrimidines (Capecitabine-Xeloda and 5-FU), EMEA/H/C/0316/LEG-033

Xeloda: Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber

Scope: PRAC advice to CHMP, consultation of PGWP

Action: For adoption

9.1.7. Adcirca-EMEA/H/C/001021/WS1066/0026, Cialis-EMEA/H/C/000436/WS1066/0086 - tadalafil - EMEA/H/C/WS1066

Eli Lilly Nederland B.V.

Lead Rapporteur: Concepcion Prieto Yerro

Scope: Request for supplementary information

Action: For adoption

"Update of sections 4.2 and 5.1 of the SmPC in order to reflect the results of study H6D-MC-LVJJ, a randomized, double-blind, placebo-controlled phase 3 trial of tadalafil in the treatment of Duchenne Muscular Dystrophy (DMD), to fulfil Adcirca P46 019.1 and Cialis P46 045.1."

See B.5.2

10. Referral procedures

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

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

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

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

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

D&A Pharma

Rapporteur: TBC, Co-Rapporteur: TBC,

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

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.

Action: For adoption

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

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

10.6.1. Dienogest/Ethinylestradiol containing products indicated in acne - Dienogest / Ethinylestradiol - EMEA/H/A-31/1435

Rapporteur: Martina Weise, Co-Rapporteur: Nithyanandan Nagercoil,

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 15.12.2016, 15.09.2016, 23 June 2016.

10.6.2. Symbioflor 2, Escherichia Coli bacteria (cells and autolysate) - EMEA/H/A-31/1441

Symbiopharm GmbH,

Rapporteur: Harald Enzmann, Co-rapporteur: Milena Stain;

Scope: List of experts for the ad hoc expert group meeting adopted via written procedure on 12 January 2017.

Action: For information

Article 31 triggered by the BfArM in Germany in March 2016 requesting the review of the benefit-risk balance for Symbioflor 2 and associated names following concerns that the effectiveness of the medicine(s) has not been adequately demonstrated.

10.6.3. Human coagulation (plasma-derived) factor VIII: human coagulation factor VIII (antihemophilic factor A) (NAP); human coagulation factor VIII (inhibitor bypassing fraction) (NAP); human coagulation factor VIII, human von Willebrand factor - Voncento (CAP) Recombinant factor VIII: antihemophilic factor (recombinant) (NAP); moroctocog alfa – Refacto AF (CAP) octocog alfa – Advate (CAP), Helixate Nexgen (CAP), Iblias (CAP), Kogenate (CAP), Kovaltry (CAP) - EMEA/H/A-31/1448

Baxter AG (Advate), Bayer Pharma AG (Helixate Nexgen, Iblias, Kogenate, Kovaltry), CSL Behring GmbH (Voncento), Pfizer Limited (Refacto AF), various

PRAC led referral - PRAC Rapporteur: Rafe Suvarna; PRAC Co-rapporteur: Brigitte Keller-Stanislawski

Scope: List of experts for ad hoc expert group meeting

Action: For adoption

Review of the benefit-risk balance of factor VIII following notification by Germany of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

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

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

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

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

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

11. Pharmacovigilance issue

11.1. Early Notification System

January 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

Action: For information

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

ITF briefing meeting

Meeting date: 1 February 2017

Action: For discussion

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

13.4. Nanomedicines activities

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Presentation on Classification of Post-Authorisation Studies (CPAS)

Action: For information

14.1.2. Release of additional dashboards for Art 57 data

Action: For information

14.1.3. Co-opted membership of the CHMP

The mandate of Robert J. Hemmings as Co-opted member of the CHMP expires in February 2017

Scope: Election of 5th co-opted member; Agreed expertise: Medical statistics (clinical-trial methodology / epidemiology)

Action: For adoption

14.1.4. Patient involvement in CHMP

Scope: Pilot report and analysis

Action: For discussion

14.1.5. Feedback on IMI-PREFER project

Action: For information

14.1.6. Myeloma UK-EMA-UMCG study on patient preferences

Action: For information

14.1.7. Proposals for future patient preference studies

Action: For information

14.1.8. Survey to committee members on the service provided by the Scientific Committees Service

Scope: Findings of the survey to Committee Members

Action: For information

14.1.9. Follow-up actions from the joint CHMP-PDCO Strategic Review and Learning meeting in Brussels under the Slovak EU Presidency

Action: For adoption

Draft minutes of meeting held on 19-21 October 2016

Action: For information

14.1.10. CHMP meetings to be held in Valletta 28 February - 3 March 2017 under the Maltese Presidency of the Council of the European Union

Scope: Information about the draft agenda topics of the upcoming Strategic Review and Learning meeting 28 February - 2 March 2017

Action: For discussion

Scope: Information about the draft agenda topics of the upcoming meeting on - Making Article 58 and other European Medicines Agency outputs more relevant for non-EU regulators to be held in Valetta 2 March - 3 March 2017

Action: For discussion

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on 09-12 January 2017

Action: For information

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

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 18-20 January 2017
Action: For information

14.2.3. Paediatric Committee (PDCO)

PIPs reaching D30 at January 2017 PDCO

Action: For information

Report from the PDCO meeting held on 24-27 January 2017

Action: For information

PIP for Levoglutamide for sickle cell anaemia

Action: For discussion

14.2.4. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 17-19 January 2017
Action: For information

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

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 23-25 January 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 09-12 January 2017. Table of conclusions

Action: For information

Scientific advice letters: See Annex G

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

14.3.2. Blood Products Working Party (BPWP)

Chair: Anneliese Hilger

Nomination of new Austrian member Daniela Philadelphy and alternate member Lisa Rosner to the BPWP after resignation of Brigitte Mueller

Action: For adoption

Scope: Call for nomination of a new Chairperson of the Blood Products Working Party (BPWP).

Nominations should be sent to the BPWP Secretariat by 9 February 2017. Elections will take place at February 2017 CHMP.

Action: For information

14.3.3. Pharmacokinetics Working Party (PKWP)

Chair: Jan WelinkPKWP response to CHMP Question on biowaiver classification of paracetamol (EMA/CHMP/715158/2016)

Action: For adoption

14.3.4. Infectious Diseases Working Party (IDWP)

Scope: Nomination of Bettina Klug (DE/PEI) as observer to IDWP

- current membership list

Action: For adoption

14.3.5. Gastroenterology Drafting Group (GDG)

Chair: Elmer Schabel

Scope: Call for nomination of a new Chairperson of Gastroenterology Drafting Group (GDG)

Nominations to be sent to the GDG Secretariat by 31 January 2017

Action: For information

14.3.6. EMA Human Scientific Committees Working Parties with Patients and Consumers Organisations (PCWP) and Healthcare Professionals Organisations (HCPWP) joint meeting

Scope: Minutes of the PCWP/HCPWP joint meeting – 20 Sep 2016 (EMA/625038/2016)

Action: For information

14.3.7. Biologics Working Party (BWP)

Scope: Call for nomination for a new Chairperson of the Biologics Working Party (BWP).

Nominations should be sent to the BWP Secretariat by 9 February 2017.

Action: For information

14.3.8. Safety Working Party (SWP)

Chair: Jan Willem van der Laan,

Nomination of Henry Stemplewski to the SWP to replace Karen van Malderen as drafting group member for the ERA guideline

Action: For adoption

Nomination of Roland Frötschl (DE/BfArM) to the SWP replacing Peter Kasper

Action: For adoption

14.3.9. Vaccine Working Party (VWP)

Chair: Mair Powell,

Nomination of new observers Ingrid Schellens (NL) and Marta Soler (ES) to the VWP

Action: For adoption

14.3.10. Biosimilar Medicinal Product Working Party (BMWP)

Chair: Elena Wolff-Holz,

Request to attend the BMWP meeting in March 2017

Action: For adoption

14.3.11. Modelling and simulation Working Group (MSWG)

Chair: Ine Skottheim Rusten,

Activity report and MSWG Work Plan

Action: For information

14.4. Cooperation within the EU regulatory network

14.5. Cooperation with International Regulators

14.5.1. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)

Scope: Nomination of Peter Mol (MEB) and Mick Foy (MHRA) as experts to the E19 Informal WG.

Nomination of Roland Frötschl (BfArM) in replacement of Peter Kasper (BfArM) as expert to the Q3C and M7 Maintenance WG

Action: For adoption

Draft Concept Paper Outline: Safety Data Collection - E19

Action: For information

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

14.7. CHMP work plan

14.7.1. CHMP 2017 Work Plan

Action: For adoption

14.8. Planning and reporting

14.9. Others

15. Any other business

15.1. AOB topic

15.1.1. Operation and Relocation Preparedness - Workstream 2 - Operational Preparedness

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)*

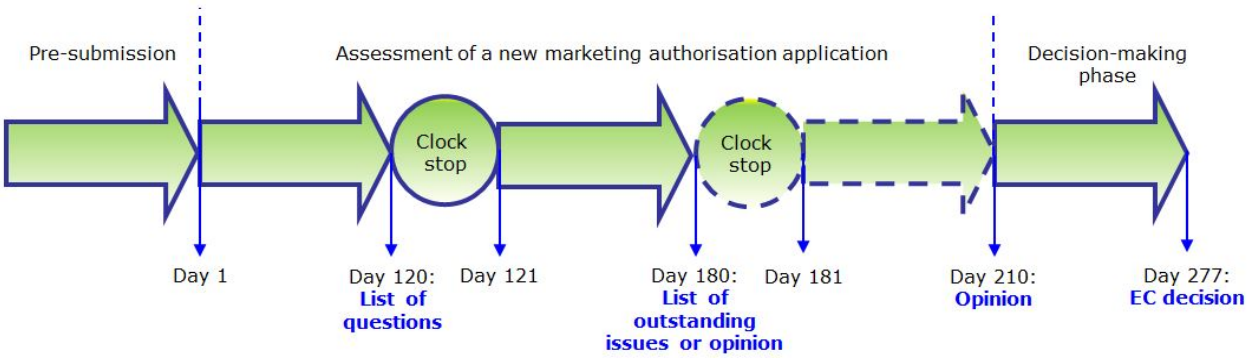
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

23 January 2017
EMA/38835/2017

Annex to January 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 January 2017: **For adoption**

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

Final Outcome of Rapporteurship allocation for January 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

Glybera - alipogene tiparvovec - EMEA/H/C/002145/S/0057, Orphan, ATMP
MAH: uniQure biopharma B.V., Rapporteur: Christiane Niederlaender, PRAC Rapporteur: Julie Williams

Ilaris - canakinumab - EMEA/H/C/001109/S/0047
MAH: Novartis Europharm Ltd, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski

Orphacol - cholic acid - EMEA/H/C/001250/S/0016, Orphan
MAH: LABORATOIRES CTRS - BOULOGNE BILLANCOURT, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Rafe Suvarna

Raxone - idebenone - EMEA/H/C/003834/S/0005, Orphan
MAH: Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Carmela Macchiarulo

Vedrop - tocofersolan - EMEA/H/C/000920/S/0019

MAH: Orphan Europe S.A.R.L., Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Fycompa - perampanel - EMEA/H/C/002434/R/0035
MAH: Eisai Europe Ltd., Rapporteur: Robert James Hemmings, PRAC Rapporteur: Julie Williams

Jentadueto - linagliptin / metformin - EMEA/H/C/002279/R/0036
MAH: Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Karsten Bruins Slot, PRAC Rapporteur: Menno van der Elst

Kalydeco - ivacaftor - EMEA/H/C/002494/R/0052, Orphan
MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Dolores Montero Corominas

Siklos - hydroxycarbamide - EMEA/H/C/000689/R/0030, Orphan
MAH: Addmedica, Rapporteur: Koenraad Norga, Co-Rapporteur: Eleftheria Nikolaidi, PRAC Rapporteur: Jean-Michel Dogné

Zyclara - imiquimod - EMEA/H/C/002387/R/0012
MAH: Meda AB, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Rafe Suvarna

B.2.3. Renewals of Conditional Marketing Authorisations

Bosulif - bosutinib - EMEA/H/C/002373/R/0023, Orphan
MAH: Pfizer Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber
Request for Supplementary Information adopted on 15.12.2016.

Deltyba - delamanid - EMEA/H/C/002552/R/0017, Orphan
MAH: Otsuka Novel Products GmbH, Rapporteur: Greg Markey, PRAC Rapporteur:

Rafe Suvarna

Pixuvri - pixantrone -
EMEA/H/C/002055/R/0034
MAH: CTI Life Sciences Limited, Rapporteur: Greg Markey, PRAC Rapporteur: Rafe Suvarna

Zykadia - ceritinib -
EMEA/H/C/003819/R/0009
MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Ulla Wändel Liminga

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on on 9-12 January 2017 PRAC:

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

EMEA/H/C/PSUSA/00000311/201606
(belatacept)
CAPS:
Nulojix (EMEA/H/C/002098) (belatacept), MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, “15 June 2015 - 14 June 2016”

EMEA/H/C/PSUSA/00000476/201606
(cabazitaxel)
CAPS:
Jevtana (EMEA/H/C/002018) (cabazitaxel), MAH: Sanofi-Aventis Groupe, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard, “18-Jun-2015 to 17-Jun-2016”

EMEA/H/C/PSUSA/00010341/201606
(secukinumab)
CAPS:
Cosentyx (EMEA/H/C/003729) (secukinumab), MAH: Novartis Europharm Ltd, Rapporteur: Tuomo Lapveteläinen, PRAC Rapporteur: Eva A. Segovia, “26 December 2015 to 25 June 2016”

EMEA/H/C/PSUSA/00010379/201607
(nivolumab)
CAPS:
OPDIVO (EMEA/H/C/003985) (nivolumab), MAH: Bristol-Myers Squibb Pharma EEIG,

Rapporteur: Aranzazu Sancho-Lopez, PRAC
Rapporteur: Brigitte Keller-Stanislawski, “04 January 2016 - 03 July 2016”

B.4. EPARs / WPARs

Alecensa - alectinib - EMEA/H/C/004164
Applicant: Roche Registration Limited, treatment of adult patients with anaplastic lymphoma kinase (ALK)-positiveNew active substance (Article 8(3) of Directive No 2001/83/EC)

Graspa - eryaspase - EMEA/H/C/004055, Orphan
Applicant: ERYTECH Pharma S.A., treatment of leukaemia, New active substance (Article 8(3) of Directive No 2001/83/EC)
WPAR

Ledaga - chlormethine - EMEA/H/C/002826, Orphan
Applicant: Actelion Registration Ltd., treatment of mycosis fungoides-type cutaneous T-cell lymphoma (MF-type CTCL), Hybrid application (Article 10(3) of Directive No 2001/83/EC)

Lifmior - etanercept - EMEA/H/C/004167
Applicant: Pfizer Limited, treatment of arthritis, ankylosing spondylitis, plaque psoriasis and paediatric plaque psoriasis, Generic, Generic of Enbrel, Generic application (Article 10(1) of Directive No 2001/83/EC)

Olumiant - baricitinib - EMEA/H/C/004085
Applicant: Eli Lilly Nederland B.V., treatment of moderate to severe active rheumatoid arthritis (RA), New active substance (Article 8(3) of Directive No 2001/83/EC)

Pregabalin Zentiva k.s. - pregabalin - EMEA/H/C/004277
Applicant: Zentiva k.s., treatment of neuropathic pain, epilepsy and Generalised Anxiety Disorder (GAD), Generic, Generic of Lyrica, Generic application (Article 10(1) of Directive No 2001/83/EC)

Truxima - rituximab - EMEA/H/C/004112
Applicant: Celltrion Healthcare Hungary Kft., treatment of Non-Hodgkin's lymphoma (NHL), Chronic lymphocytic leukaemia (CLL), Rheumatoid arthritis and Granulomatosis with

polyangiitis and microscopic polyangiitis, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	
Vihuma - simoctocog alfa - EMEA/H/C/004459 Applicant: Octapharma AB, treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency). Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency),	

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Azarga - brinzolamide / timolol - EMEA/H/C/000960/II/0035/G MAH: Alcon Laboratories (UK) Ltd, Rapporteur: Hanne Lomholt Larsen	Weekly start timetable.
Bexsero - meningococcal group B vaccine (rDNA, component, adsorbed) - EMEA/H/C/002333/II/0048 MAH: GSK Vaccines S.r.l, Rapporteur: Kristina Dunder	Weekly start timetable.
Biopoin - epoetin theta - EMEA/H/C/001036/II/0036/G MAH: TEVA GmbH, Rapporteur: Pierre Demolis	Weekly start timetable.
Eporatio - epoetin theta - EMEA/H/C/001033/II/0035/G MAH: ratiopharm GmbH, Rapporteur: Pierre Demolis	Weekly start timetable.
Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0093 MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege	Weekly start timetable.
Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0013 MAH: Sanofi Pasteur MSD SAS, Rapporteur: Kristina Dunder	Weekly start timetable.
HyQvia - human normal immunoglobulin - EMEA/H/C/002491/II/0033/G MAH: Baxalta Innovations GmbH, Rapporteur:	Weekly start timetable.

Jan Mueller-Berghaus	
Kalydeco - ivacaftor - EMEA/H/C/002494/II/0053/G, Orphan MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Concepcion Prieto Yerro	Weekly start timetable.
Levemir - insulin detemir - EMEA/H/C/000528/II/0083 MAH: Novo Nordisk A/S, Rapporteur: Hanne Lomholt Larsen	Weekly start timetable.
Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0017 MAH: GSK Biologicals SA, Rapporteur: Jan Mueller-Berghaus	Weekly start timetable.
NovoRapid - insulin aspart - EMEA/H/C/000258/II/0115 MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder	Weekly start timetable.
Nuwiq - simoctocog alfa - EMEA/H/C/002813/II/0012/G MAH: Octapharma AB, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 13.10.2016, 14.07.2016.	Weekly start timetable.
Opdivo - nivolumab - EMEA/H/C/003985/II/0020 MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez Opinion adopted on 22.12.2016. Request for Supplementary Information adopted on 17.11.2016.	Positive Opinion adopted by consensus on 22.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Opdivo - nivolumab - EMEA/H/C/003985/II/0026 MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez	Weekly start timetable.
Prezista - darunavir - EMEA/H/C/000707/II/0083/G MAH: Janssen-Cilag International NV, Rapporteur: Johann Lodewijk Hillege	
Revestive - teduglutide - EMEA/H/C/002345/II/0035, Orphan MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Sinan B. Sarac	Weekly start timetable.
Umbipro (TM) - chlorhexidine -	Weekly start timetable.

EMEA/H/W/003799/II/0002/G MAH: GlaxoSmithKline Trading Services, Rapporteur: Patrick Salmon	
Xofigo - radium-223 - EMEA/H/C/002653/II/0022/G MAH: Bayer Pharma AG, Rapporteur: Harald Enzmann	Weekly start timetable.
Zevalin - ibritumomab tiuxetan - EMEA/H/C/000547/II/0046/G MAH: Spectrum Pharmaceuticals B.V., Rapporteur: Sinan B. Sarac	Weekly start timetable.
WS1022/G **Neulasta-** **EMEA/H/C/000420/WS1022/0091/G** **Ristempa-** **EMEA/H/C/003910/WS1022/0008/G** MAH: Amgen Europe B.V., Lead Rapporteur: Robert James Hemmings	Weekly start timetable.

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

Abasaglar - insulin glargine - EMEA/H/C/002835/II/0010/G MAH: Eli Lilly Regional Operations GmbH, Rapporteur: Robert James Hemmings, "C.I.Z (Type II): Update of section 4.4 and 4.6 of the SmPC of the cartridge presentations (EU/1/44/94/001-4,9) to only recommend the use of cartridges in Lilly reusable pens and to remove the suggestion to withdraw insulin from a syringe. C.I.2 (Type IB): Update of section 4.2 of the SmPC in order to align the wording on switching from 3000 U/ml to 100 U/ml with the reference product, Lantus. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to replace U/ml by units/ml, to amend the details of the Polish affiliate, to correct the image of the KwikPen and to bring the PI in line with the latest QRD template version 10.0."	Weekly start timetable.
Adempas - riociguat - EMEA/H/C/002737/II/0018/G, Orphan MAH: Bayer Pharma AG, Rapporteur: Johann Lodewijk Hillege, "C.I.13 Submission of the final clinical study report of study 12166: A multicentre, non-randomized, non-blinded, non-	Weekly start timetable.

controlled study to investigate the impact of multiple doses of riociguat on safety, tolerability, pharmacokinetics and pharmacodynamics in patients with pulmonary hypertension in a 12 week 3 times a day individual dose titration scheme. C.I.13 Submission of the final clinical study report of study 16097: An open-label phase IIIb study of riociguat in patients with in-operable chronic thromboembolic pulmonary hypertension (CTEPH) or recurrent or persisting pulmonary hypertension after surgical treatment who are not satisfactorily treated and cannot participate in any other CTEPH trial."	
Adempas - riociguat - EMEA/H/C/002737/II/0019, Orphan MAH: Bayer Pharma AG, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.5 of the SmPC in order to add information about interactions of riociguat when administered concomitantly with combined oral contraceptives containing levonorgestrel and ethinyl estradiol to healthy female subjects. Furthermore, section 4.5 of the SmPC was updated to correct the list of CYP isoforms involved in the metabolism of riociguat based on in vitro data. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the Product Information in line with the latest QRD template version 10.0 and to update the contact details of the German local representative."	Weekly start timetable.
Aerinaze - desloratadine / pseudoephedrine sulphate - EMEA/H/C/000772/II/0033 MAH: Merck Sharp & Dohme Limited, Rapporteur: Koenraad Norga, "Update of sections 4.4 and 4.8 of the SmPC to include information on acute generalised exanthematous pustulosis (AGEP). In addition, the MAH takes the opportunity to correct minor typographical errors in the SmPC and Package Leaflet and to align the annexes with the revised QRD template v10."	Weekly start timetable.
Avastin - bevacizumab - EMEA/H/C/000582/II/0093 MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, "Update of sections 4.2	Weekly start timetable.

Posology and method of administration, 4.8 Undesirable effects, 5.1 Pharmacodynamic properties and 5.2 Pharmacokinetic properties of the SmPC in order to include the paediatric results from the HERBY (BO25041) study. Study BO25041 (HERBY) is an open-label, randomized, multicenter, comparator Phase II study of the addition of bevacizumab to adjuvant chemoradiation with temozolomide (TMZ) followed by adjuvant TMZ in pediatric patients from ≥ 3 years to < 18 years of age with newly diagnosed, localized, supratentorial or infratentorial cerebellar or peduncular high-grade glioma. The package leaflet (PIL) is updated accordingly."	
BLINCYTO - blinatumomab - EMEA/H/C/003731/II/0009, Orphan MAH: Amgen Europe B.V., Rapporteur: Pierre Demolis, "Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to update the safety information with the data from the study 103311. This study is fulfilling the specific obligation for the conditional MA. The SO is removed from annex II. The Package Leaflet is updated accordingly. The MAH takes this opportunity to amend the format of the preparation instructions to improve clarity. The content is not impacted."	
Cerdelga - eliglustat - EMEA/H/C/003724/II/0010, Orphan MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1. of the SmPC in order to update the safety and efficacy of eliglustat from studies in the GD1 patient population (studies ENGAGE & EDGE). In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet for Bulgaria and Romania."	Weekly start timetable.
Cinryze - C1-esterase inhibitor, human - EMEA/H/C/001207/II/0048 MAH: Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus, "To replace Unit (U) by International Unit (IU) in labelling for harmonization with the registration dossier Module 3 information"	
EVOTAZ - atazanavir / cobicistat - EMEA/H/C/003904/II/0010	Weekly start timetable.

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, “Proposed changes to the EVOTAZ SmPC to aling with the current Company Core Data Sheet (CCDS). During the EVOTAZ MAA procedure, an interim Week 144 CSR for Gilead study GS-US-216-0114 was submitted and the SmPC efficacy and safety data were updated and approved accordingly. However, the resistance data were not updated at that time. As a result, the MAH proposes to update the resistance sub-section in SmPC section 5.1 with study GS-US-216-0114 Week 144 resistance data that were submitted in the context of the MAA. In addition, for clarification purposes, the MAH proposes to use the specific designation of tenofovir disoproxil fumarate throughout the EVOTAZ Product Information (PI) to differentiate this pharmaceutical entity from the tenofovir alafenamide (for which no studies with EVOTAZ have been conducted). Finally, the MAH would like to take this opportunity to implement QRD version 10.” Request for Supplementary Information adopted on 29.09.2016.	
Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0094 MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update the safety information on paediatric study after its assessment in procedure EMEA/H/C/000370/P46/063. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Bulgaria, Romania and France in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.0.”	Weekly start timetable.
Gilenya - fingolimod - EMEA/H/C/002202/II/0039 MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, “Update of sections 4.4 and 4.8 of the SmPC to add an approximate time of onset of multifocal leukoencephalopathy (PML) and for cryptococcal meningitis (CM), and to remove the term isolated from "isolated cases	

of CM".”
Request for Supplementary Information adopted on 13.10.2016.

Helicobacter Test INFAI - 13C-urea - EMEA/H/C/000140/II/0019

MAH: INFAI GmbH, “Update of the SmPC section 4.2, 4.3, 5.1 and 6.5 in order to add information on use of Refex test meal prior to the Helicobacter Test INFAI administration. The Package leaflet has been updated accordingly. Additionally, the MAH has taken the opportunity to align the PI with the latest QRD template version 9.1.”
Opinion adopted on 13.10.2016.
Request for Supplementary Information adopted on 15.09.2016, 21.07.2016, 23.06.2016, 01.04.2016, 28.01.2016.

HyQvia - human normal immunoglobulin - EMEA/H/C/002491/II/0032

MAH: Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus, “Update of section 4.2 and 4.8 of the SmPC in order to add information on infusion site leakage. 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.”

Increlex - mecasermin - EMEA/H/C/000704/II/0040, Orphan

MAH: Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, , “Update of section of 4.1 of the SmPC in order to re-word the recommendation to confirm diagnosis with an IGF-1 generation test used for diagnosis of Severe Primary IGFD”

Invokana - canagliflozin - EMEA/H/C/002649/II/0026

MAH: Janssen-Cilag International NV, Rapporteur: Martina Weise, “Update of section 4.4 of the SmPC in order to update the safety information: the term 'and fatal' is added when describing the Diabetic Ketoacidosis cases that have been reported. The Package Leaflet is updated accordingly: term 'rare but serious, sometimes life-threatening and fatal' is added when describing Diabetic Ketoacidosis.

In addition, the Marketing authorisation holder

(MAH) took the opportunity to update the list of local representatives in the Package Leaflet."	
Iressa - gefitinib - EMEA/H/C/001016/II/0027 MAH: AstraZeneca AB, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to update information on mechanisms of resistance to Iressa in patients with EGFR mutation positive Non-Small Cell Lung Cancer (NSCLC) as proposed during assessment of LEG 21. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some editorial changes in the SmPC"	Weekly start timetable.
Kisplyx - lenvatinib - EMEA/H/C/004224/II/0001 MAH: Eisai Europe Ltd., Rapporteur: Bart Van der Schueren, "Update of sections 4.2, 4.4 and 4.8 of the SmPC to add warnings on "haemorrhage" and "non-gastrointestinal fistula" in line with what was aproved for Lenvima. The package leaflet is updated accordingly. In addition, the format of the EU authorisation numbers is corrected throughout the product information."	
Kuvan - sapropterin - EMEA/H/C/000943/II/0046, Orphan MAH: BioMarin International Limited, Rapporteur: Patrick Salmon, "Update of section 4.5 to delete the statement that no interaction studies have been performed and section 5.2 to reflect the relevant results of in vitro pharmacokinetic drug interactions studies BMN162-14-021, 022, 023, BMN162-15-036 and 101. In addition, the MAH took the opportunity of this procedure to improve the wording of section 4.2 and implement minor administrative changes in the SmPC."	Weekly start timetable.
Kyprolis - carfilzomib - EMEA/H/C/003790/II/0010, Orphan MAH: Amgen Europe B.V., Rapporteur: Aranzazu Sancho-Lopez, "Update of section 4.5 of the SmPC in order to inform the prescriber that no Drug Drug Interaction (DDI) studies were conducted at the higher dose (56mg/m2)."	Weekly start timetable.
M-M-RVAXPRO - measles, mumps and rubella vaccine (live) -	Weekly start timetable.

EMEA/H/C/000604/II/0080 MAH: Sanofi Pasteur MSD SAS, Rapporteur: Jan Mueller-Berghaus, “Update of section 4.8 of the SmPC in order to add acute haemorrhagic oedema of infancy and Henoch-Schönlein purpura with a frequency rare in the tabulated list of adverse reactions. In addition, the MAH took the opportunity to make some editorial changes in the product information.”	
Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0015 MAH: GSK Biologicals SA, Rapporteur: Jan Mueller-Berghaus, “The SOH submitted the final study report of study Malaria-066, a non-interventional ancillary study to Malaria-055 to evaluate the genetic polymorphism of the circumsporozoite (CS) protein of P. falciparum found in infants and children who developed clinical malaria in Malaria-055 study or with prevalent parasitaemia at cross-sectional survey. The SOH did not propose any changes to the product information.”	Weekly start timetable.
NovoThirteen - catridecacog - EMEA/H/C/002284/II/0018 MAH: Novo Nordisk A/S, Rapporteur: Joseph Emmerich, “Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to consolidate the outcome of the clinical development programme (studies F13CD-3720 and F13CD-3835) submitted in procedures P46/014 and P46/016. Briefly, section 4.4 was updated to reflect that on-demand treatment was used in the extension study F13CD-3720, section 4.8 was updated to reflect the data on number of patients/paediatric patients and exposures, in section 5.1 the bleeding rate was updated, in section 5.2 minor amendments were made to the half-life of NovoThirteen. In addition, the Marketing authorisation holder (MAH) took the opportunity to update Annex II with minor administrative amendments in line with QRD template 9.1 and Annex III in line with QRD template version 10.0.”	Weekly start timetable.
Odefsey - emtricitabine / rilpivirine / tenofovir alafenamide - EMEA/H/C/004156/II/0008/G MAH: Gilead Sciences International Ltd,	

Rapporteur: Robert James Hemmings, “Update of sections 4.8, 5.1 and 5.2 of the SmPC with 48 weeks data from Study GS-US-366-1216 and Study GS-US-366-1160 in fulfilment of MEA 001 and MEA 002 respectively. Study GS-US-366-1216 is a Phase 3b, Randomized, Double-Blind Switch Study to Evaluate the Safety and Efficacy of Emtricitabine/Rilpivirine/Tenofovir Alafenamide (FTC/RPV/TAF) Fixed Dose Combination (FDC) in HIV-1 Positive Subjects who are Virologically Suppressed on Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate (FTC/RPV/TDF) Study GS-US-366-1160 is a Phase 3b, Randomized, Double-Blind Study to Evaluate Switching from a Regimen Consisting of Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate (EFV/FTC/TDF) Fixed Dose Combination (FDC) to Emtricitabine/Rilpivirine/Tenofovir Alafenamide (FTC/RPV/TAF) FDC in Virologically-Suppressed, HIV-1 Infected Subjects. The Marketing Authorisation Holder took the opportunity to make minor administrative corrections in the SmPC, Annex II, Labelling and Package Leaflet”	
Olysio - simeprevir - EMEA/H/C/002777/II/0027/G MAH: Janssen-Cilag International NV, Rapporteur: Aranzazu Sancho-Lopez, “Update of sections 4.4 and 4.5 of the SmPC in order to update Pharmacokinetics data of drug-drug interactions following the submission of final clinical study reports for phase 2 studies: TMC435HPC2017 and TMC435HPC3016.”	Weekly start timetable.
Opdivo - nivolumab - EMEA/H/C/003985/II/0023 MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez, “Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and pharmacological information with the 24 months data from the completed NSCLC studies CA209017 and CA209057.”	Weekly start timetable.
Prialt - ziconotide - EMEA/H/C/000551/II/0052 MAH: Eisai Ltd, Rapporteur: Koenraad Norga,	

"Update of sections 4.4, 4.6 and 4.8 of the SmPC in order to update the safety information following receipt of final PRAC PSUR assessment report (Procedure no.: EMEA/H/C/PSUSA/00003142/201512). The Package Leaflet sections 2 and 4 are updated accordingly."	
ProQuad - measles, mumps, rubella and varicella vaccine (live) - EMEA/H/C/000622/II/0114 MAH: Sanofi Pasteur MSD SAS, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC in order to add acute haemorrhagic oedema of infancy with a frequency rare in the tabulated list of adverse reactions."	Weekly start timetable.
Revestive - teduglutide - EMEA/H/C/002345/II/0034, Orphan MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Sinan B. Sarac, "Submission of the Clinical Study Report of study TED-C10-004 ('A Randomized, Double-blind, Multiple-dose, Placebo controlled, Parallel-group, Single-center Study to Assess the Effects of Teduglutide on Postprandial Gallbladder Motility and Biliary Luminal Diameters in Healthy Volunteers') that was not submitted to the EMA by the previous MAH NPS Pharmaceuticals."	Weekly start timetable.
Revestive - teduglutide - EMEA/H/C/002345/II/0036/G, Orphan MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Sinan B. Sarac, "Submission of the 7 non- clinical study reports (study 8248957, 8248958, TED-P10-007, P10-005, XGW00009, V7674M-SHP633 and 19498) that was not submitted to the EMA by the previous MAH NPS Pharmaceuticals."	
Sutent - sunitinib - EMEA/H/C/000687/II/0064 MAH: Pfizer Limited, Rapporteur: Daniela Melchiorri, "Update of section 4.1 of the SmPC in order to remove statement 'Experience with SUTENT as first-line treatment is limited (see section 5.1)' based on the final CSR of study A6181202 in fulfilment of MEA 037.2."	
Tivicay - dolutegravir - EMEA/H/C/002753/II/0027 MAH: ViiV Healthcare UK Limited, Rapporteur: Filip Josephson, "Update of section 4.8 of the	Weekly start timetable.

SmPC for the 50mg film-coated tablets to add the ADRs arthralgia and myalgia with a frequency of uncommon. The Package Leaflet has been updated accordingly. In addition, the MAH has taken the opportunity to make minor corrections in section 5.1 of the SmPC and to update the contact details of the local representative in Norway in the Package Leaflet."	
Travatan - travoprost - EMEA/H/C/000390/II/0053 MAH: Alcon Laboratories (UK) Ltd, Rapporteur: Concepcion Prieto Yerro, "Following the submission of final CSR for study C-01-79 and a review of supporting clinical studies and post-marketing data, update to SmPC section 4.8 is proposed. The package leaflet is updated accordingly. In addition, MAH took the opportunity to update number of the Spanish representative in the PL."	Weekly start timetable.
Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/II/0035 MAH: ViiV Healthcare UK Limited, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC to include Week 48 data from the Phase IIIb clinical study ING117172 (ARIA) to support the use of Triumeq in HIV-infected antiretroviral (ART)-naïve women."	Weekly start timetable.
Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/II/0036 MAH: ViiV Healthcare UK Limited, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC to include Week 24 (primary analysis) and Week 48 data from the Phase IIIb clinical study 201147 (STRIIVING), to support the use of Triumeq in HIV-infected antiretroviral (ART)-experienced adults."	Weekly start timetable.
Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/II/0037 MAH: ViiV Healthcare UK Limited, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC to add the ADR myalgia with a frequency of common, and to update the source of observed ADRs with the combination of dolutegravir + abacavir/lamivudine, based on post-marketing experience with dolutegravir."	Weekly start timetable.

Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0173 MAH: Gilead Sciences International Ltd, Rapporteur: Joseph Emmerich, “Submission of final long-term safety and efficacy data (480 weeks) from two completed Phase 3 studies in HBeAg-negative and HBeAg-positive patients with chronic hepatitis B (CHB), Studies GS-US-174-0102 and GS-US-174-0103.”	Weekly start timetable.
Vokanamet - canagliflozin / metformin - EMEA/H/C/002656/II/0023 MAH: Janssen-Cilag International NV, Rapporteur: Martina Weise, “Update of section 4.4 of the SmPC in order to update the safety information: the term 'and fatal' is added when describing the Diabetic Ketoacidosis cases that have been reported. The Package Leaflet is updated accordingly: term 'rare but serious, sometimes life-threatening and fatal' is added when describing Diabetic Ketoacidosis. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.”	
Xagrid - anagrelide - EMEA/H/C/000480/II/0074, Orphan MAH: Shire Pharmaceutical Contracts Ltd., Rapporteur: Pierre Demolis, “Submission of the final Clinical Study Report of the study SPD422-403, a phase IIIb, randomised, open-label study conducted as a specific obligation to compare the safety, efficacy, and tolerability of anagrelide hydrochloride versus hydroxyurea in high-risk essential thrombocythaemia patients. No changes to the approved product information have been requested as a consequence of this study report.”	
Xagrid - anagrelide - EMEA/H/C/000480/II/0075, Orphan MAH: Shire Pharmaceutical Contracts Ltd., Rapporteur: Pierre Demolis, “Update of sections 4.4, 4.5 and 5.1 of the SmPC in order to change the terminology of myeloproliferative disorders to neoplasms, add text regarding platelet count rebound above baseline following dosage interruption, incorporate a section in drug interactions on Cyp 1A2 inducers and update information on the mode of action. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of	Weekly start timetable.

local representatives in the Package Leaflet, correct typographical errors and bring the PI in line with the latest QRD template. No changes were proposed to the RMP."	
Xyrem - sodium oxybate - EMEA/H/C/000593/II/0063/G MAH: UCB Pharma Ltd., Rapporteur: Bruno Sepodes, "Update of section 4.4 to update the warning on neuropsychiatric events and update of section 4.8 to include increased appetite, homicidal ideation, aggression, irritability and dyskinesia as undesirable effects with an unknown frequency. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 10)."	Weekly start timetable.
Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0029 MAH: AstraZeneca AB, Rapporteur: Greg Markey, "Update of sections 4.2, 4.4 and 5.1 to amend the S.aureus breakpoints (Susceptible and Resistant). Consequently the package leaflet is amended." Request for Supplementary Information adopted on 21.07.2016.	
WS1041 **CONTROLOC Control- EMEA/H/C/001097/WS1041/0025** **PANTOLOC Control- EMEA/H/C/001100/WS1041/0029** **PANTOZOL Control- EMEA/H/C/001013/WS1041/0027** **SOMAC Control- EMEA/H/C/001098/WS1041/0026** MAH: Takeda GmbH, Lead Rapporteur: Greg Markey, "Update of sections 4.3, 4.4, 4.5, 4.6 and 4.8 of the SmPC to reflect that co-administration with HIV protease inhibitors in contraindicated (not only atazanavir), to include a warning about the reduction of the absorption of vitamin B12, and a warning about the increased risk of bone fractures and hypomagnesemia, to include drug interactions with HIV protease inhibitors in section 4.5 of the SmPC, to include that animal studies have shown excretion of pantoprazole in breast milk, and to include fracture of wrist, hip and spine as undesirable effects with unknown frequency.	Weekly start timetable.

The package leaflet is updated accordingly."	
WS1055 **Ebymect-** **EMEA/H/C/004162/WS1055/0016** **Edistride-** **EMEA/H/C/004161/WS1055/0012** **Forxiga-** **EMEA/H/C/002322/WS1055/0031** **Qtern-EMEA/H/C/004057/WS1055/0004** **Xigduo-EMEA/H/C/002672/WS1055/0027** MAH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to update the safety information related to rash. The Package Leaflet is updated accordingly. Additional editorial changes were made in sections 5.1, 5.2 of the SmPC to Qtern."	Weekly start timetable.
WS1056 **Ebymect-** **EMEA/H/C/004162/WS1056/0015** **Edistride-** **EMEA/H/C/004161/WS1056/0011** **Forxiga-** **EMEA/H/C/002322/WS1056/0030** **Qtern-EMEA/H/C/004057/WS1056/0003** **Xigduo-EMEA/H/C/002672/WS1056/0026** MAH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder, "Update of sections 4.5 to add information on the interaction between 1,5-anhydroglucitol assay (monitoring glycaemic control method) and the SGLT2 inhibitors. In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10. Combined SmPCs are introduced in line with the EMA Policy on combined Summaries of Product Characteristics (SmPCs) (EMA/333423/2015)."	Weekly start timetable.
WS1062 **Descovy-** **EMEA/H/C/004094/WS1062/0011** **Genvoya-** **EMEA/H/C/004042/WS1062/0023** **Odefsey-** **EMEA/H/C/004156/WS1062/0009** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings, "Update of sections 4.8 and 5.1 of the SmPC in order to	

provide information about Studies GS-US- 292-0104 and GS-US- 292-0111. In addition, the Worksharing applicant (WSA) took the opportunity to make minor administrative corrections to the Product Information of Genvoya, Descovy and Odefsey and linguistic amendments in Slovakian, Swedish, Polish, Latvian, Czech and Portuguese.”	
WS1070 **Bretaris Genuair-** **EMEA/H/C/002706/WS1070/0032** **Eklira Genuair-** **EMEA/H/C/002211/WS1070/0032** MAH: AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, “Update of section 4.3 of the SmPC in order to modify the contraindication section deleting reference to hypersensitivity to atropine or its derivative providing justification for the claim that the chemical structure of aclidinium is unrelated to that of atropine or its derivatives. The Package Leaflet is updated accordingly.”	
WS1079 **Exviera-EMEA/H/C/003837/WS1079/0023** **Viekirax-** **EMEA/H/C/003839/WS1079/0028** MAH: AbbVie Ltd., Lead Rapporteur: Filip Josephson, “Update of section 4.5 to include information on the drug-drug interaction with mTOR inhibitors sirolimus and everolimus. The Package Leaflet is updated accordingly.”	Weekly start timetable.
WS1066 **Adcirca-EMEA/H/C/001021/WS1066/0026** **Cialis-EMEA/H/C/000436/WS1066/0086** MAH: Eli Lilly Nederland B.V., Lead Rapporteur: Concepcion Prieto Yerro “Update of sections 4.2 and 5.1 of the SmPC in order to reflect the results of study H6D-MC-LVJJ, a randomized, double-blind, placebo-controlled phase 3 trial of tadalafil in the treatment of Duchenne Muscular Dystrophy (DMD), to fulfil Adcirca P46 019.1 and Cialis P46 045.1.”	Weekly start timetable. Discussion at January Plenary see 9.1

B.5.3. CHMP-PRAC assessed procedures

Cinqaero - reslizumab - **EMEA/H/C/003912/II/0005/G**	

MAH: Teva Pharmaceuticals Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 4.2 of the SmPC in order to include a revised dosing regimen as a result of the new 25mg vial presentation. Consequential B.II.e.5c variation to change the pack size of the finished product and update sections 6.5 and 6.6 of the SmPC. The Annex II, Package Leaflet, Labelling and Risk Management Plan v. 2.0 are updated accordingly."

Cometriq - cabozantinib - EMEA/H/C/002640/II/0024, Orphan

MAH: Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "Submission of the final study report of the non-clinical study (XL184-NC-036) to assess the carcinogenicity potential in rat. Update of section 5.3 of the SmPC to reflect the results of this study. In addition, the risk management plan (RMP) is being updated accordingly."

Exjade - deferasirox - EMEA/H/C/000670/II/0052, Orphan

MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, Co-Rapporteur: Luca Pani, PRAC Rapporteur: Claire Ferard, "Update of sections 4.4 and 5.1 of the SmPC to include final results of study ICL670F2201: 'a randomized, open-label, multicentre, two-arm phase II study to evaluate the safety of deferasirox film-coated tablet (FCT) formulation and deferasirox dispersable tablet (DT) formulation in patients with transfusion dependent thalassemia or myelodysplastic syndrome (MDS) at very low, low or intermediate risk requiring chelation therapy due to iron overload' and consequent warnings (in order to fulfil ANX 047). The MAH took the opportunity to update Annex II and the RMP (version 14) are updated accordingly." Request for Supplementary Information adopted on 10.11.2016.

Fampyra - fampridine - EMEA/H/C/002097/II/0036/G

See also 9.1 in the main part of the agenda.

MAH: Biogen Idec Ltd, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus, "This is a grouped variation proposing updates:

- to the SmPC sections 4.2, 5.1, Annex II and

Package Leaflet based on the clinical study Enhance,

- to the SmPC section 4.6 based on the data from pregnancy registry.

- Further changes to the PI, section 4.2 and 5.2 of the SmPC have been introduced based on the Core Data Sheet (CDS) and PRAC review of the Fampyra PSUR 03.

The RMP (version 11) 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.

With this application the MAH requests to switch the marketing authorisation from conditional to standard."

Firdapse - amifampridine - EMEA/H/C/001032/II/0043, Orphan
MAH: BioMarin Europe Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams,
"Update of sections 4.4 and 5.3 of the SmPC respectively in order to delete the statements that amifampridine has not been fully tested in carcinogenicity models and to provide the findings from the carcinogenicity reports required for the completion of SOB 004.

The RMP (v.9) is proposed to be updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to request the removal of the requirement to complete carcinogenicity testing in an appropriate model in section E of the Annex II."
Request for Supplementary Information adopted on 10.11.2016, 15.09.2016.

Gilenya - fingolimod - EMEA/H/C/002202/II/0040
MAH: Novartis Europharm Ltd, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard,
"Update of section 4.6 of the SmPC to add information on the use of the product in pregnancy. In addition, update of section 5.3 of the SmPC to include information about the dose correspondence between human and the species used for the preclinical tests of teratogenicity.
An updated RMP is submitted (version 12.0).
The MAH took the opportunity to make minor

editorial changes in sections 4.4, 4.5, 4.6 and 5.2 and also in Annex II.D."
Request for Supplementary Information adopted on 13.10.2016.

Kalydeco - ivacaftor -
EMEA/H/C/002494/II/0054, Orphan
MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Dolores Montero Corominas, "Submission of the final clinical study report (CSR) for Study VX12-770-112 (Study 770-112), to fulfil a Risk Management Plan commitment. Study 112 was a rollover study to evaluate the long-term safety and efficacy of IVA treatment in subjects ≥6 years of age with cystic fibrosis (CF) and a non-G551D mutation in the CFTR gene. The RMP has been amended consequently with final results of Study 770-112 (ver. 5.4)."

Keytruda - pembrolizumab -
EMEA/H/C/003820/II/0018/G
MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus, "Update of section 5.1 of the SmPC to reflect the data from the post-authorisation efficacy studies (PAES) in melanoma; studies P001, P002 and P006. Annex II has been revised to reflect that these three final CSRs have been submitted.

An updated RMP version 6.0 was provided as part of the application. The following summarizes the changes to the updated RMP:
• □The fin
melanoma studies P001/002/006 and removed as PAES commitments from the RMP;
• □Me
validation report for anti-MK-3475 neutralizing antibody assay were included as Completed Pharmacovigilance Activities;
• □The M
term safety' as missing information in the list of ongoing safety concerns."

Lonsurf - trifluridine / tipiracil -
EMEA/H/C/003897/II/0002/G
MAH: Les Laboratoires Servier, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Ulla Wändel Liminga, "1) C.I.4 (type II) - Update of sections 4.2, 4.4 and 5.2 of the SmPC

following availability of the final clinical study report for the study TO-TAS-102-106, A phase I, open-label study evaluating the safety, tolerability, and pharmacokinetics of TAS-102 in patients with advanced solid tumours and varying degrees of hepatic impairment (requested in MEA 002). As a consequence of TO-TAS-102-106 study results, the RMP (ver. 5.0) is updated to remove the missing information “Use in patients with moderate to severe hepatic impairment”, and to add “Hyperbilirubinaemia in patients with baseline moderate to severe hepatic impairment” as important potential risk.
2) C.I.4 (type II) - Update of sections 4.5 and 5.2 of the SmPC following availability of the results of the in vitro CYP induction study of tipiracil hydrochloride (TPI) using the appropriate concentration of TPI (requested in a recommendation). Section SVII.4 of the RMP is updated accordingly.
3) C.I.4 (type II) - Update of section 4.2 of the SmPC in order to correct inconsistencies in the dose calculation according to body surface area. The package leaflet is updated to add ‘interstitial lung disease’ in the serious side effects part of section 4.
In addition, the MAH took the opportunity to update Annex IIIA in accordance with the latest QRD template.”

Odomzo - sonidegib - EMEA/H/C/002839/II/0007

MAH: Novartis Europharm Ltd, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Julie Williams, “To provide the final study report from the nonclinical Study No. 1070056: A study to perform an evaluation of a subset of tissues from the 6-month rat study using Ki-67 immunohistochemistry and to quantify cell proliferation.”

Odomzo - sonidegib - EMEA/H/C/002839/II/0008/G

MAH: Novartis Europharm Ltd, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Julie Williams, “C.I.13 (Type II): To provide the final study report from the Clinical Pharmacology Study CLDE225A2120: A relative bioavailability study to evaluate timing of meal relative to dose and fast conditions and effect of light meal (low fat meal), which is a category 3

study in the Odomzo Risk Management Plan (RMP).

C.I.11.z (Type IB): to change the Clinical Study Report due date for a category 3 study in version 5.0 of the EU RMP: The CSR submission date for study X2116 is changed from Q1 2017 to Q4 2018.

C.I.11.z (Type IB): to change the Clinical Study Report due date for a category 3 study in version 5.0 of the EU RMP: The study CLDE225A2404 timelines and the CSR submission date for study CLDE225A2404 are changed from Q4 2024 to Q1 2025."

Opdivo - nivolumab - EMEA/H/C/003985/II/0024

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 5.1 of the SmPC in order to reflect the final overall survival and response data, including duration of response with longer follow-up, following completion of PAES CA209037 (Randomized, Open-Label, Phase 3 Trial of nivolumab vs Investigator's Choice in Advanced (Unresectable or Metastatic) Melanoma Patients Progressing Post Anti-CTLA-4 Therapy) and its addendum on predictability of efficacy with biomarkers.
This application fulfils ANX 001 and 003.1.
Annex II has been updated accordingly.
RMP version 5.5 has been submitted within this application."

Prolia - denosumab - EMEA/H/C/001120/II/0065

MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of a revised RMP (version 18) in order to update the following information: "important potential risk of hypercalcemia following treatment discontinuation in patients with growing skeletons to: "important potential risk: hypercalcemia following treatment discontinuation in patients with growing skeletons and the adult population. This RMP update is based on Amgen's updated safety assessment conducted earlier this year.
The applicant also took the opportunity to request the removal of the important potential risk of fracture healing complications following

the PRAC recommendation in procedure EMEA/H/C/PSUSA/00000954/201509. In addition, to add study 20090601: a post-marketing active safety surveillance programmeprogram for soliciting adverse events of special interest in the United States, as a category 4 study pharmacovigilance activity."

Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0108

MAH: GSK Biologicals SA, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "Update of sections 4.2 4.4, 4.8 and 5.1 of the SmPC in order to add information obtained from two clinical studies in subjects at risk for pneumococcal infections (study 10PN-PD-DIT-034 and study 10PN-PD-DIT-064)
In addition, the Marketing authorisation holder (MAH) took the opportunity to make consequential changes to the RMP and to change the final due date of a post-marketing surveillance study."
Request for Supplementary Information adopted on 15.09.2016.

Tagrisso - osimertinib - EMEA/H/C/004124/II/0004

MAH: AstraZeneca AB, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Sabine Straus, "Update of section 5.2 of the SmPC to reflect the results of study 20 which was performed to assess the absolute bioavailability and to evaluate the PK parameters of Tagrisso in plasma following a single oral dose and a radio-labelled intravenous (IV) microdose of[14C] Tagrisso in healthy male subjects. In addition, the MAH took the opportunity to make a minor correction in SmPC section 6.5 and the Package Leaflet, where blister strips have been amended to blisters. Further, the MAH provided an updated RMP version 5.0 as part of the application."
Request for Supplementary Information adopted on 10.11.2016, 15.09.2016.

Translarna - ataluren - EMEA/H/C/002720/II/0027, Orphan

MAH: PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus, "Update of section

4.8 of the SmPC to add that the safety profile of ataluren in nonambulatory patients was similar to the safety profile in ambulatory patients to reflect the results of a 48-week open label extension study in patients with nmDMD."
Request for Supplementary Information adopted on 15.09.2016.

Tresiba - insulin degludec - EMEA/H/C/002498/II/0024/G
MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "Grouping of two variations to update sections 4.2 and 5.1 of the SmPC in order to include updated information on the use of Tresiba in terms of transfer from other basal insulin regimens and the effects of Tresiba on hypoglycaemia.

The Package Leaflet and Labelling are proposed to be updated accordingly.

An updated RMP (version 7.0) is being submitted.

The proposed changes reflect the findings from two studies submitted:
NN1250-3995 (SWITCH 1) and NN1250-3998 (SWITCH 2), comparing the safety and efficacy of Tresiba and insulin glargine U-100, mainly to document the hypoglycaemia profile in type 1 diabetes and type 2 diabetes, respectively.

In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0.

Finally, minor changes have been made to the SmPC section 4.2 and the corresponding section of the Package Leaflet to clarify the correct use of Tresiba."

Xadago - safinamide - EMEA/H/C/002396/II/0014
MAH: Zambon SpA, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Almath Spooner, "Submission of study VDD4193 (Safinamide: In Vitro Metabolic Stability in Human Cryopreserved Hepatocytes, by Fatty Acid Amide Hydrolase enzyme (FAAH), Recombinant Human N-Acylethanolamine Acid Amidase (NAAA) and Recombinant Human Acid Ceramidase (ASAHI)) conducted in

order to identify specific substances blocking the amidases (inhibitors of amidases) involved in the metabolism of safinamide. The study fulfils the MEA 001.2."

Xgeva - denosumab - EMEA/H/C/002173/II/0051

MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of a revised Risk Management Plan (RMP) (version 23) in order to update the following information: a newly categorised important potential risk of hypercalcemia following treatment discontinuation in patients other than those with growing skeletons. This RMP update is based on Amgen's updated safety assessment conducted earlier this year. The applicant also took the opportunity to include minor changes for correction and/or to add clarification."

Zykadia - ceritinib - EMEA/H/C/003819/II/0010

MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Ulla Wändel Liminga, "Provision of an update for study A2303, listed in SOB004. Sections 4.8 and 5.1 of the SmPC are proposed to be updated to reflect the safety and efficacy findings of the study. The Package Leaflet and Labelling are updated accordingly.

Annex II and the Risk Management Plan are also proposed to be updated to reflect the potential fulfilment the only outstanding specific obligation and the efficacy and safety results of Study A2303, respectively."

WS0991
Actos-EMEA/H/C/000285/WS0991/0075
Competact-EMEA/H/C/000655/WS0991/0062
Glubrava-EMEA/H/C/000893/WS0991/0047
Glustin-EMEA/H/C/000286/WS0991/0073
Tandemact-EMEA/H/C/000680/WS0991/0051

MAH: Takeda Pharma A/S, Lead Rapporteur: Patrick Salmon, Lead PRAC Rapporteur: Almath Spooner, "Submission of the final study report for the Clinical Practice Research Datalink (CPRD) GOLD linkage study (Pioglitazone_5018) conducted to investigate a possible association

of the use of pioglitazone with prostate cancer and data on the incidence of adjudicated prostate cancer in patients receiving pioglitazone in the long-term Insulin Resistance Intervention after Stroke (IRIS) trial."
Request for Supplementary Information adopted on 13.10.2016.

WS1031
Anoro-EMEA/H/C/002751/WS1031/0013
Laventair-
EMEA/H/C/003754/WS1031/0014
MAH: Glaxo Group Ltd, Lead Rapporteur: Nithyanandan Nagercoil, Lead PRAC Rapporteur: Carmela Macchiarulo, "Update of section 4.8 of the SmPC in order to add the adverse reactions "vision blurred", "intraocular pressure increased" and "paradoxical bronchospasm" and to change the frequency of the adverse reaction "glaucoma" from "not known" to "rare". The Package Leaflet (PL) is updated accordingly.
In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.
The risk management plan is submitted to reflect the changes proposed for the SmPC and also includes revision requested as part of the outcome of previous PSURs."
Request for Supplementary Information adopted on 10.11.2016.

WS1047
Kalydeco-
EMEA/H/C/002494/WS1047/0055
Orkambi-
EMEA/H/C/003954/WS1047/0016
MAH: Vertex Pharmaceuticals (Europe) Ltd., Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, "Submission of final clinical study report (CSR) for Study VX12-770-115 (Study 770-115), an ocular safety study of ivacaftor-treated paediatric patients 11 years of age or younger with Cystic Fibrosis (CF) as a follow up of Kalydeco MEA 023 and Orkambi MEA 004.
The RMPs are being updated accordingly (ver. 5.3 for Kalydeco and ver. 2.6 for Orkambi)."

WS1075
Epclusa-
EMEA/H/C/004210/WS1075/0006

Harvoni-
EMEA/H/C/003850/WS1075/0043
Sovaldi-EMEA/H/C/002798/WS1075/0037
MAH: Gilead Sciences International Ltd, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, "Submission of the final non-clinical study report PC-334-2035 assessing the potential for a pharmacokinetic interaction via transporter or enzyme based inhibition when sofosbuvir and other Direct Acting Antivirals (DAAs) are used concomitantly with amiodarone
The RMPs (Epclusa – RMP version 1.0, Harvoni – RMP version 2.0, Sovaldi – RMP version 5.0) have been updated accordingly."

B.5.4. PRAC assessed procedures

PRAC Led
Enbrel - etanercept -
EMEA/H/C/000262/II/0198
MAH: Pfizer Limited, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Rafe Suvarna, , "Submission of the final clinical study report for the BSPAR (British society for paediatric and adolescent rheumatology) entanercept registry, a cohort study (category 3 study in the RMP)" Request for Supplementary Information adopted on 15.09.2016.

PRAC Led
Eperzan - albiglutide -
EMEA/H/C/002735/II/0029/G
MAH: GlaxoSmithKline Trading Services, PRAC Rapporteur: Julie Williams, , "II: C.I.11.b - Update of the RMP to amend Study 201805 (category 3 study): "Observational Study of the Risk of Common Malignant Neoplasms and Malignant Neoplasms of Special Interest (Thyroid and Pancreatic Cancer) in Subjects Prescribed
Albiglutide Compared to Those Prescribed Other Antidiabetic Agents", in order to use a different database to study the risk of neoplasms in association with albiglutide exposure
II: C.I.11.b – Update of the RMP to add a new category 3 study as an additional pharmacovigilance activity – Study 207351: "Observational Study to Assess Maternal and Fetal Outcomes following exposure to Albiglutide

during Pregnancy""

PRAC Led

Humira - adalimumab - EMEA/H/C/000481/II/0162

MAH: AbbVie Ltd., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, , "Submission of the final national report for the Swedish biologics registry ARTIS (Anti-Rheumatic Treatment in Sweden) after ending AbbVie's support by end 2015. This fulfils MEA 066.5. No changes to the product information have been proposed."

PRAC Led

Ozurdex - dexamethasone - EMEA/H/C/001140/II/0025

MAH: Allergan Pharmaceuticals Ireland, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, , "In line with the RMP commitment, submission of the final report for the Post-Authorisation Safety Study 206207-025 (A Prospective Observational Study to Evaluate Long-Term Safety in Real-World Clinical Practice.)"

PRAC Led

Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0039

MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Eva A. Segovia, , "Submission of final report of the Drug Utilization Study REVIEU (CETB115B2406) in fulfilment of MEA 21.1."

PRAC Led

Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0040

MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Eva A. Segovia, "Submission of the final data from the nested eltrombopag HCV-TARGET cohort study. An updated RMP version 44.0 has also been submitted."

PRAC Led

Vfend - voriconazole - EMEA/H/C/000387/II/0121

MAH: Pfizer Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus, , "Submission of study A1501102 evaluating the effectiveness of aditional risk minimisation measure that aim to reduce the

risks of phototoxicity, squamous cell carcinoma (SCC) of the skin and hepatic toxicity in patients receiving Voriconazole in the European Union (EU). As a consequence, the RMP (version 5) is updated accordingly."
Request for Supplementary Information adopted on 15.09.2016.

PRAC Led
WS0943
Saxenda-
EMEA/H/C/003780/WS0943/0009
Victoza-EMEA/H/C/001026/WS0943/0041
MAH: Novo Nordisk A/S, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, , "Submission of the final results from the main "Liraglutide safety and surveillance program using the Optum Research Database" study and sub-study on breast cancer - RMP category 3 study."
Request for Supplementary Information adopted on 15.09.2016.

PRAC Led
WS0960/G
Komboglyze-
EMEA/H/C/002059/WS0960/0033/G
Onglyza-
EMEA/H/C/001039/WS0960/0040/G
MAH: AstraZeneca AB, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, , "Group of variations consisting of final epidemiological study results for:
1- study D1680R00011
2- study D1680R00012
3- study D1680R00013
4- study D1680R00014
5- study D1680R00015
6- update of the RMP to reflect the submission of the 5 epidemiological studies. As a consequence, the RMP (version 11) is updated accordingly. In addition, routine changes are made in parts III (pharmacovigilance plan, overview of planned pharmacovigilance actions) and IV. A safety review based on literature has also been included to investigate acute kidney injury associated with saxagliptin/saxagliptin and metformin at the PRAC request."
Request for Supplementary Information adopted on 15.09.2016.

PRAC Led

WS1059 **Prezista-** **EMEA/H/C/000707/WS1059/0084** **Rezolsta-** **EMEA/H/C/002819/WS1059/0015** MAH: Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, , "Submission of an updated RMP version 3.1 in order to propose the deletion of the cat 3 study TMC114HIV3015 in HIV-1 infected pregnant women and replace the commitment by the assessment of the pharmacokinetics data in HIV-1 pregnant women."	

B.5.5. CHMP-CAT assessed procedures

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

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

WS1029 **M-M-RVAXPRO-** **EMEA/H/C/000604/WS1029/0078** **ProQuad-** **EMEA/H/C/000622/WS1029/0112** MAH: Sanofi Pasteur MSD SAS, Lead Rapporteur: Jan Mueller-Berghaus,	Weekly start timetable.
WS1048/G **Infanrix hexa-** **EMEA/H/C/000296/WS1048/0212/G** MAH: GSK Biologicals SA, Lead Rapporteur: Bart Van der Schueren	
WS1049 **Infanrix hexa-** **EMEA/H/C/000296/WS1049/0210** MAH: GSK Biologicals SA, Lead Rapporteur: Bart Van der Schueren, "To update SmPC section 6.6 in order to reflect the currently registered information regarding the plastic rigid tip cap (PRTC) type pre-filled syringe (PFS). The package leaflet is updated accordingly."	
WS1065 **Entresto-**	Weekly start timetable.

EMEA/H/C/004062/WS1065/0010 **Neparvis-** **EMEA/H/C/004343/WS1065/0008** MAH: Novartis Europharm Ltd, Lead Rapporteur: Johann Lodewijk Hillege,	
WS1071 **Hexacima-** **EMEA/H/C/002702/WS1071/0054** **Hexaxim-** **EMEA/H/W/002495/WS1071/0061** **Hexyon-** **EMEA/H/C/002796/WS1071/0058** MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus, This WS also includes Nationally Authorised Products (NAPs) as listed in Annex B.”	Weekly start timetable.
WS1093 **Genvoya-** **EMEA/H/C/004042/WS1093/0025** **Stribild-EMEA/H/C/002574/WS1093/0076** **Tybost-EMEA/H/C/002572/WS1093/0033** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings, “To update the product information annexes with the PRAC adopted wording on interaction between cobicistat-containing products and corticosteroids. Section 4.5 of the SmPC and Section 2 of the PIL have been updated with the PRAC adopted text. The MAH is proposing an additional minor update in Section 4.5 in line with the adopted PRAC recommendation (update to the type of corticosteroids impacted by this interaction). For Tybost only, the MAH is adding another minor edit in Section 4.5 of the SmPC in line with the adopted PRAC recommendation and the opportunity is used to apply the following administrative changes: streamlining the text in SmPC Section 4.4 to remove the reference to elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate in consideration of the approval of Genvoya (elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide) and other COBI-containing products. Tybost is also aligned to the latest QRD 10 template.”	
WS1109 **Cymbalta-** **EMEA/H/C/000572/WS1109/0070**	

Duloxetine Lilly- EMEA/H/C/004000/WS1109/0006 MAH: Eli Lilly Nederland B.V., Duplicate, Duplicate of Ariclaim, Yentreve, Lead Rapporteur: Aranzazu Sancho-Lopez, “To update the annexes in line with the latest QRD template. In addition the fertility information in section 4.6 of the SmPC has been improved as requested by the rapporteur. Furthermore the addition of multipack labelling was added”	

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

Armisarte - pemetrexed - EMEA/H/C/004109/II/0010 MAH: Actavis Group PTC ehf, Rapporteur: Alar Irs Withdrawal request submitted on 09.01.2017.	The MAH withdrew the procedure on 09.01.2017.

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

B.5.11. Worksharing variations according to Article 20 of Commission Regulation (EC) No 1234/2008 (listing intended submissions of type II variations for CAPs and NAPS with the outcome regarding the Lead Rapporteur)

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

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

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

- dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171 indicated for the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4, List of Questions adopted on 21.07.2016.
Mimpara - cinacalcet - EMEA/H/C/000570/X/0055/G MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Ulla Wändel Liminga, “Extension application to introduce a new pharmaceutical form associated with new strengths (1 mg, 2.5

mg and 5 mg hard capsules) grouped with a type II variation (C.1.6.a) to include paediatric use in the approved indication.

As a consequence, sections 4.2 and 4.4 of the SmPC are updated to detail posology in paediatric patients and to update the safety information, respectively.

The Package Leaflet and Labelling are updated in accordance.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.

Furthermore, the PI is brought in line with the latest QRD template version 10."
List of Questions adopted on 13.10.2016.

- etirinotecan pegol - EMEA/H/C/003874
treatment of breast cancer with brain metastases,
List of Questions adopted on 10.11.2016.

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

Defitelio - defibrotide -
EMEA/H/C/002393/S/0020, Orphan
MAH: Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams

SCENESSE - afamelanotide -
EMEA/H/C/002548/S/0011, Orphan
MAH: Clinuvel (UK) Limited, Rapporteur: Harald Enzmann, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Valerie Strassmann

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

ECALTA - anidulafungin -
EMEA/H/C/000788/R/0033
MAH: Pfizer Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Sabine Straus

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

Cubicin - daptomycin -
EMEA/H/C/000637/II/0061
MAH: Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, Co-Rapporteur: Karsten Bruins Slot, PRAC Rapporteur: Julie Williams, “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.”

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Armisarte - pemetrexed -
EMEA/H/C/004109/II/0008/G
MAH: Actavis Group PTC ehf, Rapporteur: Alar Irs

Envarsus - tacrolimus -
EMEA/H/C/002655/II/0008/G
MAH: Chiesi Farmaceutici S.p.A., Rapporteur: John Joseph Borg

Fortacin - lidocaine / prilocaine -
EMEA/H/C/002693/II/0015
MAH: Plethora Solutions Ltd., Rapporteur: Concepcion Prieto Yerro

Inhixa - enoxaparin sodium -
EMEA/H/C/004264/II/0004/G
MAH: Techdow Europe AB, Duplicate, Duplicate of Thorinane, Rapporteur: Andrea Laslop

Keytruda - pembrolizumab -
EMEA/H/C/003820/II/0020/G
MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri

Lonquex - lipegfilgrastim -
EMEA/H/C/002556/II/0030/G
MAH: Sicor Biotech UAB, Rapporteur: Greg Markey

MabThera - rituximab -
EMEA/H/C/000165/II/0129/G
MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac

MabThera - rituximab -
EMEA/H/C/000165/II/0130/G
MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac

Nucala - mepolizumab -
EMEA/H/C/003860/II/0007
MAH: GlaxoSmithKline Trading Services, Rapporteur: Nithyanandan Nagercoil

Omnitrope - somatropin -
EMEA/H/C/000607/II/0045
MAH: SANDOZ GmbH, Rapporteur: Johann Lodewijk Hillege

Ratiograstim - filgrastim -
EMEA/H/C/000825/II/0053/G
MAH: ratiopharm GmbH, Rapporteur: Outi Mäki-Ikola

Tevagrastim - filgrastim -
EMEA/H/C/000827/II/0063/G
MAH: TEVA GmbH, Duplicate, Duplicate of Biograstim, Rapporteur: Outi Mäki-Ikola

Zostavax - shingles (herpes zoster) vaccine (live) - EMEA/H/C/000674/II/0109/G
MAH: Sanofi Pasteur MSD SAS, Rapporteur: Jan Mueller-Berghaus

WS1099/G
Neulasta-
EMEA/H/C/000420/WS1099/0092/G
Ristempa-
EMEA/H/C/003910/WS1099/0009/G
MAH: Amgen Europe B.V., Lead Rapporteur: Robert James Hemmings

WS1125/G
Helixate NexGen-
EMEA/H/C/000276/WS1125/0187/G
KOGENATE Bayer-
EMEA/H/C/000275/WS1125/0195/G
MAH: Bayer Pharma AG, Lead Rapporteur: Jan Mueller-Berghaus

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

Aclasta - zoledronic acid -
EMEA/H/C/000595/II/0068
MAH: Novartis Europharm Ltd, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to add the adverse reaction hypophosphataemia with an unknown frequency based on post-marketing spontaneous reports and internal databases. The package leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to remove the lower level term 'should pain' which is covered by the corresponding preferred term 'musculosketal pain', to update the list of local representatives in the Package Leaflet and to bring the product information in line with the latest QRD template version 10."

Afinitor - everolimus -
EMEA/H/C/001038/II/0051/G
MAH: Novartis Europharm Ltd, Rapporteur: Harald Enzmann, "C.I.13 Submission of the final clinical study report of study RAD001J2301: A randomized phase-III, double-blind, placebo-controlled multicenter trial of everolimus in combination with trastuzumab and paclitaxel, as first line therapy in women with HER2 positive locally advanced or metastatic breast cancer
C.I.13 Submission of the final clinical study report of study RAD001W2301: A randomized Phase III, double-blind, placebo-controlled multicenter trial of everolimus in combination with trastuzumab and vinorelbine, in pretreated women with HER2/neu over-expressing locally advanced or metastatic breast cancer
In addition, the MAH included a report on exposure-response relationship combining data from these two trials."

Effentora - fentanyl -

EMEA/H/C/000833/II/0045
MAH: Teva B.V., Rapporteur: Martina Weise, "Update of sections 4.4 and 4.5 of the SmPC in order to add a warning on increased risk of increased depressant effects with the concomitant use of alcohol and possibility of a fatal outcome with concomitant use of other CNS depressants following a cumulative review on spontaneous reporting and literature review of these risks. The package leaflet has been updated accordingly.

In addition, the marketing authorisation holder took the opportunity to introduce editorial clarifications in Annex I and Annex IIIB and changes in accordance to QRD template 10."

EVRA - ethinylestradiol / norelgestromin - EMEA/H/C/000410/II/0041
MAH: Janssen-Cilag International NV, Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.3 and 4.5 of the SmPC in order to add a contraindication for patients receiving drug combinations with Direct-acting antiviral (DAA) agents that contain paritaprevir/ritonavir, ombitasvir, and/or dasabuvir as these DAAs have the potential for a drug-drug interaction with ethinyl estradiol (EE)-containing combined hormonal contraceptives resulting in ALT elevations. The Package Leaflet has been updated accordingly."

Kuvan - sapropterin - EMEA/H/C/000943/II/0048/G, Orphan
MAH: BioMarin International Limited, Rapporteur: Patrick Salmon, "Update of section 4.9 to add information regarding shortening of QT interval at high doses following review of data of study QTC-001.

Submission of the clinical study report EMR700773-004 (pilot study assessing the effect of sapropterin on cognitive abilities, study prematurely terminated due to enrolment issues)

In addition, the MAH took the opportunity of this procedure to clarify the wording of section 4.2 and section 3 of the PL."

Lonsurf - trifluridine / tipiracil - EMEA/H/C/003897/II/0003
MAH: Les Laboratoires Servier, Rapporteur: Paula Boudewina van Hennik, "Submission of

the final report from the pharmacogenomics study (NP35044) of TAS-102 in patients with metastatic colorectal cancer refractory to standard chemotherapy (10040080) in order to fulfil a Recommendation made at the time of the initial MA."

Lumigan - bimatoprost - EMEA/H/C/000391/II/0052

MAH: Allergan Pharmaceuticals Ireland, Rapporteur: Hanne Lomholt Larsen, "Update of section 4.8 to add 4 adverse events in the Eye disorders SOC in line with the Company Core Data Sheet. The Package Leaflet has been updated accordingly.
Section 3 of the PL was also amended to improve clarity of instructions.
In addition, the MAH took the opportunity to update the Product Information in line with the QRD template version 10 and implement the unique identifier 2D barcode."

Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0042

MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, "Submission of the ASPIRE (TRC114968) final study report, a Three-Part Study of Eltrombopag in Thrombocytopenic Subjects with Myelodysplastic Syndromes or Acute Myeloid Leukemia (Part 1: Open-Label, Part 2: Randomized, Double-Blind, Part 3: Extension) assessing the potential risk of haematological changes, optimal dose escalation scheme and eltrombopag pharmacokinetics."

Rotarix - human rotavirus, live attenuated - EMEA/H/C/000639/II/0094

MAH: GlaxoSmithKline Biologicals S.A., Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Jean-Michel Dogné, "Submission of the final study report for EPI-ROTA-007 VS US DB (A phase IV, open, observational study of the safety of Rotarix, administered to a birth cohort in US States health insurance plans) which is listed in the section III.4.3 of the Risk Management Plan (RMP) version 16.
Consequently a revised RMP (version 17) is submitted in order to update information in relation to: the EPI-ROTA-007 VS US DB study; the EPI-ROTA-052 BOD EU SUPP as agreed during variation EMEA/H/C/0639/II/0086. In

addition, the MAH took this opportinity to further update the RMP with the new due date for submission of the final study report for ROTA-085 PMS."

Teysuno - tegafur / gimeracil / oteracil - EMEA/H/C/001242/II/0029
MAH: Nordic Group B.V., Rapporteur: Paula Boudewina van Hennik, "Submission of the final clinical study report for Study Salto - A phase III randomized study of S-1 versus capecitabine as first line treatment in metastatic colorectal cancer."

Torisel - temsirolimus - EMEA/H/C/000799/II/0066, Orphan
MAH: Pfizer Limited, Rapporteur: Harald Enzmann, "Submission of the further analysis of a possible association of corticosteroid (pre-)treatment and frequency and severity of hypersensitivity/infusion reactions in study 3066K1-4438-WW (B1771007), as requested by the CHMP during procedures EMEA/H/C/799/MEA 023.1 and EMEA/H/C/799/MEA 024.1. No changes to the PI are proposed."

Torisel - temsirolimus - EMEA/H/C/000799/II/0067, Orphan
MAH: Pfizer Limited, Rapporteur: Harald Enzmann, "Submission of the final report from the Japanese post marketing surveillance (PMS) studies 3066K5-4406 and B1771016 together with the response to the questions raised by the CHMP on the interim report within procedure LEG 031.4.
No changes to the PI are proposed."

Uptravi - selexipag - EMEA/H/C/003774/II/0007
MAH: Actelion Registration Ltd., Rapporteur: Martina Weise, "Update of sections 4.4 and 4.5 of the SmPC in order to add information on pharmacokinetic interactions with gemfibrozil and rifampicin in healthy subjects, based on the final clinical study report of the completed clinical pharmacology drug-drug interaction study AC-065-113. The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update information on the hydrolysis of selexipag based

on data from the previously submitted absolute bioavailability study AC-065-110, make minor amendments to sections 5.1 and 5.2 of the SmPC and to bring the PI in line with the latest QRD template version 10."

WS1106
Exviera-EMEA/H/C/003837/WS1106/0027
Viekirax-
EMEA/H/C/003839/WS1106/0031
MAH: AbbVie Ltd., Lead Rapporteur: Filip Josephson, "Update of sections 4.4 and 4.5 of the SmPC in order to add a warning stating that concomitant use of tacrolimus with dasabuvir and ombitasvir/paritaprevir/ritonavir should be avoided unless the benefit outweigh the risks."

WS1113
Stribild-EMEA/H/C/002574/WS1113/0078
Tybost-EMEA/H/C/002572/WS1113/0035
MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings, "Submission of the final report from Study GS-US-236-0128 listed as a category 3 study in the RMP.

This is a randomized, double-blind phase 3B study to evaluate the safety and efficacy of Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Disoproxil Fumarate versus Ritonavir-boosted Atazanavir plus Emtricitabine/Tenofovir Disoproxil Fumarate in HIV-1 infected, antiretroviral treatment-naive women."

B.6.10. CHMP-PRAC assessed procedures

Emtricitabine/Tenofovir disoproxil Mylan - emtricitabine / tenofovir disoproxil - EMEA/H/C/004050/II/0001
MAH: MYLAN S.A.S, Generic, Generic of Truvada, Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Rafe Suvarna, "Update of the SmPC following the assessment of the extension of indication for the reference product, Truvada, for pre-exposure prophylaxis. The Package Leaflet, Annex II and Labelling are updated in accordance."

Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0064
MAH: MedImmune LLC, Rapporteur: Bart Van

der Schueren, PRAC Rapporteur: Jean-Michel Dogné, “C.I.13: Submission of the final Clinical Study Report for the study number MI-MA194: A Postmarketing Observational Evaluation of the Safety of Fluenz in Children and Adolescents with High-risk Conditions.”

Mozobil - plerixafor - EMEA/H/C/001030/II/0030/G, Orphan

MAH: Genzyme Europe BV, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, “Submission of the final report from study ARD12858 (MOZ23510) “A pilot, exploratory, randomized, phase 2 safety study evaluating tumor cell (plasma cell) mobilization and apheresis product contamination in plerixafor plus non-pegylated G-CSF mobilized patients and in non pegylated G-CSF alone mobilized patients” listed as a category 3 study in the RMP .

Submission of the final report from study OBS13611 (MOZ18009), a multicenter, noninterventional registry designed to evaluate the long-term outcomes for patients who received plerixafor for stem cell mobilization and completed hematopoietic stem cell transplantation (HSCT) compared with patients who received other mobilization methods and completed HSCT, listed as a category 3 study in the RMP.

Submission of the final report from study OBS13612 (MOZ19310), monitoring the plerixafor off-label transplant use, in patients and donors in EBMT centers performing autologous transplants and/or allogeneic transplants, listed as a category 3 study in the RMP.”

Orencia - abatacept - EMEA/H/C/000701/II/0107

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, “Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information following the MAH’s initiative to update its clinical trials safety database to include all currently completed Orencia clinical trials for both the IV and SC formulations. The adverse reactions table in section 4.8, as well as the description of selected adverse reactions of special interest is being amended. Section 4.4 is

being brought in line with the updated section 4.8. The package leaflet is being revised accordingly. An updated Risk Management Plan (Version 22) is also being submitted within this variation.”	
Remicade - infliximab - EMEA/H/C/000240/II/0204 MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “Submission of the final registry report from the C0168T71 study (a review and analysis of birth outcomes from Swedish, Danish and Finish medical birth registers) and an evaluation of pregnancy data from multiple sources. Section 4.6 of the SmPC, relevant section of the PL and the RMP version 13.2 has been updated to reflect the study results. The MAH has also taken the opportunity to bring the product in line with the QRD template and update the local representative section of the PL.”	
Xtandi - enzalutamide - EMEA/H/C/002639/II/0034 MAH: Astellas Pharma Europe B.V., Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Eva A. Segovia, “Update of section 5.1 of the SmPC in order to reflect the final results of the post authorisation efficacy study (PAES) CL-9785-0410 which was a study of enzalutaimide in patients with progressive mCRPC previously treated with abiraterone Acetate, listed as a category 3 in the RMP. The RMP version 11.0 has also been submitted.”	
Xtandi - enzalutamide - EMEA/H/C/002639/II/0035 MAH: Astellas Pharma Europe B.V., Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Eva A. Segovia, “Update of sections 4.4 and 4.8 of the SmPC to reflect the final results of the post authorisation safety study (PASS) CL-9785-0403 which evaluated the risk of seizure among subjects with mCRPC treated with enzalutamide who were at potential increased risk of seizure (UPWARD) and was listed as a category 3 in the RMP. The RMP version 11.0 has also been submitted. In addition, the Marketing authorisation holder	

(MAH) took the opportunity to make a correction in section 5.1 of the SmPC."

Xtandi - enzalutamide - EMEA/H/C/002639/II/0036

MAH: Astellas Pharma Europe B.V., Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Eva A. Segovia, "Update of sections 4.6 and 5.3 of the SmPC to reflect the final results of study AE-7592-G, "Transfer of Radioactivity into Fetuses and Breast Milk in Rats after a Single Oral Administration of [14C] MDV3100- ISN: 9785-ME-0046". The Package Leaflet is updated accordingly. The RMP version 11.0 has also been submitted."

Xultophy - insulin degludec / liraglutide - EMEA/H/C/002647/II/0017

MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, "Update of section 4.2 of the SmPC in order to update the information on use of Xultophy in patients with hepatic impairment, based on clinical trial NN2211-1328, the LEAD 1-6 meta-analysis as well as other liraglutide trials.

In addition, 'fatigue' has been added to the tabulated list of adverse reactions in Section 4.8 of the SmPC. The Package Leaflet is updated accordingly.

RMP version 6.0 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."

WS1086
Stribild-EMEA/H/C/002574/WS1086/0077
Tybost-EMEA/H/C/002572/WS1086/0034

MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Rafe Suvarna, "Submission of the final report from Study GS-US-236-0140. This is a randomized, open-label, phase 4 study evaluating the renal effect of Elvitegravir/ Cobicistat/ Emtricitabine/Tenofovir DF or other Tenofovir DF-containing Regimens (Ritonavir-boosted Atazanavir plus Emtricitabine /Tenofovir DF or Efavirenz /Emtricitabine/Tenofovir DF) compared to Ritonavir-boosted Atazanavir plus Abacavir/ Lamivudine in Antiretroviral Treatment-naïve HIV-1 Infected Adults with

eGFR ≥70 mL/min."

WS1089/G
Prezista-
EMEA/H/C/000707/WS1089/0086/G
Rezolsta-
EMEA/H/C/002819/WS1089/0018/G
MAH: Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, "Submission of the final report from Study GS-US-236-0140 listed as a category 3 study in the RMP. This is a randomized, open-label, phase 4 study evaluating the renal effect of Elvitegravir/ Cobicistat/ Emtricitabine/Tenofovir DF or other Tenofovir DF-containing Regimens (Ritonavir-boosted Atazanavir plus Emtricitabine /Tenofovir DF or Efavirenz /Emtricitabine/Tenofovir DF) compared to Ritonavir-boosted Atazanavir plus Abacavir/ Lamivudine in Antiretroviral Treatment-naïve HIV-1 Infected Adults with eGFR ≥70 mL/min.
The RMP has been updated accordingly and the important potential risks of renal toxicity removed.

Based on cumulative review of the available data, the Prezista and Rezolsta RMPs are updated to remove the important risks of 'pancreatis', 'convulsions' and 'cardiac conduction abnormalities' and the important risk 'development of drug resistance' in the Rezolsta RMP."

B.6.11. PRAC assessed procedures

PRAC Led
Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0086
MAH: GSK Biologicals SA, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Jean-Michel Dogné, , "Submission of the final report from study HPV-039, listed in the RMP as one of the measures to bring additional information on the theoretical risk of acquiring vaccine-induced autoimmune diseases and on pregnancy outcomes after vaccination.

With this submission the MAH fulfils post-authorisation measure MEA 081."

PRAC Led

Corbilta - levodopa / carbidopa / entacapone - EMEA/H/C/002785/II/0009

MAH: Orion Corporation, PRAC Rapporteur: Kirsti Villikka, , "Submission of the final report of pharmacoepidemiological registry study CCOM998A2001, as requested in PRAC PSUR Assessment report EMEA/H/C/PSUSA/00000547/201510. The study is listed as category III studies in the Risk Management plan (RMP) of Corbilta and the summary results indicate that treatment with entacapone does not increase the risk of myocardial infarction in patients with Parkinson´s disease.

The RMP of Corbilta is updated accordingly from version 1.1 to version 2.0.

MA holder does not propose any changes to the Product Information of Corbilta as a consequence of this Type II variation."

PRAC Led

Corbilta - levodopa / carbidopa / entacapone - EMEA/H/C/002785/II/0010

MAH: Orion Corporation, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, , "Submission of the final report of pharmacoepidemiological registry study ER11-9411 was requested in PRAC PSUR assessment report EMEA/H/C/PSUSA/00000547/201510. The study is listed as category III study in the Risk Management Plan (RMP) and the summary results indicate that treatment with entacapone does not increase the risk of prostate cancer in patients with Parkinson´s disease.

The RMP of Corbilta is updated accordingly from version 1.1 to version 2.0.

MA holder does not propose any changes to the Product Information of Corbilta as a consequence of this Type II variation."

PRAC Led

Orencia - abatacept - EMEA/H/C/000701/II/0108/G

MAH: Bristol-Myers Squibb Pharma EEIG, PRAC Rapporteur: Kirsti Villikka, "This grouping of two type II variations (category C.I.13) covers the submission of the final clinical study reports from epidemiological studies IM101045A & IM101045B, listed as category 3 studies in the

RMP.

IM101045A & IM101045B are both observational studies, sharing overlapping safety objectives (e.g.: to assess the risk of infections, infusion-related reactions, autoimmune disorders, injection reactions and combination use)."

PRAC Led

Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0100

MAH: Boehringer Ingelheim International GmbH, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Torbjorn Callreus, , "Submission of the final report for study 1160.144, which evaluated the potential off-label use of dabigatran etexilate in Europe: A drug utilisation study in Cegedim France, Denmark, and CPRD UK."

PRAC Led

Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0101

MAH: Boehringer Ingelheim International GmbH, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Torbjorn Callreus, , "Submission of the final report of study 1160.162, an observational study assessing the management of gastrointestinal and urogenital bleeding events in patients with non valvular atrial fibrillation treated with dabigatran etexilate."

PRAC Led

Suboxone - buprenorphine / naloxone - EMEA/H/C/000697/II/0035

MAH: Indivior UK Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, , "Submission of the final study report for PEUS004 , a retrospective observational survey on Suboxone use in France. Consequently , the RMP (RMP 12.1) has been updated."

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

WS0972/G
Infanrix hexa-
EMEA/H/C/000296/WS0972/0211/G
MAH: GSK Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1111
Entresto-
EMEA/H/C/004062/WS1111/0011
Neparvis-
EMEA/H/C/004343/WS1111/0009
MAH: Novartis Europharm Ltd, Lead Rapporteur: Johann Lodewijk Hillege

WS1126
Gardasil-
EMEA/H/C/000703/WS1126/0070
Silgard-EMEA/H/C/000732/WS1126/0061
MAH: Sanofi Pasteur MSD SAS, Lead Rapporteur: Kristina Dunder

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

B.7.1. Line listing for Variation Type I and Variation Type II (MMD only) post authorisation procedures from the beginning of the year.

B.7.2. Line listing overview of all applications under the centralised procedure (MMD only). line listing - products - authorised, under evaluation, suspended.xls

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:

A.O.B.:

HTA:

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 23-26 January 2017 CHMP plenary:

G.3.2. List of procedures starting in December 2016 for February 2017 CHMP adoption of outcomes

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