9 February 2017
EMA/CHMP/57606/2017 Rev. 1
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Minutes of the meeting on 12-15 December 2016

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

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 document 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 is a working document primarily designed for CHMP members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in this document 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).

Rev. 1 - amendment of wording of indiciation 8.1.3

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1. Introduction

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

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified as included in the list of participants and restrictions. See (current) December 2016 CHMP minutes for the list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session held 12-15 December 2016 (to be published post January 2017 CHMP meeting).

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 22 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

1.2. Adoption of agenda

CHMP agenda for 12-15 December 2016

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 7-10 November 2016.

The CHMP adopted the minutes.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

No items

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

No items

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Alecensa - alectinib - EMEA/H/C/004164

Roche Registration Limited; treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 15.09.2016. List of Questions adopted on 28.01.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a conditional marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to medical prescription.

The CHMP noted the letter of recommendation dated 13.12.2016.

The summary of opinion was circulated for information.

3.1.2. Ledaga - chlormethine - Orphan - EMEA/H/C/002826

Actelion Registration Ltd.; treatment of mycosis fungoides-type cutaneous T-cell lymphoma (MF-type CTCL)

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 15.09.2016. List of Questions adopted on 24.09.2015.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The CHMP noted the letter of recommendation dated 14.12.2016.

The summary of opinion was circulated for information.

3.1.3. Lifmior - etanercept - EMEA/H/C/004167

Pfizer Limited; treatment of arthritis, ankylosing spondylitis, plaque psoriasis and paediatric plaque psoriasis

Scope: Opinion

Action: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Enbrel

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to medical prescription.

The summary of opinion was circulated for information.

3.1.4. Olumiant - baricitinib - EMEA/H/C/004085

Eli Lilly Nederland B.V.; treatment of moderate to severe active rheumatoid arthritis (RA)

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 13.10.2016. List of Questions adopted on 23.06.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

3.1.5. Pregabalin Zentiva k.s. - pregabalin - EMEA/H/C/004277

Zentiva k.s.; treatment of neuropathic pain, epilepsy and Generalised Anxiety Disorder (GAD)

Scope: Opinion

Action: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Lyrica

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to medical prescription.

The CHMP noted the letter of recommendation dated 14.12.2016.

The summary of opinion was circulated for information.

3.1.6. Truxima - rituximab - EMEA/H/C/004112

Celltrion Healthcare Hungary Kft.; treatment of Non-Hodgkin's lymphoma (NHL), Chronic lymphocytic leukaemia (CLL), Rheumatoid arthritis and Granulomatosis with polyangiitis and microscopic polyangiitis

Scope: Opinion

Action: For adoption

Similar biological application (Article 10(4) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 13.10.2016. List of Questions adopted on 25.02.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

The CHMP adopted the BWP report.

3.1.7. Vihuma - simoctocog alfa - EMEA/H/C/004459

Octapharma AB; Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency)

Scope: Opinion

Action: For adoption

Informed consent application (Article 10c of Directive No 2001/83/EC)

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

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

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

treatment of haemophilia A

Scope: Day 180 list of outstanding issue, report from ad-hoc expert group meeting

Action: For adoption

List of Questions adopted on 21.07.2016.

List of Experts to ad-hoc expert group meeting adopted by written procedure on 28.11.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues

The Committee adopted a list of outstanding issues with a specific timetable.

The CHMP adopted the BWP report.

3.2.2. - 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: Day 180 list of outstanding issue

Action: For adoption

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

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a 2nd list of outstanding issues with a specific timetable.

The CHMP adopted the BWP report.

3.2.3. - fluciclovine (18F) - EMEA/H/C/004197

diagnostic agent for PET of adult men with suspected recurrence of prostate cancer

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 28.04.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues .

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues with a specific timetable.

3.2.4. - ivabradine - EMEA/H/C/004241

treatment of angina pectoris

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 01.04.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues with a specific timetable.

3.2.5. - pemetrexed - EMEA/H/C/004488

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

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.07.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.6. - vosaroxin - Orphan - EMEA/H/C/004118

Sunesis Europe Ltd; treatment acute myeloid leukaemia

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 28.04.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

The CHMP agreed to consult a SAG and adopted a list of questions to this group.

3.2.7. - 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: Day 180 list of outstanding issue

Action: For adoption

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

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a 2nd list of outstanding issues with a specific timetable.

The CHMP adopted the BWP report.

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

treatment of prostate cancer

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 26.05.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

The CHMP agreed to consult a SAG.

3.2.9. - abaloparatide - EMEA/H/C/004157

treatment of osteoporosis

Scope: Day 180 list of outstanding issue

Letter from the applicant dated 13 December 2016 requesting an extension to the clock stop to respond to the Day 180 List of Outstanding issues adopted

Action: For adoption

List of Questions adopted on 01.04.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues.

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

treatment of active rheumatoid arthritis

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.07.2016.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.11. - human IgG1 monoclonal antibody specific for human interleukin-1 alpha - EMEA/H/C/004388

treatment of metastatic colorectal cancer

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.07.2016

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues.

The CHMP agreed to the request by the applicant for an extension to the clock stop to

respond to the list of outstanding issues with a specific timetable.

The CHMP adopted the BWP report.

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

3.3.1. - cerliponase alfa - Orphan - EMEA/H/C/004065

Accelerated assessment

BioMarin International Limited; treatment of neuronal ceroid lipofuscinosis type 2

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

The CHMP agreed to consult an ad-hoc expert group and adopted a list of questions to this group.

The CHMP adopted the BWP report.

3.3.2. - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/004240

treatment of HIV-1 infection

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.3. - levamisole - Orphan - EMEA/H/C/004330

ACE Pharmaceuticals BV; treatment of Steroid Sensitive Nephrotic syndrome

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.4. - entecavir - EMEA/H/C/004458

treatment of chronic hepatitis B virus infection

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.5. - entecavir - EMEA/H/C/004377

treatment of chronic hepatitis B virus infection

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

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

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions .

The CHMP adopted the BWP report.

3.3.7. - miglustat - EMEA/H/C/004366

treatment of Gaucher disease

Scope: Day 120 list of questions, Similarity Assessment Report

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.8. - neratinib - EMEA/H/C/004030

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

Scope: Day 120 list of questions

Action: For adoption

The Committee was reminded of the status of this application and its remaining outstanding issues. The Committee adopted a list of outstanding issues with a specific timetable.

3.3.9. - trastuzumab - EMEA/H/C/004346

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

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

The CHMP adopted the BWP report.

3.3.10. - d-biotin - EMEA/H/C/004153

treatment of progressive multiple sclerosis (primary or secondary)

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.11. - midostaurin - Orphan - EMEA/H/C/004095

Novartis Europharm Ltd; treatment of mastocytosis and treatment of acute myeloid leukaemia

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application. In addition, it was considered not feasible to continue along the accelerated assessment timetable.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

The CHMP agreed to revert back to a normal timetable.

3.3.12. - solithromycin - EMEA/H/C/004179

treatment of bacterial infections

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

3.4.1. - paclitaxel - Orphan - EMEA/H/C/004154

Oasmia Pharmaceutical AB; treatment of ovarian cancer

Scope: Request from the applicant for an extension of clock stop to respond to the List of Questions adopted on 23 June 2016 .

Action: For adoption

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 23 June 2016 .

3.4.2. - pacritinib - Orphan - EMEA/H/C/004193

Baxalta Innovations GmbH; treatment of myelofibrosis

Scope: Letter from the applicant dated 9 December 2016 requesting extension of clock stop to respond to the List of Questions adopted on 15 September 2016.

Action: For adoption

List of Questions adopted on 15.09.2016.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 15 September 2016.

3.4.3. - etanercept - EMEA/H/C/004192

treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, axial spondyloarthritis, ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis, plaque psoriasis and paediatric plaque psoriasis

Scope: Letter from the applicant dated 5 December 2016 requesting extension of clock stop to respond to the List of Questions adopted on 1 April 2016.

Action: For adoption

List of Questions adopted on 01.04.2016.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 01.04.2016.

3.4.4. - pegfilgrastim - EMEA/H/C/004262

treatment of neutropenia

Scope: Letter from the applicant dated 1 December 2016 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

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 13 October 2016.

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

treatment of multiple sclerosis

Scope: Letter from the applicant dated 23 November 2016 requesting an extension of clock stop to respond to the List of Questions adopted on 15 September 2016.

Action: For adoption

List of Questions adopted on 15.09.2016.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 15 September 2016.

3.4.6. - nonacog beta pegol - Orphan - EMEA/H/C/004178

Novo Nordisk A/S; treatment of haemophilia B

Scope: Report from ad-hoc expert group meeting

Action: For information

List of Outstanding Issues adopted on 15.09.2016. List of Questions adopted on 26.05.2016.

The CHMP noted the report from ad-hoc expert group.

List of Experts to ad-hoc expert group meeting were adopted by written procedure on 28.11.2016.

3.4.7. - atezolizumab - EMEA/H/C/004143

treatment of metastatic urothelial treatment of urothelial carcinoma and non-small cell lung cancer (NSCLC)

Scope: Letter from the applicant dated 30 November 2016 requesting an extension of clock stop to respond to the List of Questions adopted on 15 September 2016.

Action: For information

List of Questions adopted on 15.09.2016.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 15 September 2016.

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

treatment of Gaucher disease

Scope: Similarity Assessment Report

Action: For adoption

Oral explanation held in June 2016. List of Outstanding Issues adopted on 23.06.2016, 01.04.2016. List of Questions adopted on 23.07.2015.

The CHMP adopted a list of questions with a specific timetable.

3.4.9. - niraparib - Orphan - EMEA/H/C/004249

Tesaro UK Limited; Treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer

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

Scope: Similarity Assessment Report.

Action: For adoption

The CHMP adopted the assessment report on similarity.

3.4.10. - parathyroid hormone - Orphan - EMEA/H/C/003861

NPS Pharma Holdings Limited; treatment of hypoparathyroidism

Scope: Letter from the applicant dated 9 December 2016 requesting an extension to the clock stop to respond to the Day 180 List of Outstanding issues adopted during the September 2016 meeting

Action: For adoption

List of Outstanding Issues adopted on 15.09.2016, 21.07.2016, 28.04.2016, 24.09.2015. List of Questions adopted on 26.03.2015.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the Day 180 List of Outstanding issues adopted during the September 2016 meeting.

3.4.11. - lutetium (177 Lu) dotatate - Orphan - EMEA/H/C/004123

Advanced Accelerator Applications; Treatment of gastro-entero-pancreatic neuroendocrine tumours

Scope: Letter from the applicant dated 8 December 2016 requesting extension of clock stop to respond to the List of Questions adopted on 15 September 2016.

Action: For adoption

List of Questions adopted on 15.09.2016.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 15 September 2016.

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

No items

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. Cavoley - pegfilgrastim - EMEA/H/C/004342

STADA Arzneimittel AG; treatment of neutropenia

Scope: Withdrawal of initial marketing authorisation application

Action: For information

Similar biological application (Article 10(4) of Directive No 2001/83/EC), Duplicate of Efgratin

Oral explanation 10.11.2016, List of Outstanding Issues adopted on 13.10.2016, 21.07.2016. List of Questions adopted on 01.04.2016.

The CHMP noted the letter from the applicant informing of the decision to withdraw the MAA.

3.7.2. Efgratin - pegfilgrastim - EMEA/H/C/004023

Gedeon Richter Plc.; treatment of neutropenia

Scope: Withdrawal of initial marketing authorisation application

Action: For information

Similar biological application (Article 10(4) of Directive No 2001/83/EC)

Oral explanation 10.11.2016, List of Outstanding Issues adopted on 13.10.2016, 21.07.2016. List of Questions adopted on 01.04.2016.

The CHMP noted the letter from the applicant informing of the decision to withdraw the MAA.

3.7.3. Graspa - eryaspase - Orphan - EMEA/H/C/004055

ERYTECH Pharma S.A.; treatment of leukaemia

Scope: Withdrawal of initial marketing authorisation application

Action: For information

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

Oral explanation 10.11.2016, List of Outstanding Issues adopted on 15.09.2016. List of Questions adopted on 28.01.2016.

The CHMP noted the letter from the applicant informing of the decision to withdraw the MAA.

3.7.4. Kepnetic - aceneuramic acid - Orphan - EMEA/H/C/004176

Ultragenyx UK Limited; treatment of Hereditary Inclusion Body Myopathy (HIBM)

Scope: Withdrawal of initial marketing authorisation application

Action: For information

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

Oral explanation 10.11.2016, List of Outstanding Issues adopted on 15.09.2016. List of Questions adopted on 28.01.2016.

The CHMP noted the letter from the applicant informing of the decision to withdraw the MAA.

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. Ilaris - canakinumab - EMEA/H/C/001109/X/0045/G

Novartis Europharm Ltd

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur:

Brigitte Keller-Stanislawski

Scope: “Grouped application comprising an extension application covering an additional formulation (150 mg/ml solution for injection) and a type II variation (C.I.6.a) to add a new indication.
The proposed new indication is based on the results of the pivotal phase 3 study CACZ885N2301 and covers the treatment of adults and children of 2 years of age and older with one of the following Periodic Fever Syndromes:
- Tumour Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS);
- Hyperimmunoglobulin D Syndrome (HIDS) / Mevalonate Kinase Deficiency (MKD);
- Familial Mediterranean Fever (FMF) in patients in whom colchicine is contraindicated, is not tolerated, or does not provide an adequate response.
As a consequence sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are proposed to be updated and the Package Leaflet is proposed to be updated accordingly. In addition, the annexes have been aligned with the latest QRD template v.10. A revised RMP version 11 was provided as part of the application.”

Action: For adoption

List of Questions adopted on 15.09.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The CHMP noted the letter of recommendations dated 02.12.2016.

The summary of opinion was circulated for information.

4.1.2. Repatha - evolocumab - EMEA/H/C/003766/X/0002

Amgen Europe B.V.

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola

Scope: Opinion

“To add a new strength of 420 mg (120 mg/mL) for evolocumab solution for injection in cartridge, for subcutaneous (SC) administration by an automated mini-doser device.”

Action: For adoption

List of Outstanding Issues adopted on 26.05.2016. List of Questions adopted on 25.02.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

4.1.3. Tivicay - dolutegravir - EMEA/H/C/002753/X/0018/G

ViiV Healthcare UK Limited

Rapporteur: Filip Josephson, Co-Rapporteur: Joseph Emmerich, PRAC Rapporteur: Julie Williams

Scope: "An extension application to add two new strengths (10mg and 25mg tablets) to support the extension (variation type II C.I.6) of the target population covered by the authorised therapeutic indication for Tivicay to treat paediatric patients from 6 years of age infected with HIV. Data from cohort I and II A of the clinical trial ING112578 are presented in support of the new therapeutic indication."

Action: For adoption

List of Outstanding Issues adopted on 15.09.2016. List of Questions adopted on 26.05.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

The Committee noted the letter of recommendation dated 15.12.2016.

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

4.2.1. Esbriet - pirfenidone - Orphan - EMEA/H/C/002154/X/0035/G

Roche Registration Limited

Rapporteur: Greg Markey, Co-Rapporteur: David Lyons, PRAC Rapporteur: Julie Williams

Scope: "Extension application to introduce a new pharmaceutical form associated with 3 new strengths (267mg, 534mg and 801mg film-coated tablets).

Action: For adoption

List of Questions adopted on 15.09.2016.

The Committee discussed the issues identified in this application concerning some quality issues and the RMP.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of outstanding issues and a specific timetable.

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. Benepali - etanercept - EMEA/H/C/004007/X/0016

Samsung Bioepis UK Limited (SBUK)

Rapporteur: Andrea Laslop, PRAC Rapporteur: Rafe Suvarna

Scope: “To add a new strength of 25 mg solution for injection in pre-filled syringe.”

Action: For adoption

The Committee discussed the issues identified in this application, which were related to clinical data.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

No items

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

No items

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

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

5.1.1. Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0024

Biofrontera Bioscience GmbH

Rapporteur: Harald Enzmann, Co-Rapporteur: Patrick Salmon, PRAC Rapporteur: Martin Huber

Scope: Extension of Indication from "Treatment of actinic keratosis of mild to moderate severity on the face and scalp (Olsen grade 1 to 2; see section 5.1) and of field cancerization" to the following:
Treatment of superficial and/or nodular basal cell carcinoma unsuitable for surgical treatment due to possible treatment-related morbidity and/or poor cosmetic outcome in adults.
Consequently, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the SmPC are updated. Editorial changes

have been proposed in sections 4.2, 4.4, 5.2, 6.6 and 9 of the SmPC. The Package Leaflet and Labelling are updated accordingly. There are two new warnings that have been included in section 4.4 that the use of immunosuppressants during treatment with Ameluz is not recommended and of the risk of transient global amnesia. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.

The variation leads to amendments to the Summary of Product Characteristics, Package Leaflet and to the Risk Management Plan (RMP).

Action: For adoption

Request for Supplementary Information adopted on 10.11.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.2. Avastin - bevacizumab - EMEA/H/C/000582/II/0092

Roche Registration Limited

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Doris Stenver

Scope: “Extension of Indication to include the use of Avastin in combination with paclitaxel and carboplatin for the treatment of adult patients with first recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer.
As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated with efficacy and safety information from study GOG-0213. The Package Leaflet is updated in accordance. An update RMP is also included (version 27).”

Similarity Assessment Report

Action: For adoption

The Committee discussed the issues identified in this application. The main discussion focused on the change to the indication wording as to remove the current limitation of prior bevacizumab use. The members discussed the presented clinical data and whether it was considered sufficient to support the proposed change. It was also considered that the removal of the limitation for prior bevacizumab use would also apply to carboplatin and gemcitabine for which no data had been presented. The CHMP agreed to request further clarification on the proposed change.

The Committee adopted a request for supplementary information with a specific timetable.

The CHMP adopted the Assessment Report on similarity

The CHMP adopted the BWP report.

5.1.3. Benepali - etanercept - EMEA/H/C/004007/II/0019/G

Samsung Bioepis UK Limited (SBUK)

Rapporteur: Andrea Laslop, PRAC Rapporteur: Rafe Suvarna

Scope: "Extension of indication to include two new indications for the treatment of juvenile idiopathic arthritis and paediatric plaque psoriasis already approved for the reference medicinal product (Enbrel) for Benepali.

As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. Annex II, the Package Leaflet and Labelling are updated in accordance. The RMP (version 4.2) is also updated accordingly. Furthermore, the PI is brought in line with the latest QRD template version 10."

Action: For adoption

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

See B.5.3

5.1.4. Cinryze - c1-esterase inhibitor, human - EMEA/H/C/001207/II/0045

Shire Services BVBA

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

Scope: "Extension of Indication in children with hereditary angioedema (HAE) to include the treatment and pre-procedure prevention of angioedema attacks from 2 years and the routine prevention of angioedema attacks from 6 years; as a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2, 6.5 and 6.6 of the SmPC are updated. The key messages of educational materials in the Annex II, the Package Leaflet and the Labelling are updated in accordance. In addition, an update of regional information in module 3.2.R due to the proposed dose recommendation for children is submitted."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2016.

The Committee discussed the dose recommendation for children below 6 years of age and how to best include the available data in the SmPC.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.5. Darzalex - daratumumab - Orphan - EMEA/H/C/004077/II/0002

Janssen-Cilag International NV

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "Extension of Indication for Darzalex in the treatment of adult patients with multiple myeloma who have received at least 1 prior therapy.
As a consequence, sections 4.2, 4.4, 4.5, 5.1 and 5.2 of the SmPC are updated in order to update the information on posology, warnings, interactions, efficacy and pharmacokinetics. A new warning is introduced in section 4.4 regarding neutropenia/thrombocytopenia induced by background therapy.

Annex II is updated to remove all the specific obligations following submissions of the final results of studies MMY3003 and MMY3004.

The Package Leaflet and Risk Management Plan (RMP version 2) 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.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Similarity Assessment Report

Action: For adoption

The Committee discussed the issues identified in this application, which were related to the wording of indication and request for 1 year of market protection for a new indication.

The Committee adopted a request for supplementary information with a specific timetable.

The CHMP adopted the similarity assessment report for Darzalex.

The CHMP adopted the BWP report.

5.1.6. Firazyr - icatibant - Orphan - EMEA/H/C/000899/II/0034/G

Shire Orphan Therapies GmbH

Rapporteur: Kristina Dunder, Co-Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Qun-Ying Yue

Scope: "A type II variation (C.I.6) to modify the existing marketing authorization to include a recommendation for use in children (study HGT-FIR-086) following completion of the PIP (EMEA-000408-PIP01-08-M05)
In addition, it is proposed to reflect the conduct of a juvenile toxicity study (JE049-0172) in SmPC section 5.3 in order to fulfill article 37 of regulation 1901/2006. Study JE049-0172 has previously been assessed by EMA.

Section 5.2. of the SmPC has been updated to reflect the effect on age (elderly), gender

and race on PK of icatibant."

Action: For adoption

The Committee discussed the issues identified in this application. The main discussions focused on pharmacokinetics and the posology in children.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.7. Inovelon - rufinamide - Orphan - EMEA/H/C/000660/II/0037

Eisai Ltd

Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard

Scope: "Update of sections 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC in order to include additional information relevant to the paediatric population based on the results of study 303 in patients aged 1 to less than 4 years with Lennox-Gastaut Syndrome and the results from toxicity studies in juvenile animals. Section 5.1 was furthermore updated to add additional information on the design of study 022 in LGS patients aged 4 years and older. Additional editorial amendments were made to SmPC sections 4.4 and 4.6. The Package Leaflet has been updated accordingly. Furthermore, the PI was brought in line with the latest QRD template and the SmPCs, Labelling and Package Leaflets for the three authorised strengths of the tablet formulation were combined. An updated RMP version 9.0 was agreed as part of the procedure.
The variation leads to amendments to the Summary of Product Characteristics, labelling and Package Leaflet and to the RMP."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2016.

The Committee noted that, in light of the outstanding issues regarding the population PK simulations, the MAH withdrew the original application for an extension of indication to extend the use of the medicine to children aged 1 to 4 years, whilst still pursuing an update of the product information to include relevant paediatric study data.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The Committee noted the letter of recommendation dated 14.12.2016.

The summary of opinion was circulated for information.

5.1.8. Izba - travoprost - EMEA/H/C/002738/II/0005

Alcon Laboratories (UK) Ltd

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Almath Spooner

Scope: "Extension of Indication to include treatment of paediatric patients aged 2 months to < 18 years with ocular hypertension or paediatric glaucoma in order to decrease of elevated intraocular pressure. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package leaflet has been updated accordingly. In addition, the marketing authorisation holder took the opportunity to introduce minor corrections in the SmPC and to update the list of local representatives in the PL. The RMP has updated to version 9.0"

Action: For adoption

The Committee discussed the issues identified in this application, mainly relating to the indication and the available clinical data for the different age groups. The members considered the need for further clarification in the age group below 3 years of age.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.9. Jardiance - empagliflozin - EMEA/H/C/002677/II/0014

Boehringer Ingelheim International GmbH

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Modification of indication

Update of section 4.1, 4.4, 4.8 and 5.1 of the SmPC to reflect new data on cardiovascular outcomes, based on the final study report of the phase III clinical trial EMPA-REG OUTCOME. The Package Leaflet and RMP have been updated accordingly.

The MAH took the opportunity to make some editorial changes and bring the PI in line with the latest QRD template.

Action: For adoption

Request for Supplementary Information adopted on 15.09.2016, 23.06.2016, 25.02.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.10. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0011

Merck Sharp & Dohme Limited

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

Scope: “Extension of Indication to include first-line treatment of metastatic non-small cell lung carcinoma (NSCLC) in adults whose tumours express PD-L1 with a ≥50% tumour proportion score (TPS) with no EGFR or ALK positive tumour mutations. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. An updated RMP version 4.2 was agreed during the procedure.”, Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 10.11.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

The CHMP agreed by consensus on the one additional year of market protection for a new indication.

5.1.11. Opdivo - nivolumab - EMEA/H/C/003985/II/0019

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 the treatment of locally advanced unresectable or metastatic urothelial carcinoma in adults after failure of prior platinum-containing therapy for OPDIVO.

As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the proposed indication, add a warning about the patient populations excluded from the clinical trial, and update the safety information. The Package Leaflet is updated in accordance.
Moreover, the updated RMP version 7.0 has been submitted”

Action: For adoption

The Committee discussed the issues identified in this application, which mainly related to the efficacy. Questions were raised whether the proposed population was considered sufficiently justified by the provided uncontrolled data. The members noted a large heterogeneity in the study population as well as the subgroup outcomes. The members agreed to seek further clarification on the data.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.12. Votubia - everolimus - Orphan - EMEA/H/C/002311/II/0041

Novartis Europharm Ltd

Rapporteur: Harald Enzmann, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Martin Huber

Scope: "Extension of Indication to include adjunctive treatment of patients aged 2 years and older with refractory seizures associated with tuberous sclerosis complex (TSC) for Votubia 2 mg, 3 mg and 5 mg dispersible tablets.
Sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC were updated in parallel based on the results from the pivotal study. In addition, sections 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 were also updated for the 2.5 mg, 5 mg and 10 mg tablets to reflect on data relevant to these formulations.
The Package Leaflet was updated in accordance.
Furthermore, the PI was brought in line with the latest QRD template version 10."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

5.1.13. Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/II/0053

Bial - Portela & Cª, S.A.

Rapporteur: Martina Weise, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Martin Huber

Scope: "Extension of indication to include the use of Zebinix as monotherapy in adults, in addition to the previously authorised indication as adjunctive therapy. As a consequence, Sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. This submission includes an updated RMP (version 15.0). In addition, the MAH is claiming an additional 1-year period of market protection under Article 14(11) of Regulation (EC) No 726/2004.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 21.07.2016.

The Committee discussed the issues identified in this application. The main discussion focused on the acceptability of the request for an additional 1 year of market protection and the need for further justification to support the claim of significant benefit based on safety and major contribution to patient care (improved dosing regimen). Furthermore, the Committee requested further discussion by the MAH on the claim of non-inferiority of eslicarbazepine acetate compared to controlled-release carbamazepine and in order to

support a positive benefit-risk balance of Zebinix in the monotherapy of adults with partial onset seizures.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.14. Trajenta Jentadueto - linagliptin linagliptin / metformin - EMEA/H/C/WS0915

Boehringer Ingelheim International GmbH

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

Scope: "Extension of indication to include the use of Trajenta and Jentadueto in combination with other diabetes medicines; as a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated based on studies 1245.30, 1275.10 and 1275.1. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to make minor editorial changes in the PI. Moreover, the RMP version 10 (for Trajenta) and version 12 (for Jentadueto) have been updated. Furthermore, the PI is brought in line with the latest QRD template version 10.0."

Action: For adoption

Request for Supplementary Information adopted on 13.10.2016, 26.05.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

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. Translarna - ataluren - Orphan - EMEA/H/C/002720/II/0012

PTC Therapeutics International Limited

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Sabine Straus

Scope: "Extension of indication for Translarna to include the treatment of cystic fibrosis resulting from a nonsense mutation in at least one allele of the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Consequently, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.8, 5.1, 5.2 of the SmPC were updated. The Package leaflet and RMP are being updated accordingly.
The MAH took also the opportunity to implement the QRD template v9.1. and proposed combined SmPC for Translarna 125 mg, 250 mg and 1000 mg granules for oral suspension.

Minor editorial changes have been introduced throughout the PI.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004), .

Request by the MAH for an extension to the clock stop to respond to the RSI adopted in May 2016.

Action: For adoption

Request for Supplementary Information adopted on 26.05.2016, 17.12.2015.

The CHMP agreed to the request by the MAH for an extension to the clock stop to respond to the RSI adopted in May 2016.

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

No items

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. – Glecaprevir/ Pibrentasvir - EMEA/H/C/04430

Treatment of chronic hepatitis C (CHC) in adults

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

Action: For adoption

The CHMP agreed to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

8.1.2. - brigatinib - EMEA/H/C/04248

Treatment of patients with locally advanced or metastatic anaplastic lymphoma kinase positive (ALK+) non-small cell lung cancer (NSCLC) who have previously been treated with crizotinib

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

Action: For adoption

The CHMP did not agree to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

8.1.3. - durvalumab - EMEA/H/C/04205

indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma whose disease has progressed during or after one standard platinum-based regimen.

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

Action: For adoption

The CHMP did not agree to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

8.1.4. - Sofosbuvir, Velpatasvir, Voxilaprevir- EMEA/H/C/04350

Treatment of chronic hepatitis C (CHC) in adults

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

Action: For adoption

The CHMP agreed to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

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.

The CHMP noted the list of applications received.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

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

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 7 recommendations for eligibility to PRIME: 1 was granted and 6 were denied. The individual outcomes are listed in PRIME Monthly Report on EMA website.

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Ranexa - ranolazine - EMEA/H/C/000805/II/0051

Menarini International Operations Luxembourg S.A., treatment of angina pectoris.

Rapporteur: Kristina Dunder

Scope: “Update of section 5.1 of the SmPC in order to include the data from the final CSR of study RIVER-PCI. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the details of local representative in Bulgaria in the Package Leaflet and to bring the Annex II in line with the latest QRD template version 9.1.”

Action: For adoption

Request for Supplementary Information adopted on 21.07.2016, 14.04.2016.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

See B.5.2

9.1.2. Meropenem, ciprofloxacin: Signal of incompatibility leading to possible precipitation when co-administered intravenously

PRAC Rapporteur: Jan Neuhauser

Action: For adoption

Following the PRAC discussion of this new signal, it was agreed that a list of questions should be addressed to the Quality Working Party.

The CHMP adopted questions to QWP.

10. Referral procedures

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

10.1.1. Direct-acting antivirals (DAAV) indicated for the treatment of hepatitis C (interferon free): Daklinza - daclatasvir; Exviera - dasabuvir ; Viekirax - ombitasvir, paritaprevir, ritonavir ; Olysio – simeprevir; Sovaldi - sofosbuvir sofosbuvir, Harvoni - ledipasvir –EMEA/H/A-20/1438

Applicant: Bristol-Myers Squibb Pharma EEIG (Daklinza); AbbVie Ltd (Exviera, Viekirax); Janssen-Cilag International N.V. (Olysio); Gilead Sciences International Ltd (Harvoni, Sovaldi)

Rapporteur for the Article 20 referral:
PRAC Lead Rapporteur: Margarida Guimarães; PRAC Lead Co-rapporteur: Dolores Montero Corominas

CHMP Lead Rapporteur: Fátima Ventura; CHMP Lead Co-rapporteur: Aranzazu Sancho-Lopez

CHMP Rapporteurs: Rapporteur: Filip Josephson, Co-Rapporteur: Robert James Hemmings (Daklinza), Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege (Exviera, Viekirax), Rapporteur: Aranzazu Sancho-Lopez, Co-Rapporteur: Daniela Melchiorri (Olysio); Rapporteur: Filip Josephson, Co-Rapporteur: Alar Irs (Sovaldi), Rapporteur: Filip Josephson, Co-Rapporteur: Joseph Emmerich (Harvoni)

Scope: Opinion

Review of the benefit-risk balance of DAAV following notification by the European Commission of a referral under Article 20 of Regulation (EC) No 726/2004 based on pharmacovigilance data

Action: For adoption

The CHMP discussed the PRAC recommendation and adopted an amended recommendation by consensus. The timelines for submission of the final study report of the imposed post-authorisation safety study to evaluate the recurrence of hepatocellular carcinoma associated with direct-acting antivirals have been amended.

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

10.2.1. Desloratadine-containing products - desloratadine - EMEA/H/A-5(3)/1431

Rapporteur: Koenraad Norga, Co-Rapporteur: Andrea Laslop,

Scope: List of questions to the SWP adopted via written procedure on 07.12.2016

Prescription status of desloratadine-containing products

Action: For information

The CHMP noted the list of questions adopted via written procedure on 07.12.2016

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

No items

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

No items

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

10.5.1. Etopophos and associated names– etoposide - EMEA/H/A-30/1417

MAH: Bristol-Myers Squibb group of companies and associated companies

Rapporteur: Greg Markey, Co-Rapporteur: Paula van Hennik,

Scope: List of Outstanding Issues

Harmonisation exercise for Etopophos and associated names

Action: For adoption

List of outstanding issues adopted on 21.07.2016, 25.02.2016, List of Questions adopted on 22.10.2015.

The CHMP adopted a 3rd list of outstanding issues with a specific timetable.

Submission of responses: 09.02.2017

Re-start of the procedure: 23.02.2017

Joint Rapporteurs assessment report circulated to CHMP: 08.03.2017

Comments: 13.03.2017

Updated Joint Rapporteurs assessment report circulated to CHMP: 16.03.2017

List of outstanding issues/CHMP opinion: March 2017 CHMP

10.5.2. Vepesid and associated names - etoposide - EMEA/H/A-30/1425

MAH: Bristol-Myers Squibb group of companies and associated companies

Rapporteur: Greg Markey, Co-Rapporteur: Paula van Hennik,

Scope: List of Outstanding Issues

Harmonisation exercise for Vepesid and associated names

Action: For adoption

List of outstanding issues adopted on 21.07.2016, 25.02.2016. List of Questions adopted on 22.10.2015.

The CHMP adopted a 3rd list of outstanding issues with a specific timetable.

Submission of responses: 09.02.2017

Re-start of the procedure: 23.02.2017

Joint Rapporteurs assessment report circulated to CHMP: 08.03.2017

Comments: 13.03.2017

Updated Joint Rapporteurs assessment report circulated to CHMP: 16.03.2017

List of outstanding issues/CHMP opinion: March 2017 CHMP

10.5.3. Lovenox and associated names – enoxaparin - EMEA/H/A-30/1429

Sanofi Aventis group of companies and associated companies

Rapporteur: Joseph Emmerich, Co-Rapporteur: Johann Lodewijk Hillege,

Scope: Opinion

Harmonisation exercise for Lovenox and associated names. The review was triggered by France, due to the need of harmonisation of the Summary of Product Characteristics across Member States.

Action: For adoption

List of outstanding Issues adopted 13.10.2016, 28.04.2016. List of Questions adopted on 19.11.2015.

The Committee adopted a positive opinion by consensus recommending that the concerned marketing authorisations should be varied together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The CHMP noted the EMA question and answer document.

10.5.4. Saroten and associated names - amitriptyline - EMEA/H/A-30/1430

Lundbeck group of companies and associated companies, Bayer Vital and PNG Gerolymatos Medical

Rapporteur: George Aislaitner, Co-Rapporteur: Alar Irs,

Scope: List of Outstanding Issues

Harmonisation exercise for Saroten and associated names (amitriptyline). Review triggered by Greece due to the need to harmonise the product information across all Member States, including the therapeutic indication, the posology, the contra-indications, the adverse effects and the recommendations for use.

Action: For adoption

List of outstanding issues adopted on 13.10.2016, 23.06.2016, 01.04.2016. List of Questions adopted 17.12.2015

The CHMP discussed the approved indications for Saroten products in Europe as well as the wording for the dosing.

The CHMP adopted a 4th list of outstanding issues with a specific timetable.

CHMP fourth list of outstanding issues: 15.12.2016

Submission of responses: 12.01.2017

Re-start of the procedure: 26.01.2017

Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 08.02.2017

Comments: 13.02.2017

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 16.02.2017

CHMP opinion: February 2017 CHMP

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: List of Outstanding Issues

Action: For adoption

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

The CHMP adopted a 3rd list of outstanding issues with a specific timetable.

Submission of responses: 04.01.2017

Re-start of the procedure: 09.01.2017

Rapporteur/co-rapporteur joint assessment reports circulated to CHMP: 13.01.2017

Comments: 18.01.2017

Updated Rapporteur/co-rapporteur joint assessment reports circulated to CHMP: 20.01.2017

CHMP Opinion: January 2017 CHMP

10.6.2. Micro Therapeutics Research Labs, India - EMEA/H/A-31/1450

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Milena Stain

Scope: reliability of the data of bioequivalence studies

Appointment of (Co)Rapporteur, List of Questions and timetable

Action: For adoption

Letter from:
- the Medicines Evaluation Board (MEB) in the Netherlands dated 1 December 2016

Letter from following NCAs on 2 December 2016:
- the Norwegian Medicines Agency in Norway- the Agency for Medicinal Products and Medical Devices of the Republic of Croatia

Letter from following NCAs on 5 December 2016: - the BASG/AGES in Austria- the Danish Health and Medicines Authority in Denmark

- the State Agency of Medicines in Latvia- the Medical Products Agency in Sweden- the Icelandic Medicines Agency in Iceland

Letter from following NCAs on 7 December 2016:- the State Agency of Medicines in Estonia
- the Federal Institute for Drugs and Medical Devices BfArM in Germany
- the National Medicines Agency and Medicinal Devices in Romania
- the State Institute for Drug Control in Slovakia
- the Agency of Medicines and Medical Devices in Spain
- the Medicines and Healthcare Products Regulatory Agency in United Kingdom

Letter from following NCAs on 12 December 2016:- the National Institute of Pharmacy and Nutrition in Hungary
- the Agency for Medicinal Products and Medical Devices in Slovenia

Letter from following NCAs on 14 December 2016:

- the Drug Agency in Bulgaria

- the Medicines Agency in Finland

notifying of an official referral under Article 31 and its grounds.

The CHMP appointed Johann Lodewijk Hillege as Rapporteur (interest level 1) and Milena Stain (interest level 1) as Co-Rapporteur.

The CHMP adopted lists of questions with a specific timetable.

Submission of responses: 09.02.2017

Re-start of the procedure: 23.02.2017

Rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 08.03.2017

Comments: 13.03.2017

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 16.03.2017

CHMP list of outstanding issues/CHMP opinion: March 2017 CHMP

10.6.3. 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 to Ad-hoc expert meeting (to be held 13.01.2017), updated timetable

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.

Action: For adoption

The CHMP adopted a revised timetable. List of experts were adopted via written procedure on 12 January 2017.

CHMP list of outstanding issues: September 2016 CHMP

Ad-hoc expert meeting: 13.01.2017

Submission of responses: 09.02.2017

Re-start of the procedure: 23.02.2017

Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 08.03.2017

Comments: 13.03.2017

Updated Rapporteur/co-rapporteur joint assessment report(s) circulated to CHMP: 16.03.2017

CHMP opinion: March 2017 CHMP

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

December 2016 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

The CHMP noted the December 2016 Early Notification System.

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

The CHMP noted the minutes.

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. Completed ITF Briefing Meetings in 2016

Action: For information

The CHMP noted the meetings held in 2016.

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

No items

13.4. Nanomedicines activities

Minutes of 6th TC of the IPRF Nano Working Group on 7 December 2016

Action: For information

The CHMP noted the minutes.

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Co-opted membership of the CHMP

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

Scope: Agreement on the expertise required for Co-opted membership

Action: For adoption

The CHMP agreed on the required expertise for co-opted member to the CHMP as Medical statistics (clinical-trial methodology / epidemiology).

Call for nominations for co-opted member:

Nominations of experts with the agreed expertise should be sent by 20 January 2017, end of business.

14.1.2. Updated policy on handling competing interests for scientific committees' members and experts

Scope: Policy 0044 - European Medicines Agency policy on the handling of competing interests of scientific committees' members and experts

Action: For information

The CHMP discussed and noted the updated policy.

14.1.3. EMA report on 10 years of experience with conditional marketing authorisations

Scope: Presentation of the main findings from the analysis

Action: For information

The CHMP noted the findings from the analysis. The report will be published in January.

14.1.4. Best practice guide on measures improving predictability of submissions and adherence to communicated submission deadlines (EMA/760652/2016)

Action: For information

The CHMP noted the best practice guide. This best practice guide has been developed for Applicants and Marketing Authorisation Holders and for the Regulatory Agencies to optimise the operation and functioning of national and centralised evaluation procedures. Compliance with the principles defined in this best practice guide, will enable both the Regulatory Agencies and Industry to improve workload planning and resourcing of relevant procedures.

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

Action: For information

Postponed to January 2017

14.1.6. Survey on initial marketing authorisation – Update

Action: For information

The CHMP noted the update on the survey. Rapporteur teams were encouraged to participate in the survey.

14.1.7. Release of additional dashboards for Art 57 data

Action: For information

Postponed to January 2017

14.1.8. Call for expression of interest: the WHO benchmarking (assessment) of the Saudi Arabia Food and Drug Authority (SFDA) in 2017

Call for expression of interest for an expert in the area of Registration and Marketing Authorization (vaccine), who would participate to the WHO benchmarking (assessment) of the Saudi Arabia Food and Drug Authority (SFDA) in 2017. The benchmarking is planned from 22 to 26 January 2017. The experts will be recruited as WHO temporary advisors and travel costs and per diem will be covered by WHO.

Expressions of interest should be sent by 22nd of December 2016.

Action: For information

The CHMP noted the information.

14.1.9. Seating plan for CHMP under Maltese EU Presidency, 1 January – 30 June 2017

CHMP Seating Plan 1 January – 30 June 2017, under Maltese EU presidency

Action: For information

The CHMP noted the seating plan for the first half of 2017.

14.1.10. CHMP Strategic Review and Learning Meeting under Maltese EU Presidency

Scope: draft Agenda

Action: For information

The CHMP noted the information.

14.1.11. Amendments to the CHMP Annex under B.5.11

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): the proposal was to stop the inclusion of Letter of intent on worksharing and the appointed Rapporteur under B.5.11 of the CHMP Annex.

Action: For information

The CHMP noted the information. In the January 2017, a disclaimer will be added into CHMP Annex under B.5.11. In February 2017 CHMP Annex B.5.11 will be completely removed.

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 28 November – 1 December 2016

Action: For information

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for December 2016

Call for nomination of a CHMP representative to the ENCePP Steering Group. Nominations should be sent by 30th November 2016.

Action: For adoption

The CHMP appointed Johann Lodewijk Hillege as CHMP representative to the ENCePP Steering Group.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 7-9 December 2016
Action: For information

The CHMP noted the draft minutes.

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 21-22 November 2016

Action: For information

The CHMP noted the report.

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at December 2016 PDCO

Action: For information

The CHMP noted the information.

Report from the PDCO meeting held on 14-16 December 2016

Action: For information

The CHMP noted the report.

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 6-8 December 2016
Action: For information

The CHMP noted the report.

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

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 12-14 December 2016

Action: For information

The CHMP noted the report.

Notes regarding 'Specific scientific guidance for allergies with lower prevalence' (EMA/826761/2016)

Action: For discussion

Follow up from January 2016 CHMP. The CHMP noted the document and agreed for a drafting group to work on a concept paper.

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 28 November – 1 December 2016. Table of conclusions

Action: For information

The CHMP noted the report

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

Scope: Nomination of a replacement SAWP member and his alternate following retirement of Dr Jens Ersbøll. The required area of expertise is oncology.

Action: For adoption
The CHMP appointed Sinan Bardakci Sarac as new member and Kirstine Moll Harboe as new alternate to the SAWP.

Scope: SAWP Chair election
Action: For adoption
The CHMP re-elected Robert James Hemmings as chair of the SAWP.

Mandate, objectives and rules of procedure of the Scientific advice working party (SAWP) (EMEA/CHMP/SAWP/69686/04) - revision

Action: For adoption

The CHMP adopted the revised mandate, objectives and rules of procedure.

14.3.2. Quality Working Party (QWP)

Chair: Jean-Louis Robert

QWP Work Plan (EMA/CHMP/CVMP/QWP/601201/2016)

Action: For adoption

The CHMP adopted the QWP Work Plan 2017.

Question & answers on the removal of heavy metals tests from a specification (EMA/CHMP/CVMP/QWP/693784/2016)

Action: For adoption

The CHMP adopted the question and answer document. The reference to the general Heavy metals test (2.4.8) will be deleted from all individual monographs for substances for pharmaceutical use (except e.g. substances for veterinary use only). Instead the general monograph Pharmaceutical Preparations will make ICH Q3D mandatory for all medicines within the scope of the guideline.

Concept paper on the need for revision of Note for guidance on quality of water for pharmaceutical use (EMA/CHMP/CVMP/QWP/BWP/428135/2016)

Action: For adoption for 3-month consultation

The CHMP adopted the concept paper for 3-month public consultation. The current guideline needs to be updated to reflect imminent changes in European Pharmacopoeia. The text of guideline needs to be updated to take into account manufacturing practices using methods other than distillation for producing water of injectable quality and the consequent deletion of the monograph Water, highly purified. A new Ph. Eur. monograph “Water for preparation of extracts” (2249) is also published.

Correction to the Reflection paper on the Requirements for selection and justification of starting materials for the manufacture of chemical active substances

Action: For adoption

The CHMP adopted the correction of the reflection paper.

Q3D implementation strategy

Action: For adoption

The CHMP adopted the Q3D implementation strategy. The purpose of the document is to address specific considerations to enable the practical implementation of ICH Q3D Guideline for Elemental Impurities in the European Union. It is intended to provide guidance for MAHs, drug product, drug substance and excipient manufacturers, as well as regulators. In addition to new applications, it will also apply to variations to existing marketed products.

14.3.3. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 23 November 2016.

Action: For adoption

The CHMP adopted the table of decision.

Potential for name-related confusion identified post-authorisation with a CAP and a NAP

Scope: Adoption of NRG advice

Action: For adoption

The CHMP discussed the possible name-related confusion.

14.3.4. Biostatistics Working Party (BSWP)

Vice-Chair: Thomas Lang

Election of the BSWP Chair

Action: For adoption

The CHMP elected Anja Schiel (NO) as chair of the BSWP.

Guideline on multiplicity issues in clinical trials (EMA/CHMP/720718/2016)

Action: For adoption for a 3-month public consultation

The CHMP adopted the guideline for a 3-month public consultation. The scope of the guideline is to provide guidance on the confirmatory conclusions which are usually based on the results from pivotal Phase III trials and, to a lesser extent, on Phase II studies. The guideline mainly discusses issues in decision making for a formal proof of efficacy. Due to the precautionary principle in safety evaluations, reducing the rate of false negative conclusions

on harm is usually more important than controlling the number of false positive conclusions and rigorous multiplicity adjustments could mask relevant safety signals.

14.3.5. Central Nervous System Working Party (CNSWP)

Chair: Karl Broich CNSWP Work plan 2017 (EMA/CHMP/627427/2016)

Action: For adoption

The CHMP adopted the CNSWP Work plan 2017.

Guideline on the clinical development of medicinal products intended for the treatment of pain (EMA/CHMP/970057/2011)

Action: For adoption

The CHMP adopted the guideline. The scope of the guideline is to provide guidance on the clinical development of new medicinal products intended for the treatment of nociceptive, neuropathic or mixed pain. Requirements with regard to study design, duration, target patient population and outcome measures are described, taking into account experience with marketing authorisation applications, scientific advice procedures, and developments in basic science and clinical guidelines since publication of the separate guidelines on neuropathic and nociceptive pain which the current guideline replaces and updates.

14.3.6. Pharmacogenomics Working Party (PGWP)

Chair: Krishna Prasad/Markus Paulmichl PGWP Work plan 2017 (EMA/CHMP/389037/2016)

Action: For adoption

The CHMP adopted the PGWP Work plan 2017.

14.3.7. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink PKWP Work plan 2017 (EMA/CHMP/643117/2016)

Action: For adoption

The CHMP adopted the PKWP Work plan 2017.

Q & A Question on requirements for bioequivalence studies under fasting and fed conditions (general) (EMA/CHMP/805455/2016)

Action: For discussion

The CHMP noted the document.

Q & A PKWP clarification on Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1/Corr**); Appendix II section on oral solutions

Action: For adoption

The CHMP adopted the Q & A PKWP clarification on Guideline on the investigation of bioequivalence.

14.3.8. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus, RIWP Work plan 2017 (EMA/646364/2016)

Action: For adoption

The CHMP adopted the RIWP Work plan 2017.

14.3.9. Vaccines Working Party (VWP)

Chair: Mair Powell, Nomination of Darko Krnic (Croatia) as an observer to VWP

- current list of VWP members and observers

Action: For adoption

The CHMP nominated Darko Krnic (HR) as observer to the VWP.

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

14.7.1. CHMP 2017 Draft Work Plan

Action: For discussion

The CHMP noted the draft work plan. Comments are awaited until the 6th of January 2017.

14.8. Planning and reporting

14.8.1. 2017 forecast of the Business Pipeline report for the human scientific committees

Action: For information

The CHMP noted the 2017 forecast.

14.9. Others

No items

15. Any other business

15.1. AOB topic

16. List of participants

List of participants including any restrictions with respect to involvement of members/alternates/ experts following evaluation of declared interests for the 12 – 15 December 2016 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Tomas Salmonson	Chair	Sweden	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Milena Stain	Alternate	Austria	No interests declared	
Bart Van der Schueren	Member	Belgium	No interests declared	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Katarina Vučić	Member	Croatia	No interests declared	
Selma Arapovic Dzakula	Alternate	Croatia	No interests declared	
Panayiotis Triantafyllis	Member	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Sinan B. Sarac	Member	Denmark	No interests declared	
Hanne Lomholt Larsen	Alternate	Denmark	No interests declared	
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Tuomo Lapveteläinen	Alternate	Finland	No interests declared	
Pierre Demolis	Member via Adobe	France	No interests declared	
Joseph	Alternate	France	No interests	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Emmerich			declared	
Harald Enzmann	Member (Vice-Chair)	Germany	No interests declared	
Martina Weise	Alternate	Germany	No restrictions applicable to this meeting	
Dimitrios Kouvelas	Member	Greece	No interests declared	
George Aislaitner	Alternate	Greece	No interests declared	
Agnes Gyurasics	Member	Hungary	No interests declared	
Hrefna Gudmundsdottir	Alternate	Iceland	No interests declared	
David Lyons	Member	Ireland	No restrictions applicable to this meeting	
Patrick Salmon	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No restrictions applicable to this meeting	
Juris Pokrotnieks	Member	Latvia	No restrictions applicable to this meeting	
Romaldas Mačiulaitis	Member	Lithuania	No participation in final deliberations and voting on:	3.1.1. Alecensa - alectinib - EMEA/H/C/004164; 3.4.5. ocrelizumab - EMEA/H/C/004043; 3.4.7. - atezolizumab - EMEA/H/C/004143; 4.2.1. Esbriet - pirfenidone - Orphan - EMEA/H/C/002154/X/0035/G; 5.1.2. Avastin - bevacizumab - EMEA/H/C/000582/II/0092
Jacqueline Genoux-Hames	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	
Karsten Bruins Slot	Member	Norway	No interests declared	
Bjorg Bolstad	Alternate	Norway	No restrictions applicable to this meeting	
Piotr Fiedor	Member	Poland	No interests declared	
Bruno Sepodes	Member	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No participation in final deliberations and voting on:	3.3.10. - d-biotin - EMEA/H/C/004153
Nela Vilceanu	Member	Romania	No interests declared	
Jana Schweigertova	Alternate via Adobe	Slovakia	No restrictions applicable to this meeting	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member	Spain	No interests declared	
Aranzazu Sancho-Lopez	Alternate	Spain	No restrictions applicable to this meeting	
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Greg Markey	Member	United Kingdom	No interests declared	
Nithyanandan Nagercoil	Alternate	United Kingdom	No restrictions applicable to this meeting	
Robert James Hemmings	Co-opted member	United Kingdom	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Koenraad Norga	Co-opted member	Belgium	No restrictions applicable to this meeting	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Jean-Louis Robert	Co-opted member	Luxembourg	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Maria Escudero Galindo	Expert - in person*	Spain	No participation in discussions, final deliberations and voting on:	3.4.4. - pegfilgrastim - EMEA/H/C/004262; 3.3.2. - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/004240; 3.3.5. - entecavir - EMEA/H/C/004377; 3.3.9. - trastuzumab - EMEA/H/C/004346;
Jan Kyselovič	Expert - in person*	Slovakia	No interests declared	
Christoph Focke	Expert - in person*	Belgium	No restrictions applicable to this meeting	
Zuzana Ptackova	Expert - in person*	Czech Republic	No restrictions applicable to this meeting	
Mette Tranholm	Expert - in person*	Denmark	No interests declared	
Jorge Camarero Jimenez	Expert - in person*	Spain	No restrictions applicable to this meeting	
Mair Powell	Expert - via telephone*	United Kingdom	No interests declared	
Jan Welink	Adobe Speaker	Netherlands	No interests declared	
Henrike Potthast	Adobe Speaker	Netherlands	No interests declared	
Barbara Spruce	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Eleftheria Nikolaidi	Expert - in person*	Greece	No interests declared	
Patrick Vrijlandt	Expert - via telephone*	Netherlands	No interests declared	
Andreas Schrijvers	Expert - in person*	Netherlands	No interests declared	
Peter Salomons	Expert - in person*	Netherlands	No interests declared	
Maria Concepcion Payares	Adobe Speaker	Spain	No restrictions applicable to this meeting	
Macarena Rodriguez Mendizabal	Expert - via telephone*	Spain	No interests declared	
Dolores Montero Corominas	Expert - via telephone*	Spain	No interests declared	
Eva Malikova	Adobe Speaker	Slovakia	No interests declared	
Johannes Pohly	Adobe Speaker	Germany	No interests declared	
Clemens Mittmann	Adobe Speaker	Germany	No interests declared	
Susanne Steinecker	Adobe Speaker	Germany	No interests declared	
Sylvia Kuehn	Adobe Speaker	Germany	No restrictions applicable to this meeting	
Ralf Meyer	Expert - in person*	Germany	No interests declared	
Christoph Unkrig	Adobe Speaker	Germany	No interests declared	
Jörg Zinserling	Adobe Speaker	Germany	No interests declared	
Tom Lams	Adobe Speaker	Belgium	No interests declared	
Olga Kholmanskikh	Adobe Speaker	Belgium	No interests declared	
Stefan Bonné	Adobe Speaker	Belgium	No interests declared	
Shirley Hopper	Expert - in person*	United Kingdom	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Parvinder Singh Phul	Expert - in person*	United Kingdom	No interests declared	
Cecilia Chisholm	Expert - via telephone*	United Kingdom	No interests declared	
Elspeth Gray	Expert - via telephone*	United Kingdom	No interests declared	
Elina Rönnemaa	Expert - via telephone*	Sweden	No interests declared	
Lisbeth Bregnhoj	Expert - via telephone*	Denmark	No interests declared	
David Churchward	Expert - via telephone*	United Kingdom	No interests declared	
Stefan Vieths	Expert - via telephone*	Germany	No interests declared	
Susanne Kaul	Expert - via telephone*	Germany	No interests declared	
Andreas Bonertz	Expert - via telephone*	Germany	No interests declared	
Alan Moon	Expert - via telephone*	United Kingdom	No restrictions applicable to this meeting	
Margarida Guimarães	Expert - via telephone*	Portugal	No interests declared	
Anabel Cortés Blanco	Adobe Speaker	Spain	No interests declared	
Isabella Berger	Expert - via telephone*	Austria	No interests declared	
Representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

* Experts were only evaluated against the product(s) they have been invited to talk about.

17. 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)*

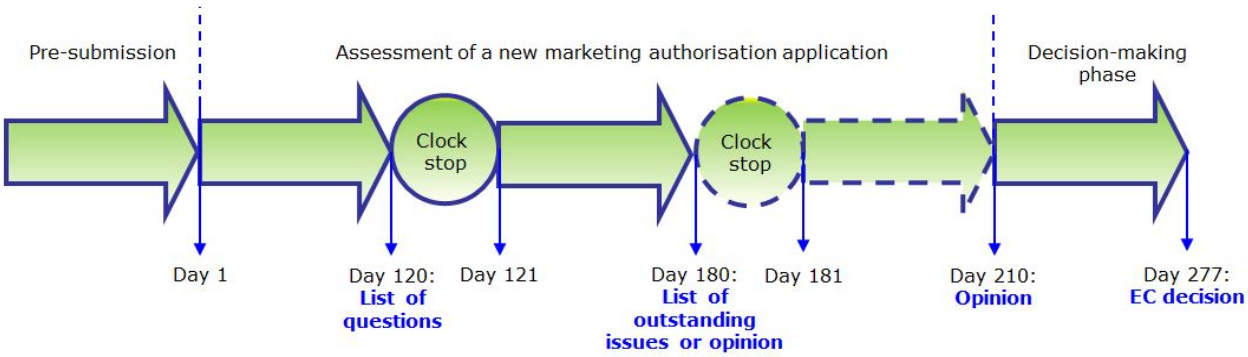
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

27 January 2017
EMA/CHMP/31422/2017

ANNEX TO DECEMBER 2016 CHMP Minutes

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 December 2016: **For adoption**	Adopted.

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

Final Outcome of Rapporteurship allocation for December 2016: **For adoption**	Adopted.

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

ATryn - antithrombin alfa - EMEA/H/C/000587/S/0028 MAH: GTC Biotherapeutics UK Limited, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard	Positive Opinion adopted by consensus together with the CHMP assessment report ‹and translation timetable›. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.
Naglazyme - galsulfase - EMEA/H/C/000640/S/0065 MAH: BioMarin Europe Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Rafe Suvarna	Positive Opinion adopted by consensus together with the CHMP assessment report ‹and translation timetable›. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.
Strensiq - asfotase alfa - EMEA/H/C/003794/S/0011, Orphan MAH: Alexion Europe SAS, Rapporteur: Greg Markey, PRAC Rapporteur: Almath Spooner	Positive Opinion adopted by consensus together with the CHMP assessment report ‹and translation timetable›. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members

	were in agreement with the CHMP opinion.

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Revlimid - lenalidomide - EMEA/H/C/000717/R/0091, Orphan MAH: Celgene Europe Limited, Rapporteur: Pierre Demolis, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Claire Ferard	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information the CHMP was of the opinion that an additional five-year renewal was required. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Docetaxel Accord - docetaxel - EMEA/H/C/002539/R/0030 MAH: Accord Healthcare Ltd, Generic, Generic of Taxotere, Rapporteur: Filip Josephson, PRAC Rapporteur: Claire Ferard	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The Committee concluded that the renewal can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Docetaxel Kabi - docetaxel - EMEA/H/C/002325/R/0015 MAH: FRESENIUS KABI ONCOLOGY PLC, Generic, Generic of Taxotere, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The Committee concluded that the renewal can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/R/0059 MAH: Pfizer Limited, Rapporteur: Greg Markey, Co-Rapporteur: Karsten Bruins Slot, PRAC Rapporteur: Rafe Suvarna Request for Supplementary Information adopted on 10.11.2016.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The Committee concluded that the renewal can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pergoveris - follitropin alfa / lutropin alfa - EMEA/H/C/000714/R/0050 MAH: Merck Serono Europe Limited, Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Julie Williams Request for Supplementary Information adopted on 15.12.2016.	Request for Supplementary Information adopted with a specific timetable.

Pioglitazone Teva - pioglitazone - EMEA/H/C/002297/R/0016 MAH: Teva B.V., Generic, Generic of Actos, Glustin, Rapporteur: Patrick Salmon, PRAC Rapporteur: Almath Spooner Request for Supplementary Information adopted on 13.10.2016.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The Committee concluded that the renewal can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pioglitazone Teva Pharma - pioglitazone - EMEA/H/C/002410/R/0013 MAH: Teva B.V., Generic, Generic of Actos, Rapporteur: Patrick Salmon, PRAC Rapporteur: Almath Spooner Request for Supplementary Information adopted on 13.10.2016.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The Committee concluded that the renewal can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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.	Request for Supplementary Information adopted with a specific timetable.
Caprelsa - vandetanib - EMEA/H/C/002315/R/0023 MAH: Genzyme Europe BV, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard, Request for Supplementary Information adopted on 10.11.2016.	Positive Opinion adopted by consensus together with the CHMP assessment report. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 28 November – 1 December 2016 PRAC:

Data collection on adverse events of anti-HIV drugs (D:A:D) study - PRAC evaluation of D:A:D data merger results Assessment report : **For adoption**	Adopted.

Proton pump inhibitors (PPIs): dexlansoprazole; esomeprazole; lansoprazole; omeprazole; pantoprazole; rabeprazole – **CONTROLOC control** EMEA/H/C/001097; pantoprazole **PANTECTA control**; EMEA/H/C/001099; pantoprazole **PANTOLOC control** EMEA/H/C/001100; pantoprazole **PANTOZOL control** EMEA/H/C/001013; pantoprazole **SOMAC control** – EMEA/H/C/001098; pantoprazole CHMP Rapporteur: Greg Markey PRAC Rapporteur: Rafe Suvarna **NEXIUM control**; EMEA/H/C/002618; esomeprazole CHMP Rapporteur: Romaldas Mačiulaitis PRAC Rapporteur: Simona Kudeliene Signal of gastric polyps • PRAC recommendation on a variation: **For adoption**	Adopted.
Vildagliptin; vildagliptin / metformin hydrochloride – **Galvus** EMEA/H/C/000771; vildagliptin **Jalra** EMEA/H/C/001048; vildagliptin **Xiliarx** EMEA/H/C/001051; vildagliptin **Eucreas** EMEA/H/C/000807; vildagliptin/metformin hydrochloride **Icandra** EMEA/H/C/001050; vildagliptin/metformin hydrochloride **Zomarist** EMEA/H/C/001049; vildagliptin CHMP Rapporteur: Kristina Dunder PRAC Rapporteur: Qun-Ying Yue - Signal of pemphigoid • PRAC recommendation on a variation: **For adoption**	Adopted.
PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its November/December 2016 PRAC meeting:	
EMEA / H / C / PSUSA / 00000226 / 201605 (apixaban) CAPS: **Eliquis** (EMEA/H/C/002148) (apixaban), MAH: Bristol-Myers Squibb / Pfizer EEIG, Rapporteur:	Based on the PRAC review of data on safety and efficacy, the PRAC considers that the risk-benefit balance of medicinal products containing apixaban remains unchanged but recommends that the terms of the marketing authorisation(s)

Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, “18 May 2015 to 17 May 2016”	should be varied as follows: Update of section 4.2 of the SmPC to clarify the wording about the dose in patients with renal impairment. In addition, the Marketing authorisation holder took the opportunity to make some editorial changes and to bring the product information in line with the latest QRD template version 10. Issues to be addressed in the next PSUR: In addition, the MAH should also address the following issues in the next PSUR: • To submit a cumulative review of liver injury cases; • To provide an analysis on the cases with 'interstitial pneumonia' or other interstitial lung disorders; • To provide a complete overview of all causes of death for the fatal cases as well as report average patient’s age overall vs. patients with a fatal event; • To investigate a specific case of potential off label use, namely under-dosing. The next PSUR should be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.
EMEA/H/C/PSUSA/00002491/201604 (pramipexole) CAPS: **Mirapexin** (EMEA/H/C/000134) (pramipexole), MAH: Boehringer Ingelheim International GmbH, Rapporteur: Hanne Lomholt Larsen **Sifrol** (EMEA/H/C/000133) (pramipexole), MAH: Boehringer Ingelheim International GmbH, Rapporteur: Hanne Lomholt Larsen NAPS: **Calmolan 0,54 mg-Tabletten 1-30129 AT** - G.L. PHARMA GMBH **Pramipexol - 1 A Pharma 0,54 mg Tabletten 77956.00.00 DE** - 1 A PHARMA GMBH **Pramipexol G.L. 0,54 mg-Tabletten 1-30123 AT** - G.L. PHARMA GMBH **Pramipexol HEXAL 0,54 mg Tabletten 77954.00.00 DE** - HEXAL AG **Pramipexol Sandoz 0,54 mg Tabletten 77955.00.00 DE** - HEXAL AG	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the medicinal products containing the above referred active substance(s), concerning the following change(s): Update of section 4.4 to add further information on “dopamine agonist withdrawal syndrome” (DAWS) with reference to section 4.2 and 4.8 where DAWS was also added as an adverse reaction with frequency not known. Section 4.8 has also been brought in line with the SmPC guideline and latest QRD template. The Package leaflet is updated accordingly.

, PRAC Rapporteur: Doris Stenver, “07/04/2013 - 06/04/2016”	The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00009118/201605 (decitabine) CAPS: **Dacogen** (EMEA/H/C/002221) (decitabine), MAH: Janssen-Cilag International NV, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard, “02 May 2015 to 01 May 2016”	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change(s): Update of sections 4.4 and 4.8 of the SmPC to add a warning on interstitial lung disease, and to add the same adverse reaction with a frequency not known. In addition, the MAH took the opportunity to implement the latest adopted version of the QRD template (version 10) and to change the contact details of local representative in the Netherlands.
EMEA/H/C/PSUSA/00010301/201605 (ibrutinib) CAPS: **Imbruvica** (EMEA/H/C/003791) (ibrutinib), MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Julie Williams, “13 November 2015 to 12 May 2016”	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change(s): Update of section 4.4 of the SmPC to add a warning on: Progressive Multifocal Leukoencephalopathy (PML). The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010307/201605 (aclidinium bromide / formoterol fumarate dihydrate) CAPS: **Brimica Genuair** (EMEA/H/C/003969) (aclidinium / formoterol fumarate dihydrate), MAH: AstraZeneca AB, Rapporteur: Nithyanandan Nagercoil **Duaklir Genuair** (EMEA/H/C/003745) (aclidinium / formoterol fumarate dihydrate), MAH: AstraZeneca AB, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, “20 November 2015 - 19 May 2016”	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 of the SmPC is recommended to add ‘angina’ with a frequency of ‘uncommon’. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned

	recommendation of the CHMP.
EMEA/H/C/PSUSA/00010316/201605 (ketoconazole (centrally authorised product only)) CAPS: **Ketoconazole HRA** (EMEA/H/C/003906) (ketoconazole), MAH: Laboratoire HRA Pharma, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Željana Margan Koletić, "20 November 2015 to 19 May 2016 Update of section 4.5 of the SmPC regarding ketoconazole inhibition of breast cancer resistant protein (BCRP). In addition, the table 1 "Interactions and recommendations for co-administration" in section 4.5 of the SmPC is updated regarding interaction with naloxegol. Section 5.2 is also updated to include new information related to ketoconazole potent inhibition of several transporters. The Package leaflet is updated accordingly."	Based on the PRAC review of data on safety and efficacy, the PRAC considers by consensus that the risk-benefit balance of medicinal product containing ketoconazole remains unchanged but recommends that the terms of the marketing authorisation should be varied as follows: Update of section 4.5 of the SmPC regarding ketoconazole inhibition of breast cancer resistant protein (BCRP). In addition, the table 1 "Interactions and recommendations for co-administration" in section 4.5 of the SmPC is updated regarding interaction with naloxegol. Section 5.2 is also updated to include new information related to ketoconazole potent inhibition of several transporters. The Package leaflet is updated accordingly. Issues to be addressed in the next PSUR: In addition, the MAH should also address the following issues in the next PSUR: • Clarify whether follow up (FU) form was sent for each reported case of hepatotoxicity as described in the RMP. Also, the MAH is requested to keep track of all sent FU forms and received responses (whether or not successful) and present them in future PSURs. When presenting the data, it should be presented according to the source type – NCA or HCP/patient directly/through the representative to the MAH. • Continuously monitor all available sources for cases of use in paediatric population; • Update the data about the results of skin biopsy regarding the case HRA-KET20160005 (PT reported 'dermatitis exfoliative'); • Carefully track and monitor all activities related to risk minimisation measures. Additionally, in future PSURs when applicable, the MAH needs to provide for every Product Information (PI) update regarding drug-drug interactions (DDIs), an analysis of relevance of observed data for Cushing'Syndrome patient population in addition to the retrieved data in order to include interaction relevant to prescribers and prevent the transformation of ketoconazole PI into clinician's handbook. The next PSUR should be submitted in accordance with the requirements set out in the

	list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.
EMEA/H/C/PSUSA/00010318/201605 (nintedanib (oncology indications)) CAPS: **Vargatef** (EMEA/H/C/002569) (nintedanib), MAH: Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Leonidas Klironomos, "22 Nov 2015 to 21 May 2016"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change: Update of section 4.8 of the SmPC to add the adverse reaction pancreatitis with a frequency 'uncommon'. The Package leaflet is updated accordingly. In addition the MAH took the opportunity to introduce small changes to the German Annexes (to align it with the latest QRD template).

B.4. EPARs / WPARs

Afstyla - lonoctocog alfa - EMEA/H/C/004075 Applicant: CSL Behring GmbH, treatment of haemophilia A, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Cavoley - pegfilgrastim - EMEA/H/C/004342 Applicant: STADA Arzneimittel AG, treatment of neutropenia, Duplicate, Duplicate of Efgratin, Similar biological application (Article 10(4) of Directive No 2001/83/EC) **WPAR**	adopted.
Darunavir Mylan - darunavir - EMEA/H/C/004068 Applicant: MYLAN S.A.S, treatment of HIV-1, Generic, Generic of Prezista, Generic application (Article 10(1) of Directive No 2001/83/EC)	adopted.
Efgratin - pegfilgrastim - EMEA/H/C/004023 Applicant: Gedeon Richter Plc., treatment of neutropenia, Similar biological application (Article 10(4) of Directive No 2001/83/EC) **WPAR**	adopted.
Fiasp - insulin aspart - EMEA/H/C/004046 Applicant: Novo Nordisk A/S, treatment of diabetes mellitus in adults, Known active	adopted.

substance (Article 8(3) of Directive No 2001/83/EC)	
Kepnetic - aceneuramic acid - EMEA/H/C/004176, Orphan Applicant: Ultragenyx UK Limited, treatment of Hereditary Inclusion Body Myopathy (HIBM), New active substance (Article 8(3) of Directive No 2001/83/EC) **WPAR**	adopted.
Lusduna - insulin glargine - EMEA/H/C/004101 Applicant: Merck Sharp & Dohme Limited, treatment of diabetes mellitusSimilar biological application (Article 10(4) of Directive No 2001/83/EC)	adopted.
Ruconest – conestat alfa - EMEA/H/C/001223/X/0034 Applicant: Pharming Group N.V, Scope: “Addition of a new pharmaceutical form "powder and solvent for solution for injection" with self-administration kit.”	adopted.
Suliqua - insulin glargine / lixisenatide - EMEA/H/C/004243 Applicant: sanofi-aventis groupe, treatment of type 2 diabetes mellitus, Fixed combination application (Article 10b of Directive No 2001/83/EC)	adopted.
Tadalafil Generics - tadalafil - EMEA/H/C/004297 Applicant: MYLAN S.A.S, treatment of pulmonary arterial hypertension (PAH), Generic, Generic of Adcirca, Cialis, Generic application (Article 10(1) of Directive No 2001/83/EC)	adopted.
Vemlidy - tenofovir alafenamide - EMEA/H/C/004169 Applicant: Gilead Sciences International Ltd, treatment of chronic hepatitis B, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Zinplava - bezlotoxumab - EMEA/H/C/004136 Applicant: Merck Sharp & Dohme Limited, indicated for the prevention of Clostridium difficile infection (CDI) recurrence, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.

Begedina - begelomab - EMEA/H/C/004144 Applicant: Adienne S.r.l. S.U., treatment of graft-versus-host disease, New active substance (Article 8(3) of Directive No 2001/83/EC) **WPAR**	adopted.
Chenodeoxycholic acid sigma-tau - Chenodeoxycholic Acid- EMEA/H/C/004061 Sigma-tau Arzneimittel GmbH, Novo mesto, treatment of inborn errors of primary bile acid synthesis, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	adopted.
Emtricitabine/Tenofovir disoproxil Krka - Emtricitabine/Tenofovir Disoproxil - EMEA/H/C/004215 Applicant: KRKA, d.d., Novo mesto, indicated in antiretroviral combination therapy for the treatment of HIV-1 infected adultsGeneric application (Article 10(1) of Directive No 2001/83/EC)	adopted.

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Aflunov - prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - EMEA/H/C/002094/II/0026/G MAH: Seqirus S.r.l, Rapporteur: Daniela Melchiorri Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 21.07.2016, 03.03.2016, 03.12.2015.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
BeneFIX - nonacog alfa - EMEA/H/C/000139/II/0138 MAH: Pfizer Limited, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 06.10.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Colobreathe - colistimethate sodium - EMEA/H/C/001225/II/0023 MAH: Teva B.V., Rapporteur: Nithyanandan	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

Nagercoil Request for Supplementary Information adopted on 17.11.2016, 12.05.2016, 03.03.2016.	
ELOCTA - efmoroctocog alfa - EMEA/H/C/003964/II/0008/G MAH: Swedish Orphan Biovitrum AB (publ), Rapporteur: Jan Mueller-Berghaus Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 13.10.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Empliciti - elotuzumab - EMEA/H/C/003967/II/0003 MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 24.11.2016. Request for Supplementary Information adopted on 13.10.2016.	Positive Opinion adopted by consensus on 24.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Foclivia - influenza virus surface antigens (inactivated) of strain A/Vietnam/1194/2004 (H5N1) - EMEA/H/C/001208/II/0023/G MAH: Seqirus S.r.l, Rapporteur: Daniela Melchiorri Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 27.10.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0013/G, Orphan MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 13.10.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ixiaro - japanese encephalitis vaccine (inactivated, adsorbed) - EMEA/H/C/000963/II/0083 MAH: Valneva Austria GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Nulojix - belatacept - EMEA/H/C/002098/II/0034/G MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson Opinion adopted on 17.11.2016. Request for Supplementary Information adopted on 15.09.2016, 09.06.2016.	Positive Opinion adopted by consensus on 17.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Opdivo - nivolumab -	Weekly start timetable. The Committee

EMEA/H/C/003985/II/0020 MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez Request for Supplementary Information adopted on 17.11.2016.	adopted a Request for Supplementary information together with a specific timetable.
Opdivo - nivolumab - EMEA/H/C/003985/II/0022/G MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez Request for Supplementary Information adopted on 01.12.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Pixuvri - pixantrone - EMEA/H/C/002055/II/0032/G MAH: CTI Life Sciences Limited, Rapporteur: Greg Markey Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Praluent - alirocumab - EMEA/H/C/003882/II/0014/G MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 08.12.2016.	Positive Opinion adopted by consensus on 08.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0147/G MAH: Pfizer Limited, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 15.12.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0110 MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Rapilysin - reteplase - EMEA/H/C/000105/II/0062 MAH: Actavis Group PTC ehf, Rapporteur: Harald Enzmann Opinion adopted on 08.12.2016. Request for Supplementary Information adopted on 20.10.2016.	Positive Opinion adopted by consensus on 08.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Repatha - evolocumab - EMEA/H/C/003766/II/0012 MAH: Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Savene - dexrazoxane - EMEA/H/C/000682/II/0031, Orphan MAH: Clinigen Healthcare Ltd, Rapporteur: Pierre Demolis Opinion adopted on 08.12.2016.	Positive Opinion adopted by consensus on 08.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Simponi - golimumab - EMEA/H/C/000992/II/0071/G MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder Opinion adopted on 08.12.2016.	Positive Opinion adopted by consensus on 08.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Soliris - eculizumab - EMEA/H/C/000791/II/0088/G, Orphan MAH: Alexion Europe SAS, Rapporteur: Aranzazu Sancho-Lopez Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Soliris - eculizumab - EMEA/H/C/000791/II/0089, Orphan MAH: Alexion Europe SAS, Rapporteur: Aranzazu Sancho-Lopez Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Stelara - ustekinumab - EMEA/H/C/000958/II/0051/G MAH: Janssen-Cilag International NV, Rapporteur: Greg Markey Opinion adopted on 24.11.2016. Request for Supplementary Information adopted on 20.10.2016.	Positive Opinion adopted by consensus on 24.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0110 MAH: GSK Biologicals SA, Rapporteur: Kristina Dunder Opinion adopted on 17.11.2016.	Positive Opinion adopted by consensus on 17.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tysabri - natalizumab - EMEA/H/C/000603/II/0098/G MAH: Biogen Idec Ltd, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 24.11.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Vimpat - lacosamide - EMEA/H/C/000863/II/0064/G MAH: UCB Pharma S.A., Rapporteur: Filip Josephson Opinion adopted on 01.12.2016. Request for Supplementary Information adopted on 29.09.2016.	Positive Opinion adopted by consensus on 01.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/II/0058 MAH: Bial - Portela & Cª, S.A., Rapporteur: Martina Weise Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 15.09.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0922/G **Hexacima-EMEA/H/C/002702/WS0922/0052/G** **Hexaxim-EMEA/H/W/002495/WS0922/0059/G** **Hexyon-EMEA/H/C/002796/WS0922/0055/G** MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 13.10.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0969 **Infanrix hexa-EMEA/H/C/000296/WS0969/0204** MAH: GSK Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 24.11.2016. Request for Supplementary Information adopted on 13.10.2016.	Positive Opinion adopted by consensus on 24.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0976/G **Infanrix hexa-EMEA/H/C/000296/WS0976/0205/G** MAH: GSK Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 13.10.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1003 **HyQvia-EMEA/H/C/002491/WS1003/0031** **Kiovig-EMEA/H/C/000628/WS1003/0075** MAH: Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1043/G **Helixate NexGen-EMEA/H/C/000276/WS1043/0182/G** **KOGENATE Bayer-EMEA/H/C/000275/WS1043/0189/G** MAH: Bayer Pharma AG, Lead Rapporteur: Jan Mueller-Berghaus	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

Request for Supplementary Information adopted on 24.11.2016.	
WS1061/G **Humalog-** **EMEA/H/C/000088/WS1061/0151/G** **Liprolog-** **EMEA/H/C/000393/WS1061/0115/G** MAH: Eli Lilly Nederland B.V., Lead Rapporteur: Robert James Hemmings Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Arzerra - ofatumumab - EMEA/H/C/001131/II/0048, Orphan MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, "Submission of final clinical study of the study OMB115991: A Phase II, Multi-Centre Study Investigating the Safety and Efficacy of Ofatumumab Plus Bendamustine in Patients with Untreated or Relapsed CLL." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cerdelga - eliglustat - EMEA/H/C/003724/II/0008, Orphan MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, "Update of SmPC section 5.1 to include 2, 3 and 4 years composite stability endpoint data based on the final results of the ENCORE study." Request for Supplementary Information adopted on 15.12.2016, 13.10.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0081 MAH: GSK Biologicals SA, Rapporteur: Bart Van der Schueren, "To submit the final effectiveness results of clinical study HPV-040, a community randomized study conducted in Finland to evaluate the effectiveness of two vaccination strategies for 12 -15 year old early adolescents using Cervarix, i.e., to vaccinate female adolescents only, or to vaccinate female and male adolescents." Request for Supplementary Information adopted on 15.12.2016, 15.09.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Effentora - fentanyl - EMEA/H/C/000833/II/0044 MAH: Teva B.V., Rapporteur: Martina Weise,	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

"Update of sections 4.6 and 4.8 with neonatal opioid withdrawal syndrome, and sections 4.8 and 5.1 regarding adrenal insufficiency and androgen deficiency information, following a request from FDA to introduce a class label safety warning. The PL was updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0 and to apply a combined SmPC" Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 10.11.2016.	recommendation.
Eperzan - albiglutide - EMEA/H/C/002735/II/0027/G MAH: GlaxoSmithKline Trading Services, Rapporteur: Kristina Dunder, "Submission of the final study reports for non-clinical toxicity studies: 2015N232567 - Investigation of blood brain barrier penetration of albiglutide in mice and 2016N269355 - Subcutaneous juvenile toxicity study in mice. In addition, the MAH submitted a literature review on glucagon like peptide 1 receptor (GLP-1R) distribution patterns in thyroid and pancreas tissue and results of two additional juvenile toxicology dose response studies as part of this group of variations." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 17.11.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Fycompa - perampanel - EMEA/H/C/002434/II/0034/G MAH: Eisai Europe Ltd., Rapporteur: Robert James Hemmings, "Update of sections 4.5 and 5.1 of the SmPC in order to add information on the conversion of patients to Fycompa monotherapy (E2007-G000-504, hereby Study 504) and to include the effect of withdrawal of concomitant enzyme-inducing antiepileptic drugs (EIAEDs) on plasma concentrations of perampanel (A supportive analysis, CPMS-E2007-0013R). In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

on 15.12.2016.	
Incruse - umeclidinium bromide - EMEA/H/C/002809/II/0013 MAH: Glaxo Group Ltd, Rapporteur: Concepcion Prieto Yerro, "Update of section 4.8 of the SmPC and relevant section of the PL to add hypersensitivity reactions including rash, urticaria, pruritus as uncommon and anaphylaxis and angioedema as rare adverse reactions. The MAH is taking the opportunity to update the Local representative section in the PL." Request for Supplementary Information adopted on 15.12.2016.	Rolling Timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Intuniv - guanfacine - EMEA/H/C/003759/II/0004 MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 (Posology and Method of Administration), 4.4 (Special Warnings and Precautions for Use), and 4.8 (Undesirable Effects) of the SmPC in order to include a warning and update the safety information as a result of a post-marketing case of hypertensive encephalopathy upon abrupt discontinuation of Intuniv (guanfacine hydrochloride). The Package Leaflet is updated accordingly. Annex II has been updated to include the parameters to be monitored during downward titration: blood pressure and pulse as an additional key element. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 13.10.2016, 23.06.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ivemend - fosaprepitant - EMEA/H/C/000743/II/0034/G MAH: Merck Sharp & Dohme Limited, Rapporteur: Filip Josephson, "C.I.4 - Update of sections 5.1 and 5.2 of the SmPC in order to include pharmacodynamic and pharmacokinetic data relevant to the paediatric population. C.I.4 - Update of sections 5.3 of the SmPC in order to include non-clinical data relevant to the paediatric population. The Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

latest QRD template version 10.0." Opinion adopted on 15.12.2016.	
Jevtana - cabazitaxel - EMEA/H/C/002018/II/0035 MAH: Sanofi-Aventis Groupe, Rapporteur: Pierre Demolis, "Update of sections 4.2, 5.1 and 5.2 of the SmPC in order to add information on study TED12689 a phase 1-2 dose finding, safety and efficacy study of cabazitaxel in pediatric patients with refractory solid tumors including tumors of the central nervous system." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 10.11.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Keppra - levetiracetam - EMEA/H/C/000277/II/0162 MAH: UCB Pharma S.A., Rapporteur: Koenraad Norga, PRAC Rapporteur: Laurence de Fays, "Update of the RMP to include an additional epidemiological study (EPD172) to further characterise the risk of acute kidney injury with levetiracetam and other AEDs (RMP version 7.0)." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 15.09.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0013 MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, "Update of section 4.4 of the SmPC with information regarding the possible occurrence of simultaneous immune-related adverse reactions. The Package Leaflet has been updated accordingly." Request for Supplementary Information adopted on 17.11.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Levemir - insulin detemir - EMEA/H/C/000528/II/0082 MAH: Novo Nordisk A/S, Rapporteur: Hanne Lomholt Larsen, "Update of sections 4.4 of the SmPC with additional information regarding avoidance of accidental mix-ups and medication errors. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 9.1 and 10.0 and to correct a mistake in the recommendation for use of the first of the two	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

titration algorithms in section 4.2 of the SmPC." Opinion adopted on 15.12.2016.	
NovoMix - insulin aspart - EMEA/H/C/000308/II/0087 MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, "Update of section 4.4 f the SmPC to include a warning on the risk of medication errors. The package leaflet 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." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
NovoSeven - eptacog alfa / eptacog alfa (activated) - EMEA/H/C/000074/II/0092 MAH: Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.4 of the SmPC in order to delete sucrose warning (also affecting section 2 of the SmPC). The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes/corrections and updates in sections 4.8, 6.4, 6.5 and 6.6 of the SmPC and in the Package Leaflet. Moreover, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10 (combined SmPC has been introduced)." Opinion adopted on 08.12.2016. Request for Supplementary Information adopted on 06.10.2016, 04.08.2016.	Positive Opinion adopted by consensus on 08.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Orfadin - nitisinone - EMEA/H/C/000555/II/0056 MAH: Swedish Orphan Biovitrum International AB, Rapporteur: Luca Pani, "Update of section 5.1 of the SmPC in order to present the efficacy data based on a complementary analysis of the pivotal study for Orfadin (NTBC study). In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the Product Information in line with the latest QRD template version 10." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 15.09.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0014 MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Nithyanandan Nagercoil, "Update of	Positive Opinion adopted by consensus on 08.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

section 5.3 of the SmPC in order to revise the ivacaftor animal:human exposure ratio. The Package Leaflet is updated accordingly." Opinion adopted on 08.12.2016.	recommendation.
Otezla - apremilast - EMEA/H/C/003746/II/0011 MAH: Celgene Europe Limited, Rapporteur: Patrick Salmon, "Submission of study report CC-10004-PSOR-010; a Phase 3b, multicenter, randomized, placebo-controlled, double-blind, double-dummy, study of the efficacy and safety of apremilast (CC-10004), etanercept, and placebo, in subjects with moderate to severe plaque psoriasis. The submission of this clinical study report fulfils PAM EMEA/H/C/003746/MEA/003." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0097 MAH: Boehringer Ingelheim International GmbH, Rapporteur: Hanne Lomholt Larsen, "Submission of final study report of study 1160.173 "A prospective, open label study to evaluate the pharmacokinetics of dabigatran in non-valvular atrial fibrillation (NVAF) patients with severely impaired renal function on dabigatran etexilate 75 mg BID therapy"." Request for Supplementary Information adopted on 01.12.2016.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0145 MAH: Pfizer Limited, Rapporteur: Kristina Dunder, "Update of the SmPC section 5.1 with information on Prevenar 13 effects on invasive pneumococcal disease, antimicrobial resistance and otitis media caused by nontypeable H. influenzae. Editorial changes have also been proposed throughout the SmPC." Request for Supplementary Information adopted on 15.12.2016, 13.10.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0146 MAH: Pfizer Limited, Rapporteur: Kristina Dunder, "Update of the SmPC section 4.5 to include information on Prevenar 13 co-	Positive Opinion adopted by consensus on 17.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

administration with the tetanus toxoid conjugated meningococcal polysaccharide serogroups A, C, W and Y vaccine based on the results of study MenACWY-TT-104. Minor editorial changes have been introduced throughout the PI. Additionally the MAH took the opportunity to align the PI with the latest QRD template version 10.0." Opinion adopted on 17.11.2016.	
Ranexa - ranolazine - EMEA/H/C/000805/II/0051 MAH: Menarini International Operations Luxembourg S.A., Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to include the data from the final CSR of study RIVER-PCI. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the details of local representative in Bulgaria in the Package Leaflet and to bring the Annex II in line with the latest QRD template version 9.1." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 21.07.2016, 14.04.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Rapamune - sirolimus - EMEA/H/C/000273/II/0163/G MAH: Pfizer Limited, Rapporteur: Kristina Dunder, "Update of section 4.4 of the SmPC to update the current warning on angioedema to include a possible dose-dependent effect between sirolimus and angioedema based on post-marketing data. Update of section 4.8 of the SmPC to include neuroendocrine carcinoma of the skin and malignant carcinoma as new ADRs and to include squamous cell carcinoma of the skin and basal cell carcinoma as part of the ADR 'skin cancer' based on post-marketing data. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to combine the 0.5 mg, 1 mg and 2 mg tablets SmPC, to fully detail all components of the Rapamune printing ink in section 6.1 of the SmPC and in the Package Leaflet, to align the wording in section 4 of the Package Leaflet with section 4.8 of the SmPC regarding Clostridium difficile, to update the list of local representatives for the Czech republic, Norway and Sweden in the Package Leaflet and to bring the PI in line with the latest QRD template	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

version 10." Request for Supplementary Information adopted on 01.12.2016.	
Revestive - teduglutide - EMEA/H/C/002345/II/0032, Orphan MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Sinan B. Sarac, "Update of sections 4.3, 4.4, and 4.8 of the SmPC in order to update the safety information in line with updated CCDS following review of the MAH's safety database. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in section 5.1 of the SmPC." Request for Supplementary Information adopted on 15.12.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0037/G MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, "Update of SmPC section 4.8 to add a new ADR 'skin discolouration' with the frequency 'not known'. The PL has been updated accordingly. Additionally, minor editorial changes have been introduced throughout the PI. The MAH took also the opportunity to align the PI with the latest version of the QRD template 10.0." Opinion adopted on 24.11.2016.	Positive Opinion adopted by consensus on 24.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Rotarix - human rotavirus, live attenuated - EMEA/H/C/000639/II/0086 MAH: GlaxoSmithKline Biologicals S.A., Rapporteur: Bart Van der Schueren, "Submission of the final report of study EPI-ROTA-052 BOD EU SUPP (201433) in which the strain surveillance data of the European Rotavirus Network (EuroRotaNet) during the rotavirus seasons from September 2006 to August 2015 is presented." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 15.09.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Saxenda - liraglutide - EMEA/H/C/003780/II/0010 MAH: Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 5.1 of the SmPC in order to update the documented treatment effect currently limited to 1 year. The proposed update of the current	Positive Opinion adopted by consensus on 01.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

labelling for long-term efficacy, safety and tolerable use in the management of obesity is based on 3-year data from trial 1839. In addition, the Marketing authorisation holder took the opportunity to bring the PI in line with the latest QRD template version 10 and implement minor linguistic updates." Opinion adopted on 01.12.2016. Request for Supplementary Information adopted on 29.09.2016.	
Stivarga - regorafenib - EMEA/H/C/002573/II/0018 MAH: Bayer Pharma AG, Rapporteur: Paula Boudewina van Hennik, "Update the SmPC section 4.2, 4.5 and 5.2 based on results from phase 1 study which evaluated pharmacokinetics and safety of regorafenib in cancer subjects with severe renal impairment compared to cancer subjects without or with mild renal impairment. The package leaflet is updated accordingly." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 13.10.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Strensiq - asfotase alfa - EMEA/H/C/003794/II/0008, Orphan MAH: Alexion Europe SAS, Rapporteur: Greg Markey, PRAC Rapporteur: Almath Spooner, "Update of sections 4.3, 4.4 and 4.8 of the SmPC in order to reinforce the wording on the risk of anaphylaxis. The Package Leaflet is updated accordingly. The MAH took the opportunity to include the Pharmacotherapeutic group in section 5.1." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 13.10.2016, 21.07.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tamiflu - oseltamivir - EMEA/H/C/000402/II/0122 MAH: Roche Registration Limited, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "Update of section 5.1 of the SmPC and RMP to reflect the results of study IRIS (NV20237) a prospective, multicenter, information-gathering study, comprising virological surveillance and assessment of clinical outcomes, which enrolled patients over a 7-year period.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 21.07.2016.	
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0034 MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, "To update Section 5.3 (Preclinical Safety Data) of the Summary of Product Characteristics (SmPC) to reflect that exposure margins have been re-calculated based on the area under the concentration-time curve (AUC) rather than based on body surface area (mg/m2)." Opinion adopted on 17.11.2016.	Positive Opinion adopted by consensus on 17.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/II/0025 MAH: AbbVie Ltd., Rapporteur: Filip Josephson, "Update of sections 4.3 and 4.5 of the SmPC to add three additional contraindication medications with dronedarone, lurasidone and ranolazine. The Package Leaflet is updated accordingly." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vimpat - lacosamide - EMEA/H/C/000863/II/0066/G MAH: UCB Pharma S.A., Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC in order to update the safety information regarding the use of lacosamide in patients with hepatic impairment, section 4.8 to add a new adverse drug reaction (hepatic enzyme increased (> 2x ULN)) and section 4.9 regarding lacosamide overdose based on postmarketing reports. 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 make minor editorial change in the SmPC." Request for Supplementary Information adopted on 15.12.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Zydelig - idelalisib - EMEA/H/C/003843/II/0029 MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson, "Submission of the final study report for the clinical study 101-07	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

"A Phase I Study To Investigate the Safety and Clinical Activity of Idelalisib in Combination with Chemotherapeutic Agents, Immunomodulatory Agents and Anti-CD-20 mAb in Subjects with Relapsed or Refractory Indolent B-cell Non-Hodgkin Lymphoma, Mantle Celle Lymphoma or Chronic Lymphocytic Leukemia", in order to fulfil of the Post Approval Measure (PAM) MEA 009 for Zydelig." Opinion adopted on 15.12.2016.	
WS1019 **Clopidogrel Zentiva-EMEA/H/C/000975/WS1019/0055** **Clopidogrel/Acetylsalicylic acid Zentiva-EMEA/H/C/001144/WS1019/0047** **DuoPlavin-EMEA/H/C/001143/WS1019/0046** **Iscover-EMEA/H/C/000175/WS1019/0128** **Plavix-EMEA/H/C/000174/WS1019/0124** MAH: Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, "Update of section 4.8 of the SmPC in order to add Kounis syndrome as a new ADR. The Package Leaflet is updated accordingly. In addition the Worksharing applicant (WSA) took the opportunity to make minor amendments to Annex II for Clopidogrel Zentiva, Iscover and Plavix, to update the contact details of the Bulgarian local representative in the Package Leaflet for all the products involved and the Italian, Hungarian and Lithuanian local representatives for Clopidogrel Zentiva, Iscover and Plavix, to combine the two strengths SmPCs for all the products involved in this Worksharing application, to combine the two strengths Package Leaflet for DuoPlavin and Clopidogrel/Acetylsalicylic acid Zentiva. Furthermore, the PI is brought in line with the latest QRD template version 10." Opinion adopted on 08.12.2016.	Positive Opinion adopted by consensus on 08.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1020 **Clopidogrel/Acetylsalicylic acid Zentiva-EMEA/H/C/001144/WS1020/0046** **DuoPlavin-EMEA/H/C/001143/WS1020/0045** MAH: Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, "Update of sections 4.4 and 4.5 of the SmPC in order to add a new drug-drug interaction between nicorandil and NSAIDs including acetylsalicylic acid (ASA) and lysine-	Positive Opinion adopted by consensus on 08.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

acetylsalicylate (LAS) and its increased risk for severe complications including gastrointestinal ulceration, perforation and haemorrhage. The Package Leaflet is updated accordingly. In addition the Worksharing applicant (WSA) took the opportunity to make a minor correction in Annex II (typographical change)." Opinion adopted on 08.12.2016.	
WS1034 **Descovy-** **EMEA/H/C/004094/WS1034/0007** **Genvoya-** **EMEA/H/C/004042/WS1034/0021** **Odefsey-** **EMEA/H/C/004156/WS1034/0005** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings, "Update of section 4.5 of the SmPC with new pharmacology date from the final Study GS-US-311-1790." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1045 **Entresto-** **EMEA/H/C/004062/WS1045/0008** **Neparvis-** **EMEA/H/C/004343/WS1045/0006** MAH: Novartis Europharm Ltd, Lead Rapporteur: Johann Lodewijk Hillege, "Submission of study no. 1570187: Effect of LBQ657 on cloned hERG potassium channels expressed in human embryonic kidney cells. No changes to PI have been proposed." Opinion adopted on 01.12.2016.	Positive Opinion adopted by consensus on 01.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.3. CHMP-PRAC assessed procedures

Aluvia - lopinavir / ritonavir - **EMEA/H/W/000764/II/0100** MAH: AbbVie Ltd., Rapporteur: Joseph Emmerich, PRAC Rapporteur: Claire Ferard, "Update of sections 4.2 and 5.1 of the SmPC in order to update information following the analysis of the published 48-week study results "Kaletra ONCE daily randomised Trial of the pharmacokinetics, safety and efficacy of twice-daily versus once-daily lopinavir/ritonavir tablets dosed by weight as part of combination antiretroviral therapy in HIV-1–infected children" (PENTA 18/KONCERT) in fulfilment of a	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Post Authorisation Measure (Additional PhV activity in the Risk Management Plan). In addition, the SOH takes the opportunity to remove the Missing Information safety concern of Limited Information of the Aluvia 100 mg/25 mg film-coated tablets in the paediatric population as part of the agreed RMP version 8.1." Opinion adopted on 15.12.2016.	
Amyvid - florbetapir (18F) - EMEA/H/C/002422/II/0022 MAH: Eli Lilly Nederland B.V., Rapporteur: Harald Enzmann, PRAC Rapporteur: Valerie Strassmann, "Update of sections 4.4 and 5.1 of the SmPC in order to introduce quantitative read as an adjunct to visual read of florbetapir (18F) PET scans. In addition, the Marketing authorisation holder (MAH) took the opportunity bring the PI in line with the latest QRD template version 10.0. The updated RMP version 2.0 has been submitted" Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 10.11.2016, 15.09.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Benepali - etanercept - EMEA/H/C/004007/II/0019/G MAH: Samsung Bioepis UK Limited (SBUK), Rapporteur: Andrea Laslop, PRAC Rapporteur: Rafe Suvarna, "Extension of indication to include two new indications for the treatment of juvenile idiopathic arthritis and paediatric plaque psoriasis already approved for the reference medicinal product (Enbrel) for Benepali. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. Annex II, the Package Leaflet and Labelling are updated in accordance. The RMP (version 4.2) is also updated accordingly. Furthermore, the PI is brought in line with the latest QRD template version 10." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 10.11.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. See 5.1 in main part of Minutes.
Bronchitol - mannitol - EMEA/H/C/001252/II/0027, Orphan MAH: Pharmaxis Pharmaceuticals Limited, Rapporteur: Nithyanandan Nagercoil, PRAC	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Rapporteur: Julie Williams, “To submit the Clinical Study Report (CSR) for a study to investigate the efficacy and safety of Bronchitol in children and adolescents with cystic fibrosis (Study DPM-CF-204).” Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 15.09.2016.	
Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0085 MAH: GSK Biologicals SA, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jean-Michel Dogné, “Submission of Study EPI-HPV-069, a meta-analysis assessing the risk of three autoimmune diseases following vaccination with Cervarix: autoimmune thyroiditis (AIT), Guillain-Barre Syndrome (GBS) and Inflammatory Bowel Disease (IBD). The EPI-HPV-069 study is a post-licensure commitment to the EMA (PASS register number EUPAS13332). As part of this submission, an updated RMP (version 18) is provided, including changes related to the EPI-HPV-069 meta-analysis submitted and minor updates related to other studies.” Request for Supplementary Information adopted on 15.12.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0054 MAH: UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “To submit the final clinical study report for study AS001. Sections 4.8 and 5.1 of the Summary of Product Characteristics (SmPC) are revised in order to update the efficacy and safety information (Week 204) for study AS001. Minor changes to the Package Leaflet have been implemented. A revised RMP (version 11.1) is also submitted.” Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 13.10.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0055 MAH: UCB Pharma S.A., Rapporteur: Kristina	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Final clinical study report for study PsA001 is submitted to provide data on long-term use of Cimzia in psoriatic arthritis subjects up to 216 weeks of treatment. Sections 4.8 and 5.1 of the Summary of Product Characteristics (SmPC) are revised in order to update the efficacy and safety information (Week 216) for study PsA001. The package leaflet remains unchanged. A revised RMP (veriosn 11) is also submitted. This corresponds to MEA 027" Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 13.10.2016.	recommendation.
Epclusa - sofosbuvir / velpatasvir - EMEA/H/C/004210/II/0003 MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of sections 4.4, 4.5 and 5.1 of the SmPC in order to reflect on emerging clinical data from study GS-US-342-1202 investigating efficacy and safety in subjects with chronic hepatitis C virus (HCV) and human immunodeficiency virus (HIV)-1 coinfection. In addition, minor administrative changes are implemented throughout the Product Information." Request for Supplementary Information adopted on 15.12.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Feraccru - iron - EMEA/H/C/002733/II/0002/G MAH: Shield TX (UK) Ltd, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Adam Przybylkowski, "Submission of two final study reports for in vitro studies conducted as part of post-authorisation measures MEA 001 and MEA 002 : - One drug-drug interaction study to investigate drug interactions with Feraccru - One drug-drug interaction study to identify UGT isoenzyme(s) that are responsible for metabolism of ferric maltol. Sections 4.5 and 5.2 of the SmPC and the RMP have been updated to reflect the completion and results of the studies." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 10.11.2016, 15.09.2016.	
Flixabi - infliximab - EMEA/H/C/004020/II/0009 MAH: Samsung Bioepis UK Limited (SBUK), Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final study report of study SB2-G31-RA: A Randomised, Double-blind, Parallel Group, Multicentre Clinical Study to Evaluate the Efficacy, Safety, Pharmacokinetics and Immunogenicity of SB2 Compared to Remicade® in Subjects with Moderate to Severe Rheumatoid Arthritis despite Methotrexate Therapy. The RMP (v. 4) has been updated to reflects the results from the 78 weeks CSR, to exclude 2 of the 5 registries of the pharmacovigilance plan and update in the due date for the prospective observational cohort study of Flixabi in AS (Ankylosing Spondylitis) and CD (Crohn's Disease) patients." Request for Supplementary Information adopted on 15.12.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0061 MAH: MedImmune LLC, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Jean-Michel Dogné, "Update of sections 4.3 and 4.8 of the SmPC to reflect that Fluenz Tetra is contraindicated only in children with severe hypersensitivity to eggs (instead of all children with egg allergy), and to update the safety information (update of the number of children and adolescents in the safety database). The PIL is amended accordingly. The RMP is updated to implement administrative changes to the high level description on Enhanced Safety Surveillance, and to change the milestones for study MA-VA-MEDI3250-1116." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Iclusig - ponatinib - EMEA/H/C/002695/II/0032/G, Orphan MAH: Incyte Biosciences UK Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Rafe Suvarna, "Update of sections 4.2, 4.4, 4.8, 5.1 of the SmPC based on data from the ongoing Study AP24534-07-101 with a median duration of	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

follow-up of approximately 48 months for the CP-CML patients and 3.6 months for the advanced phase Ph+ leukemia patients, as well as 48-month follow-up data from the ongoing Study AP24534-10-201 (PACE). The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC and to align the annexes with the latest QRD template v.10. An updated RMP version 15.3 was agreed during the procedure in order to include the 48-month follow up data from the phase 2 study (PACE), address the commitments made in the framework of the PSUR 4 assessment and update the educational materials in line with the changes to the SmPC. In addition, the MAH took the opportunity to update the RMP to include one additional potential risk identified in the post-marketing setting, i.e. posterior reversible encephalopathy syndrome (PRES), for which data were included in the PSUR 5 (PSUSA/00010128/201512)." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 10.11.2016, 21.07.2016.	
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0027/G, Orphan MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Julie Williams, "1. C.I.4 - Update of sections 4.8 in order to include Stevens-Johnson Syndrome (SJS) and Onychoclasis as post-marketing adverse drug reactions (ADRs). In addition the applicant has taken the opportunity to make minor editorial amendments to the SmPC, including an editorial amendment to section 4.8 to mark the existing ADR terms of tumor lysis syndrome (added in variation EMEA/H/C/003791/II/0004), erythema, angioedema, and urticaria (added in variation EMEA/H/C/003791/0008/G) with an "a" referring to the existing ADR table footnote that indicates that they originated from spontaneous post-marketing reports. 2. C.I.4 – Update of section 4.4 to include Hypertension as one of the risk factors for atrial fibrillation/flutter. The Package Leaflet is updated accordingly. Updated version 6.2 of the RMP has been submitted."	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 10.11.2016.	
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0029, Orphan MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Julie Williams, "Update of sections 4.5 of the SmPC to remove the statement that an interaction between products increasing stomach pH and ibrutinib have not been studied and section 5.2 to include the findings from study CLL1005. The Package Leaflet is not impacted by these changes. In addition, the RMP is updated to version 6.3 to reflect this new safety information." Request for Supplementary Information adopted on 15.12.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Jakavi - ruxolitinib - EMEA/H/C/002464/II/0031 MAH: Novartis Europharm Ltd, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information following the completion of two 5-year follow up studies INCB 18424-351 and INC424A2352(long-term extensions of pivotal myelofibrosis studies CONFORT-I and COMFORT-II, respectively), thereby addressing one of the outstanding Obligations in Annex II. The RMP (version 7.0) has been updated with completion of post-approval commitments of studies INCB 18424-351 and CINC424A2352." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 13.10.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0027/G MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "C.I.4 (Type II): Submission of the final study report for the study TDM4997g/BO25734 (TH3RESA study) to address the safety concerns in Left Ventricular Dysfunction and Safety in Elderly patients. The RMP and Annex II.D are updated. C.I.11.z (Type IB): To update the RMP following the submission of the third annual report of study H4621g.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

The MAH takes the opportunity to implement the following administrative changes to the RMP: - inclusion of standard post-authorization data based on PSUR number 4 (reporting period from 22 February 2015 to 21 February 2016). - change of Herceptin picture in the Kadcyla Educational Material to align the picture with the recently approved version of the Herceptin vial label and carton." Opinion adopted on 15.12.2016.	
Kaletra - lopinavir / ritonavir - EMEA/H/C/000368/II/0160 MAH: AbbVie Ltd., Rapporteur: Joseph Emmerich, PRAC Rapporteur: Claire Ferard, "Update of sections 4.2 and 5.1 of the SmPC in order to update information following the analysis of the published 48-week study results "Kaletra ONCE daily randomised Trial of the pharmacokinetics, safety and efficacy of twice-daily versus once-daily lopinavir/ritonavir tablets dosed by weight as part of combination antiretroviral therapy in HIV-1–infected children"(PENTA 18/KONCERT) in fulfilment of a Post Authorisation Measure (Additional PhV activity in the Risk Management Plan). In addition, the MAH takes the opportunity to remove the Missing Information safety concern of Limited Information of the Kaletra 100 mg/25 mg film-coated tablets in the paediatric population as part of the agreed RMP version 8.1." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Lyxumia - lixisenatide - EMEA/H/C/002445/II/0020 MAH: Sanofi-Aventis Groupe, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "Submission of the final clinical study report for study EFC12382, a randomized double-blind, placebo-controlled, 2 arm parallel group, multicentre study with a 24-week treatment period to assess the efficacy and safety of lixisenatide in patients with Type 2 Diabetes Mellitus patients insufficiently controlled with basal insulin or without metformin, in order to fulfil MEA 004. In addition the MAH took the opportunity to update the RMP (version 4.0) accordingly." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

OPDIVO - nivolumab - EMEA/H/C/003985/II/0018 MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update the safety information for toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), myositis, myocarditis and rhabdomyolysis based on findings from routine pharmacovigilance activities. The Package Leaflet is updated accordingly. In addition, the RMP is updated to version 4.5 to reflect this new safety information." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 10.11.2016, 13.10.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Orfadin - nitisinone - EMEA/H/C/000555/II/0057 MAH: Swedish Orphan Biovitrum International AB, Rapporteur: Luca Pani, PRAC Rapporteur: Carmela Macchiarulo, "Update of sections 4.2 and 5.1 of the SmPC in order to amend the dosing frequency further to the results of a clinical pharmacology study NTBC-003. The Package Leaflet and Risk Management Plan are updated accordingly." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 15.09.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Plegridy - peginterferon beta-1a - EMEA/H/C/002827/II/0031/G MAH: Biogen Idec Ltd, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Julie Williams, "II: C.I.4 Update of section 4.8 of the SmPC with data on exposure and section 5.1 of the SmPC with information on maintenance of long-term efficacy based on clinical study data (study ATTAIN) II: C.I.4 Update of section 4.8 of the SmPC in order to add information concerning the onset and duration of flu-like symptoms based on clinical study data (study ALLOW). The Package Leaflet is updated accordingly." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Prolia - denosumab - EMEA/H/C/001120/II/0057 MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga,	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

"Update of section 4.6 of the SmPC in order to delete references to the Pregnancy and Lactation Surveillance programs. The Package Leaflet is updated accordingly. The RMP (version 22.0) has been revised to remove all references to the Pregnancy and Lactation Program. In addition, it has been also updated to add to the Pharmacovigilance plan that patients and infants exposed to denosumab during pregnancy or lactation will be followed until the infant is 1 year of age. In addition, the Marketing authorisation holder took the opportunity to make minor editorial updates to the SmPC and Package Leaflet." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 13.10.2016.	
Prolia - denosumab - EMEA/H/C/001120/II/0062 MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the product information (SmPC sections 4.4, 4.8 and PL sections 3 and 4) as well as the Risk Management Plan (RMP) to update the safety information and reflect the multiple vertebral fractures (MVF) follwoing discontinuation of Prolia treatement as a new important risk. This variation follows a concluded analysis of osteoporosis-related fracture data in subjects who discontinued investigational product and remained on study in either the Prolia phase 3 pivotal fracture study (Study 20030216) or its study extension (Study 20060289) to better understand the incidence of fracture following treatment discontinuation. The results of this analysis conclude that multiple vertebral fractures may occur following discontinuation of Prolia treatment, particularly in patients with a history of vertebral fracture. In addition, the applicant took the opportunity to update the PI in line with the QRD template latest version, amend the PI previous version typographical errors from previous version, and implement minor changes in the Package leaflet local representatives." Request for Supplementary Information adopted on 15.12.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Prolia - denosumab - EMEA/H/C/001120/II/0063	The Committee adopted a Request for Supplementary information together with a

MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the SmPC section 5.1 to provide information on the clinical study data experience in patients in treatment transition from an oral Bisphosphonate to desunomab, information resulting from the assessment on data of study report 20110153 and a discussion on the issue of long term antiresorptive treatment, in particular when long-term bisphosphonate treatment is followed by denosumab." Request for Supplementary Information adopted on 15.12.2016.	specific timetable.
Reyataz - atazanavir / atazanavir sulfate - EMEA/H/C/000494/II/0105/G MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Claire Ferard, "Scope C.I.4 Update of section 4.6 of the SmPC in order to update the safety information on lactation to indicate that atazanavir has been detected in human milk. The Package Leaflet and the RMP are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Scope C.I.11.b This type II variation aims to update the RMP in order to add "IRIS" and "angioedema" to Important Identified Risks and to update the epidemiology/exposure sections. The MAH also took the opportunity to make some reformatting changes to align the RMP with the current approved EMA template. The requested group of variations proposed amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP)." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Senshio - ospemifene - EMEA/H/C/002780/II/0012/G MAH: Shionogi Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Julie Williams, "-Update of section 4.5 of the SmPC in order to add the CYP3A4 in the drug interaction studies as a result of the submission of study E1508I0242. The following post authorisation measure is fulfilled: PAM 8: The Applicant is requested to investigate the CYP induction potential of ospemifene at	The CHMP adopted a revised timetable.

clinically relevant intestinal concentrations to exclude potential CYP3A4 induction in the intestine. No CYP induction is expected for ospemifene and M-1 at clinically relevant systemic concentrations.
-Update of section 5.2 of the SmPC in order to update the elimination section of the SmPC as a result of the submission of study E1508I0242 to fulfil the following post authorisation measures:
PAM 13: The applicant committed to evaluate and the conversion of the Z-enantiomer of ospemifene to its E-enantiomer post marketing.
PAM 14: The applicant committed to evaluate the metabolism and excretion of ospemifene and its metabolites using the commercial ospemifene 60 mg under fed conditions in a postauthorization study.
-Update of section 5.2 of the SmPC in order to update the distribution section as a result of the submission of study OSP-PF-046-N and OSP-PF-047-N to fulfil the following post authorisation measures:
PAM 6: The in vitro plasma protein binding data of M-1 in the non-clinical species will be provided post-authorisation for interspecies comparison between non-clinical species and humans. However the protocol should be adapted; the Applicant is requested to investigate a concentration range, e.g. 50 to 200 ng/mL for M1.
PAM 7: The blood-to-plasma ratio data for ospemifene in monkey and rat and the blood-to plasma ratio for M-1 in rat, monkey and human will be provided post-authorisation.
However the protocol should be adapted; the Applicant is requested to investigate a concentration range, e.g. 500 to 1200 ng/mL for ospemifene and 50 to 200 ng/mL for M 1.
-Update of section 5.2 of the SmPC in order to update the biotransformation section as a result of the submission of study OSP-PF-041-N to fulfil the following post authorisation measure:
PAM 9: The Applicant will provide BSEP transporter studies post-marketing.
As a consequence, an updated RMP version 1.2 is provided accordingly."
Request for Supplementary Information adopted on 10.11.2016.
Clockstop extension of 2 months requested to respond to RSI, responses expected

04.01.2017. For adoption.	
Soliris - eculizumab - EMEA/H/C/000791/II/0086/G, Orphan MAH: Alexion Europe SAS, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Eva A. Segovia, "Type II (C.I.4): Update of section 4.8 of the SmPC with the ADR frequencies to reflect overall exposure to eculizumab in clinical trials. The Package Leaflet (section 4) is updated accordingly. Type II (C.I.3.b): update of section 4.4 of the SmPC with warning and precautions on meningococcal vaccination timing as recommended by PRAC. The Package Leaflet (sections 2 and 3) Annex II.D and the RMP (ver. 13) are updated accordingly. In addition, the MAH took the opportunity of this RMP update to implement the PRAC recommendation suggesting to remove the off label use from the missing information, to provide the exposure data from PSUR 13 and to update the epidemiology sections with more complete and recent scientific literature data. Moreover, the MAH took the opportunity of this submission to add editorial changes and to bring the PI in line with the latest QRD template." Request for Supplementary Information adopted on 15.12.2016, 15.09.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable:
Stivarga - regorafenib - EMEA/H/C/002573/II/0019 MAH: Bayer Pharma AG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "The Marketing authorisation holder (MAH) took the opportunity to update Annex II to remove condition relating to provision of data on biomarkers from the ceased COAST trial (15983). Furthermore, minor editorial changes were introduced in the Product Information. The RMP has been updated accordingly and in order to remove the safety concern in patients with severe hepatic impairment following the parallel ongoing variation EMEA/H/C/002573/II/0018." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 10.11.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
TAGRISSO - osimertinib - EMEA/H/C/004124/II/0009/G MAH: AstraZeneca AB, Rapporteur: Aranzazu	The Committee adopted a Request for Supplementary information together with a specific timetable.

Sancho-Lopez, PRAC Rapporteur: Sabine Straus, “Update of SmPC sections 4.2, 4.4, 4.8, 5.1 and 5.2 based on the results from study D5160C00003 (AURA3) and the updated CSRs for studies D5160C00001 (AURAex) and D5160C00002 (AURA2). The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make editorial changes in the SmPC and Package Leaflet. The application included an updated RMP version 6.0. The provision of the CSR from study AURA3 addresses the Specific Obligation for Tagrisso and hence the MAH requests the conversion from a Conditional Marketing Authorisation to a Marketing Authorisation not subject to Specific Obligations.” Request for Supplementary Information adopted on 15.12.2016.	
Tasigna - nilotinib - EMEA/H/C/000798/II/0087, Orphan MAH: Novartis Europharm Ltd, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, “Submission of the final CSR from the clinical drug-drug interaction study CAMN107A2132. An updated RMP version 17 was included as part of the application.” Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0035 MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, “To update section 4.8 (Undesirable effects) of the SmPC under the sub-heading 'Tabulated summary of adverse reactions', to include 'liver function abnormalities' as an adverse event, observed in the post-marketing setting, and under the sub-heading 'Hepatic transaminases' to clarify events not observed in placebo-controlled studies. The package leaflet has been updated accordingly (section 4 under heading 'Possible side effects'). The MAH has also taken the opportunity to make minor administrative changes in the package leaflet and to review and update the status timelines of clinical and nonclinical study reports in the Risk Management Plan (v8).” Request for Supplementary Information adopted on 15.12.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.

Torisel - temsirolimus - EMEA/H/C/000799/II/0064, Orphan MAH: Pfizer Limited, Rapporteur: Harald Enzmann, "Update of sections 4.4 and 4.5 of the SmPC to reflect the increased risk of angioneurotic oedema in patients taking temsilorimus concomitantly with angiotensin-converting enzyme (ACE) inhibitors and/or calcium/channel blockers, based upon the pharmacokinetic analysis of Study 3066K1-148-US and supportive literature. The Package Leaflet is updated accordingly." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Translarna - ataluren - EMEA/H/C/002720/II/0016/G, Orphan MAH: PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus, "Update of section 4.4 to remove precautions for use relating to the co-administration of ataluren with substrates or inducers of UGT1A9 and section 4.5 of the SmPC to remove statements relating to the potential effect of co-administration of ataluren with inducers or substrates of UGT1A9 and to add results from studies PTC124-GD-026-HV and PTC124-GD-027-HV (MEA 011 and MEA 012). The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to the SmPC. Moreover, the updated RMP version 4.2 has been submitted." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 10.11.2016, 15.09.2016, 23.06.2016, 28.04.2016, 28.01.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xgeva - denosumab - EMEA/H/C/002173/II/0046 MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.6 of the SmPC in order to delete references to the Pregnancy and Lactation Surveillance programs. The Package Leaflet is updated accordingly. The RMP (version 22.0) has been revised to remove all references to the Pregnancy and Lactation Program. In addition, it has been also updated to add to the Pharmacovigilance plan that patients and infants exposed to denosumab during pregnancy or lactation will be followed until the infant is 1	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

year of age. In addition, the Marketing authorisation holder took the opportunity to make minor editorial updates to the SmPC and Package Leaflet." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 13.10.2016.	
Zelboraf - vemurafenib - EMEA/H/C/002409/II/0037 MAH: Roche Registration Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.5 of the SmPC in order to include information on Drug-drug interaction with rifampicin. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the RMP (final version 10.2) and to request modification of MEA 012 part 2 "Study GO29475: Two-part steady-state interaction study with rifampin (3YP3A4 inducer). Furthermore, the MAH is requesting changes of due dates for 3 category 3 final study reports (GO29475 (MEA011), MO25515 (MEA006) and GP28492 (MEA010)). The MAH is also including request for deletion from the RMP of the study NO25390 (MEA 005) to reflect the Paediatric Product Specific Waiver for treatment of melanoma as agreed with the PDCO on 24 April 2016." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS0971 **Jardiance-EMEA/H/C/002677/WS0971/0022** **Synjardy-EMEA/H/C/003770/WS0971/0021** MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Dolores Montero Corominas, "Submission of the final clinical report for study 1245.28 (4-year data) 'A phase III randomised, double-blind, active controlled parallel group efficacy and safety study of BI 10773 compared to glimepiride administered orally during 104 weeks with a 104-week extension period in patients with type 2 diabetes mellitus and insufficient glycaemic control despite metformin treatment' . Updated RMP versions 10.3 for and version 8.3 for Synjardy are approved as part of this procedure." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Request for Supplementary Information adopted on 15.09.2016.	
WS1026 **Rasilez-EMEA/H/C/000780/WS1026/0110** **Rasilez HCT-EMEA/H/C/000964/WS1026/0080** MAH: Novartis Europharm Ltd, Lead Rapporteur: Daniela Melchiorri, Lead PRAC Rapporteur: Carmela Macchiarulo, "Update of section 5.1 of the SmPC in order to reflect the results of study SPP100F2301 (ATMOSPHERE) a multicenter, randomized, doubleblind, parallel group, active-controlled study to evaluate the efficacy and safety of both aliskiren monotherapy and aliskiren/enalapril combination therapy compared to enalapril monotherapy, on morbidity and mortality in patients with chronic heart failure (NYHA Class II - IV). The RMP (v 13) has also been updated to reflect the study results." Request for Supplementary Information adopted on 15.12.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.

B.5.4. PRAC assessed procedures

PRAC Led **ATryn - antithrombin alfa - EMEA/H/C/000587/II/0027** MAH: GTC Biotherapeutics UK Limited, Rapporteur: Pierre Demolis, PRAC Rapporteur: Claire Ferard, , "Introduction of the first version of the RMP following request in 6th Annual Re-assessment EMEA/H/C/000587/S/0021 and second renewal EMEA/H/C/000587/R/0024" Request for Supplementary Information adopted on 15.12.2016, 15.09.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
PRAC Led **Eperzan - albiglutide - EMEA/H/C/002735/II/0028/G** MAH: GlaxoSmithKline Trading Services, Rapporteur: Kristina Dunder, PRAC Rapporteur: Julie Williams, , "II: C.I.11.b - Submission of a revised RMP in order to introduce the additional risk minimisation measures addressing the important potential risk of medication errors. Annex II of the Product Information is updated accordingly. II: C.I.11.b – Update of the RMP to add a new	The Committee adopted a Request for Supplementary information together with a specific timetable.

category 3 study as an additional pharmacovigilance activity - Study 204879: A Randomized, Open-label, Active-Controlled, Parallel-Group, Exploratory Study on the Effects of Repeated Doses of Albiglutide compared to Exenatide on Gastric Myoelectrical Activity and Gastric Emptying in Subjects with Type 2 Diabetes Mellitus II: C.I.11.b - Update of the RMP to add a new category 3 study as an additional pharmacovigilance activity – Study 201840 - An Exploratory Randomized, 2-Part, Single-blind, 2-Period Crossover Study Comparing the Effect of Albiglutide with Exenatide on Regional Brain Activity Related to Nausea in Healthy Volunteers II: C.I.11.b – Update of the RMP to add a new category 3 study as an additional pharmacovigilance activity – Cross-sectional survey to assess the effectiveness of the proposed additional educational materials using Patient Connect" Request for Supplementary Information adopted on 15.12.2016.	
PRAC Led **Halaven - eribulin - EMEA/H/C/002084/II/0033** MAH: Eisai Europe Ltd., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, , "Update of the RMP version 4.2 following the revision of the protocol for a post-authorisation study to capture data on the frequency of resolution and time to resolution of eribulin-induced or aggravated peripheral neuropathy from a phase 3 study, E7389-A001-303 (ACCRU) to an observational study, E7389-M044-504 (IRENE). The submission of the corresponding study report to the EMA / PRAC remains unchanged and is planned during 2019." Request for Supplementary Information adopted on 15.12.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
PRAC Led **Inflectra - infliximab - EMEA/H/C/002778/II/0047** MAH: Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey, PRAC Rapporteur: Rafe Suvarna, , "Update of the RMP (v 7.0) to merge the RMPs for Remsima and Inflectra."	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 15.12.2016.	
PRAC Led **Lyxumia - lixisenatide - EMEA/H/C/002445/II/0019** MAH: Sanofi-Aventis Groupe, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, , "Submission of the final clinical study report for a non-interventional PASS: a retrospective database study to estimate the incidence rates of acute pancreatitis, pancreatic and thyroid cancer among adult Type 2 Diabetes Mellitus patients treated with GLP-1 receptor agonists or a DPP4-inhinitor drug versus patients treated with other anti-diabetics, a category 3 study in order to fulfil MEA 007.2." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0093** MAH: Boehringer Ingelheim International GmbH, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Torbjorn Callreus, , "Submission of the final clinical trial report of study 1160.149 (Post-authorisation study to evaluate the effectiveness of the risk minimisation activities in the treatment of SPAF) in order to address part of follow-up measure FUM 026. The risk management plan (RMP) (Ver. 31.6) has been updated with results from the clinical study 1160.149." Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 15.09.2016, 26.05.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Rapiscan - regadenoson - EMEA/H/C/001176/II/0023** MAH: Rapidscan Pharma Solutions EU Ltd., Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, , "Submission of study report 01-1-401 to assess the safety profile of Rapiscan (regadenoson) in patients with liver impairment and to observe common adverse events reported in the post marketing setting." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Remsima - infliximab - EMEA/H/C/002576/II/0039** MAH: Celltrion Healthcare Hungary Kft.,	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Rapporteur: Greg Markey, PRAC Rapporteur: Rafe Suvarna, , “Update of the RMP (v 7.0) to merge the RMPs for Remsima and Inflectra.” Opinion adopted on 15.12.2016.	recommendation.
PRAC Led **Thymanax - agomelatine - EMEA/H/C/000916/II/0031** MAH: Servier (Ireland) Industries Ltd., Duplicate, Duplicate of Valdoxan, Rapporteur: Karsten Bruins Slot, PRAC Rapporteur: Kristin Thorseng Kvande, , “Submission of the final study report for study CLE-20098-095: ‘HLA alleles as genetic risk factors for elevation of aminotransferase levels in patients treated with agomelatine’. The product information and RMP are not impacted by this change.” Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Thyrogen - thyrotropin alfa - EMEA/H/C/000220/II/0088** MAH: Genzyme Europe BV, Rapporteur: Patrick Salmon, PRAC Rapporteur: Almath Spooner, , “To transfer the RMP to the latest RMP template. As a consequence, gastrointestinal symptoms, constitutional symptoms, and injection site reactions have been downgraded to identified risks, not categorized as important and therefore have been deleted. In addition, “perceived lower TSH elevation after thyrotropin alfa administration” does not correspond to a safety risk for the patients treated with Thyrogen and was also deleted from the list of important potential risks. Finally, study results and completion date of T4 study have been included and as a consequence, "Use of Thyrogen for remnant ablation in patients originally diagnosed with T4N0-1M0-1 thyroid cancer" was removed from the missing information section. RMP version 9.0 is being submitted.” Request for Supplementary Information adopted on 15.12.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
PRAC Led **Valdoxan - agomelatine - EMEA/H/C/000915/II/0033** MAH: Les Laboratoires Servier, Rapporteur: Karsten Bruins Slot, PRAC Rapporteur: Kristin Thorseng Kvande, , “Submission of the final	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

study report for study CLE-20098-095: 'HLA alleles as genetic risk factors for elevation of aminotransferase levels in patients treated with agomelatine'. The product information and RMP are not impacted by this change." Opinion adopted on 15.12.2016.	
PRAC Led **Zypadhera - olanzapine -** **EMEA/H/C/000890/II/0032** MAH: Eli Lilly Nederland B.V., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, , "Submission of the final study report of the PASS: Post-Injection Syndrome in Patients with Schizophrenia Receiving Olanzapine Long-Acting Injection. The Risk Management Plan (version 12) has been revised to reflect the results of the study." Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS0953** **Jardiance-** **EMEA/H/C/002677/WS0953/0019** **Synjardy-** **EMEA/H/C/003770/WS0953/0019** MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Dolores Montero Corominas, , "To update the RMP with risk of diabetic ketoacidosis (DKA) under the treatment of SGLT2 inhibitors for empagliflozin. The PRAC had considered that "diabetic ketoacidosis with atypical presentation" should be included as important identified risk in the RMP for all SGLT2 inhibitors. In addition, ongoing and planned activities are being included in the RMP." Request for Supplementary Information adopted on 15.09.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1028** **Relvar Ellipta-** **EMEA/H/C/002673/WS1028/0027** **Revinty Ellipta-** **EMEA/H/C/002745/WS1028/0023** MAH: Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, , "Submission of study HZA107112 (A randomised, double-blind,	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

two-way crossover study to investigate the effect of inhaled fluticasone furoate on short-term lower-leg growth in paediatric subjects with asthma), a post-authorization safety study (PASS) (Category 3) within the EU-RMP to investigate the important potential risk of growth retardation in children. This study was conducted as part of the Paediatric Investigational Plan (EMEA-000431-PIP01-08). In addition, the due date for study 205052 is amended in the RMP version 8.2 submitted." Opinion adopted on 15.12.2016.	
PRAC Led **WS1063** **Exviera-EMEA/H/C/003837/WS1063/0022** **Viekirax-EMEA/H/C/003839/WS1063/0027** MAH: AbbVie Ltd., Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Dolores Montero Corominas, , "To update the RMP for Exviera and Viekirax with the following chnages: 1. The addition of information on cases of hepatic decompensation observed in patients with Child-Pugh B hepatic impairment, and the revision of the SmPC to change the dose recommendation of these patients to "not recommended", as well as the addition of statements recommending the monitoring of hepatic function in these patients as approved on 25 January 2016 ((Ref: EMEA/H/C/WS/0873). 2. Addition of a reference to nine drug-drug interaction studies as approved on 28 April 2016 (Ref: EMEA/H/C/WS0896/G). 3. Reference to the completion of rat 2 year carcinogenicity studies on dasabuvir (Exviera) and ombitasvir (Viekirax) as approved on 24 September 2015 (Ref: EMEA/H/C/003837/II/0006 and EMEA/H/C/003839/II/0004). 4. Update of section 4.2 of SmPC for Virkirax to recommend a decrease in treatment duration of 12 weeks in GT4 cirrhotic patients, with a consequential change to sections 4.4 and 5.1 as approved on 18 August 2016 (Ref: EMEA/H/C/003839/II/0022/G). 5. Removal of the nonclinical PAMS 1-3 in the initial RMP, (Ref: EMEA/H/C/03837/MEA/003, EMEA/H/C/038397/MEA/002,	The Committee adopted a Request for Supplementary information together with a specific timetable.

EMEA/H/C/03839/MEA/003)." Request for Supplementary Information adopted on 15.12.2016.	

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

WS0989 **M-M-RVAXPRO-EMEA/H/C/000604/WS0989/0077** **ProQuad-EMEA/H/C/000622/WS0989/0111** MAH: Sanofi Pasteur MSD SNC, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 08.12.2016.	Positive Opinion adopted by consensus on 08.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1007 **Ambirix-EMEA/H/C/000426/WS1007/0081** **Fendrix-EMEA/H/C/000550/WS1007/0056** **Infanrix hexa-EMEA/H/C/000296/WS1007/0209** **Twinrix Adult-EMEA/H/C/000112/WS1007/0115** **Twinrix Paediatric-EMEA/H/C/000129/WS1007/0116** MAH: GlaxoSmithKline Biologicals, Lead Rapporteur: Bart Van der Schueren, Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1016/G **Aclasta-EMEA/H/C/000595/WS1016/0067/G** **Zometa-EMEA/H/C/000336/WS1016/0076/G** MAH: Novartis Europharm Ltd, Lead Rapporteur: Sinan B. Sarac Opinion adopted on 15.12.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1018 **Helixate NexGen-EMEA/H/C/000276/WS1018/0179** **KOGENATE Bayer-EMEA/H/C/000275/WS1018/0186**	Positive Opinion adopted by consensus on 24.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

MAH: Bayer Pharma AG, Duplicate, Duplicate of KOGENATE Bayer, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 24.11.2016. Request for Supplementary Information adopted on 29.09.2016.	
WS1021 **Genvoya-EMEA/H/C/004042/WS1021/0018** **Stribild-EMEA/H/C/002574/WS1021/0070** **Vitekta-EMEA/H/C/002577/WS1021/0025** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings Opinion adopted on 17.11.2016.	Positive Opinion adopted by consensus on 17.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1024 **Humalog-EMEA/H/C/000088/WS1024/0147** **Liprolog-EMEA/H/C/000393/WS1024/0111** MAH: Eli Lilly Nederland B.V., Informed Consent of Humalog, Lead Rapporteur: Robert James Hemmings Opinion adopted on 15.12.2016. Request for Supplementary Information adopted on 20.10.2016.	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1027 **Genvoya-EMEA/H/C/004042/WS1027/0019** **Stribild-EMEA/H/C/002574/WS1027/0071** **Tybost-EMEA/H/C/002572/WS1027/0030** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings Request for Supplementary Information adopted on 17.11.2016.	Rolling Timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
WS1042/G **Tivicay-EMEA/H/C/002753/WS1042/0024/G** **Triumeq-EMEA/H/C/002754/WS1042/0033/G** MAH: ViiV Healthcare UK Limited, Lead Rapporteur: Filip Josephson, Opinion adopted on 24.11.2016.	Positive Opinion adopted by consensus on 24.11.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1052 **Entresto-EMEA/H/C/004062/WS1052/0009** **Neparvis-EMEA/H/C/004343/WS1052/0007** MAH: Novartis Europharm Ltd, Lead	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Rapporteur: Johann Lodewijk Hillege Opinion adopted on 15.12.2016.	
WS1064 **Comtess-** **EMEA/H/C/000170/WS1064/0054** **Entacapone Orion-** **EMEA/H/C/002440/WS1064/0013** MAH: Orion Corporation, Lead Rapporteur: Outi Mäki-Ikola In addition the MAH has removed the address of MAH from the bottle label due to space constraints. In addition the annexes are being updated to QRD version 10"	Positive Opinion adopted by consensus on 15.12.2016. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/II/0039 MAH: ViiV Healthcare UK Limited, Rapporteur: Kristina Dunder, Withdrawal request submitted on 22.12.2016.	The MAH withdrew the procedure on 22.12.2016.
Wakix - pitolisant - EMEA/H/C/002616/II/0005, Orphan MAH: BIOPROJET PHARMA, Rapporteur: Joseph Emmerich Withdrawal request submitted on 26.12.2016.	The MAH withdrew the procedure on 26.12.2016.

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

- hydrocortisone - EMEA/H/C/004416, PUMA treatment of adrenal insufficiency
- anagrelide - EMEA/H/C/004585 reduction of elevated platelet counts in at risk essential thrombocythaemia patients,
- benralizumab - EMEA/H/C/004433 treatment of severe asthma with an eosinophilic phenotype

- betrixaban - EMEA/H/C/004309
treatment of prophylaxis of venous thromboembolism (VTE)

- burosumab - EMEA/H/C/004275, Orphan
Applicant: Kyowa Kirin Limited, treatment of X-linked hypophosphataemia (XLH)

- emtricitabine / tenofovir disoproxil - EMEA/H/C/004686
, treatment of HIV-1 infection, Generic, Duplicate,

- eteplirsen - EMEA/H/C/004355, Orphan
Applicant: AVI Biopharma International Ltd, treatment of Duchenne muscular dystrophy

- fulvestrant - EMEA/H/C/004649
Treatment of breast cancer,

- guselkumab - EMEA/H/C/004271
treatment of plaque psoriasis

- bevacizumab - EMEA/H/C/004360
for treatment of adult patients with metastatic carcinoma of the colon or rectum.
for first-line treatment of adult patients with metastatic breast cancer.
for first-line treatment of adult patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer other than predominantly squamous cell histology.
for first-line treatment of adult patients with unresectable advanced, metastatic or recurrent non-squamous non-small cell lung cancer with Epidermal Growth Factor Receptor (EGFR) activating mutations.
for first-line treatment of adult patients with advanced and/or metastatic renal cell cancer.
for the front-line treatment of adult patients with advanced (International Federation of Gynecology and Obstetrics (FIGO) stages III B, III C and IV) epithelial ovarian, fallopian tube, or primary peritoneal cancer.
for treatment of adult patients with first recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer.

- bevacizumab - EMEA/H/C/004728
, for treatment of adult patients with metastatic carcinoma of the colon or rectum.
for first-line treatment of adult patients with metastatic breast cancer.

for first-line treatment of adult patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer other than predominantly squamous cell histology.
for first-line treatment of adult patients with unresectable advanced, metastatic or recurrent non-squamous non-small cell lung cancer with Epidermal Growth Factor Receptor (EGFR) activating mutations.
for first-line treatment of adult patients with advanced and/or metastatic renal cell cancer.
for the front-line treatment of adult patients with advanced (International Federation of Gynecology and Obstetrics (FIGO) stages III B, III C and IV) epithelial ovarian, fallopian tube, or primary peritoneal cancer.
for treatment of adult patients with first recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer.

- gemtuzumab ozogamicin - EMEA/H/C/004204, Orphan
Applicant: 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).

- semaglutide - EMEA/H/C/004174
to improve glycaemic control in adults with type 2 diabetes and to prevent cardiovascular events

- ritonavir - EMEA/H/C/004549
treatment of HIV-1

- rituximab - EMEA/H/C/004729
treatment of Non-Hodgkin's lymphoma (NHL), Chronic lymphocytic leukaemia (CLL), Rheumatoid arthritis and Granulomatosis with polyangiitis and microscopic polyangiitis,

- rotigotine - EMEA/H/C/004286
treatment of idiopathic Restless Legs Syndrome and Parkinson's disease

- human herpesvirus 3 - EMEA/H/C/004336
prevention of herpes zoster (HZ) and HZ-related complications

- tacrolimus - EMEA/H/C/004435
prophylaxis of transplant rejection and

treatment of allograft rejection

- fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004363
treatment of adult patients with chronic obstructive pulmonary disease (COPD)

- human fibrinogen / human thrombin - EMEA/H/C/004446
treatment of haemostasis

- ngr-htnf - EMEA/H/C/004455, Orphan
Applicant: MolMed SpA, treatment of advanced malignant pleural mesothelioma

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

Samsca - tolvaptan - EMEA/H/C/000980/X/0024
MAH: Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Julie Williams, “Extension application to add a new strength of 7.5 mg tablets.”

Signifor - pasireotide - EMEA/H/C/002052/X/0030/G, Orphan
MAH: Novartis Europharm Ltd, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, “Extension application to introduce two new strengths of the ‘powder and solvent for suspension for injection pharmaceutical form’ (10 mg and 30 mg) grouped with a type II variation (C.I.6.a) to extend the indication to include ‘Treatment of adult patients with Cushing’s disease for whom surgery is not an option or for whom surgery has failed’ to the intramuscular injection formulations.”

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

- expanded human allogeneic mesenchymal adult stem cells extracted from adipose tissue - EMEA/H/C/004258, Orphan, ATMP
treatment of complex perianal fistula(s), List of Questions adopted on 15.07.2016.

- inotuzumab ozogamicin - EMEA/H/C/004119, Orphan
treatment B-cell precursor acute lymphoblastic leukaemia (ALL),
List of Questions adopted on 15.09.2016.

Celsentri - maraviroc - EMEA/H/C/000811/X/0046/G
MAH: ViiV Healthcare UK Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Qun-Ying Yue, "Extension application to introduce new pharmaceutical form (20mg/ml oral solution) and 2 new strenghts of film-coated tablets (25mg and 75mg) to the currently approved presentations for Celsentri, grouped with extension of indication to include paediatric use (2 to 18 years).

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.

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

- spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736, ATMP
treatment of cartilage defects,
List of Questions adopted on 19.04.2013.

- etanercept - EMEA/H/C/004192
treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, axial spondyloarthritis, ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis, plaque psoriasis and paediatric plaque psoriasis,
List of Questions adopted on 01.04.2016.

- iloperidone - EMEA/H/C/004149
treatment of schizophrenia,
List of Questions adopted on 28.04.2016.

- febuxostat - EMEA/H/C/004374
treatment of hyperuricaemia,
List of Questions adopted on 15.09.2016.

- sarilumab - EMEA/H/C/004254
treatment of active rheumatoid arthritis,
List of Questions adopted on 10.11.2016.

- masitinib - EMEA/H/C/004159, Orphan
, treatment of mastocytosis
List of Questions adopted on 15.09.2016.

Pergoveris - follitropin alfa / lutropin alfa - EMEA/H/C/000714/X/0047
MAH: Merck Serono Europe Limited,
Rapporteur: Nithyanandan Nagercoil, “Extension application to introduce a new pharmaceutical form (solution for injection) associated with 3 strengths of (300 IU + 150 IU)/ 0.48 ml, (450 IU + 225 IU)/ 0.72 ml and (900 IU + 450 IU)/ 1.44 ml.”
List of Questions adopted on 10.11.2016.

- cariprazine - EMEA/H/C/002770
treatment of schizophrenia,
List of Questions adopted on 21.07.2016.

- rituximab - EMEA/H/C/003903
, treatment of Non-Hodgkin's lymphoma (NHL), Chronic lymphocytic leukaemia (CLL), Rheumatoid arthritis and Granulomatosis with polyangiitis and microscopic polyangiitis,
List of Questions adopted on 15.09.2016.

- dimethyl fumarate - EMEA/H/C/002157
treatment of moderate to severe plaque psoriasis in adults in need of systemic drug therapy, treatment of plaque psoriasis
List of Questions adopted on 28.04.2016.

- Carglumic Acid - EMEA/H/C/004019
treatment of hyperammonaemia,

- patiromer sorbitex calcium - EMEA/H/C/004180
treatment of hyperkalaemia,
List of Questions adopted on 15.09.2016.

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

Ceplene - histamine dihydrochloride - EMEA/H/C/000796/S/0030, Orphan
MAH: Meda AB, Rapporteur: David Lyons, PRAC Rapporteur: Almath Spooner

Kolbam - cholic acid - EMEA/H/C/002081/S/0020, Orphan
MAH: Retrophin Europe Ltd, Rapporteur: Robert

James Hemmings, PRAC Rapporteur: Rafe Suvarna

Vyndaqel - tafamidis - EMEA/H/C/002294/S/0036, Orphan
MAH: Pfizer Limited, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Claire Ferard

Xagrid - anagrelide - EMEA/H/C/000480/S/0077, Orphan
MAH: Shire Pharmaceutical Contracts Ltd., Rapporteur: Pierre Demolis, Co-Rapporteur: Koenraad Norga, PRAC Rapporteur: Claire Ferard

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

Cuprymina - copper (64Cu) chloride - EMEA/H/C/002136/R/0014
MAH: Sparkle S.r.l., Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Rafe Suvarna

Dacogen - decitabine - EMEA/H/C/002221/R/0030, Orphan
MAH: Janssen-Cilag International NV, Rapporteur: Pierre Demolis, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Claire Ferard

Darzalex - daratumumab - EMEA/H/C/004077/R/0003, Orphan
MAH: Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Ana Sofia Diniz Martins

Enurev Breezhaler - glycopyrronium bromide - EMEA/H/C/002691/R/0020
MAH: Novartis Europharm Ltd, Duplicate, Duplicate of Seebri Breezhaler, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Torbjorn Callreus

Inlyta - axitinib - EMEA/H/C/002406/R/0021
MAH: Pfizer Limited, Rapporteur: Karsten Bruins Slot, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Helga Haugom Olsen

NovoThirteen - catridecacog - EMEA/H/C/002284/R/0020
MAH: Novo Nordisk A/S, Rapporteur: Joseph Emmerich, Co-Rapporteur: Jan Mueller-

Berghaus, PRAC Rapporteur: Claire Ferard

Pandemic influenza vaccine H5N1 MedImmune - pandemic influenza vaccine (H5N1) (live attenuated, nasal) - EMEA/H/C/003963/R/0003

MAH: MedImmune LLC, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jan Neuhauser

Revestive - teduglutide - EMEA/H/C/002345/R/0038, Orphan

MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Harald Enzmann, PRAC Rapporteur: Torbjorn Callreus

Seebri Breezhaler - glycopyrronium - EMEA/H/C/002430/R/0020

MAH: Novartis Europharm Ltd, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Torbjorn Callreus

Torisel - temsirolimus - EMEA/H/C/000799/R/0065, Orphan

MAH: Pfizer Limited, Rapporteur: Harald Enzmann, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Martin Huber

Tovanor Breezhaler - glycopyrronium - EMEA/H/C/002690/R/0022

MAH: Novartis Europharm Ltd, Duplicate, Duplicate of Seebri Breezhaler, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Torbjorn Callreus

Zoledronic acid Mylan - zoledronic acid - EMEA/H/C/002482/R/0013

MAH: MYLAN S.A.S, Generic, Generic of Zometa, Rapporteur: Milena Stain, PRAC Rapporteur: Doris Stenver

Zoledronic acid Teva - zoledronic acid - EMEA/H/C/002439/R/0018

MAH: Teva B.V., Generic, Generic of Zometa, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Zoledronic acid Teva Pharma - zoledronic acid - EMEA/H/C/002437/R/0014

MAH: Teva B.V., Generic, Generic of Aclasta, Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

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

Genvoya - elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004042/II/0026 MAH: Gilead Sciences International Ltd, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Amelia Cupelli, "Extension of indication Extension of Indication to include paediatric patients from 6 of age to less than 12 years of age, with body weight of at least 25kg, infected with human immunodeficiency virus-1 (HIV-1) without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir, for Genvoya. As a consequence, sections 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated based on the analysis of the paediatric study GS-US-292-0106 (Cohort 2) "A Phase 2/3, Open-Label Study of the Pharmacokinetics, Safety, and Antiviral Activity of the Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) Single Tablet Regimen (STR) in HIV-1 Infected Antiretroviral Treatment Naive Adolescents and Virologically Suppressed Children". The Package Leaflet and the Risk Management Plan (v. 3) are updated in accordance."	
Humira - adalimumab - EMEA/H/C/000481/II/0163 MAH: AbbVie Ltd., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Extension of Indication to include new indication for treatment of chronic non-infectious uveitis in paediatric patients for Humira. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and the RMP are updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity implement an alternative format statement for blind/partially sighted patients into the Package Leaflet as it was introduced with procedure EMEA/H/C/000481/N/0155. Furthermore, the MAH has made some editorial	

changes to the Package leaflet."

Nplate - romiplostim -
EMEA/H/C/000942/II/0060/G, Orphan
MAH: Amgen Europe B.V., Rapporteur: Aranzazu Sancho-Lopez, Co-Rapporteur: Paula Boudewina van Hennik, "C.I.6.a - Extension of Indication to include paediatric population for Nplate: to register Nplate for the use in the paediatric chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients: 1 year of age and older.
As a consequence Product information has been updated accordingly.
The RMP version 18 has also been submitted.
Furthermore, the PI is brought in line with the latest QRD templare version 10.
B.II.e.5.c – To add a low-dose romiplostim 125 microgram vial presentation for powder for solution for injection (4 vials pack).
B.II.e.5.a.1 – To add a 1 vial pack size of a low-dose romiplostim 125 microgram presentation."

Opdivo - nivolumab -
EMEA/H/C/003985/II/0029
MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension of Indication to include the treatment of hepatocellular carcinoma after prior sorafenib therapy in adults for OPDIVO.
As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.
Moreover, the updated RMP version 8.0 has been submitted."

Opdivo - nivolumab -
EMEA/H/C/003985/II/0030
MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Aranzazu Sancho-Lopez, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension of indication to include treatment of adults with mismatch repair deficient (dMMR) or microsatellite instability high (MSI-H) metastatic colorectal cancer after prior fluoropyrimidine based therapy for OPDIVO.
As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated in order to add the new indication and update the safety

information. The Package Leaflet is updated in accordance.
RMP version 9.0 is submitted with this application"

RoActemra - tocilizumab - EMEA/H/C/000955/II/0066

MAH: Roche Registration Limited, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension of indication to include an indication in adult patients for the treatment of giant cell arteritis for the subcutaneous formulation of RoActemra. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated to reflect information relevant to this indication. The Package Leaflet is updated in accordance."

Soliris - eculizumab - EMEA/H/C/000791/II/0090, Orphan

MAH: Alexion Europe SAS, Rapporteur: Aranzazu Sancho-Lopez, PRAC Rapporteur: Eva A. Segovia, "Extension of Indication of Soliris to include the 'treatment of Refractory generalized Myasthenia Gravis (gMG) patients who are antiacetylcholine receptor (AChR) antibody-positive'.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated to include information on the new indication and to include the new methodology to calculate the Adverse Drug Reaction frequencies (section 4.8).
The RMP is updated accordingly (version 14.0)."

Zykadia - ceritinib - EMEA/H/C/003819/II/0012

MAH: Novartis Europharm Ltd, Rapporteur: Aranzazu Sancho-Lopez, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ulla Wändel Liminga, "Extension of Indication to include new indication/population for Zykadia as first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC).
As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 of the SmPC are updated to update the information based primarily on the supporting study, CLDK378A2301 (ASCEND-4).
The Package Leaflet is updated in accordance.
An updated Risk Management Plan (Version 6) is also included in the application."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Adcetris - brentuximab vedotin -
EMEA/H/C/002455/II/0041/G, Orphan
MAH: Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik

Advate - octocog alfa -
EMEA/H/C/000520/II/0082/G
MAH: Baxter AG, Rapporteur: Jan Mueller-Berghaus

Bemfola - follitropin alfa -
EMEA/H/C/002615/II/0011
MAH: Gedeon Richter Plc., Rapporteur: Paula Boudewina van Hennik,

Cerezyme - imiglucerase -
EMEA/H/C/000157/II/0099/G
MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege

Cimzia - certolizumab pegol -
EMEA/H/C/001037/II/0058/G
MAH: UCB Pharma S.A., Rapporteur: Kristina Dunder, Procedure Manager: Helena Matos, EPL: Catherine Drai

Cosentyx - secukinumab -
EMEA/H/C/003729/II/0017
MAH: Novartis Europharm Ltd, Rapporteur: Tuomo Lapveteläinen

Darzalex - daratumumab -
EMEA/H/C/004077/II/0004, Orphan
MAH: Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac

Darzalex - daratumumab -
EMEA/H/C/004077/II/0005/G, Orphan
MAH: Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac

Emtricitabine/Tenofovir disoproxil Zentiva - emtricitabine / tenofovir disoproxil -
EMEA/H/C/004137/II/0001
MAH: Zentiva k.s., Generic, Generic of Truvada, Rapporteur: Alar Irs

HBVAXPRO - hepatitis B vaccine (rDNA) -
EMEA/H/C/000373/II/0055
MAH: Sanofi Pasteur MSD SNC, Rapporteur: Jan Mueller-Berghaus

Hemoprostol - misoprostol -
EMEA/H/W/002652/II/0006/G

MAH: Linepharma International Limited,
Rapporteur: Johann Lodewijk Hillege

Herceptin - trastuzumab -
EMEA/H/C/000278/II/0121
MAH: Roche Registration Limited, Rapporteur:
Jan Mueller-Berghaus

Herceptin - trastuzumab -
EMEA/H/C/000278/II/0127/G
MAH: Roche Registration Limited, Rapporteur:
Jan Mueller-Berghaus

Hizentra - human normal immunoglobulin -
EMEA/H/C/002127/II/0074/G
MAH: CSL Behring GmbH, Rapporteur: Jan
Mueller-Berghaus

IDELVION - albutrepenonacog alfa -
EMEA/H/C/003955/II/0003/G, Orphan
MAH: CSL Behring GmbH, Rapporteur: Jan
Mueller-Berghaus

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

Inhixa - enoxaparin sodium -
EMEA/H/C/004264/II/0005/G
MAH: Techdow Europe AB, Duplicate, Duplicate
of Thorinane, Rapporteur: Andrea Laslop

Lantus - insulin glargine -
EMEA/H/C/000284/II/0107/G
MAH: Sanofi-aventis Deutschland GmbH,
Rapporteur: Johann Lodewijk Hillege

Nimenrix - meningococcal group A, C,
W135 and Y conjugate vaccine -
EMEA/H/C/002226/II/0062
MAH: Pfizer Limited, Rapporteur: Greg Markey

Onivyde - irinotecan hydrochloride
trihydrate - EMEA/H/C/004125/II/0002,
Orphan
MAH: Baxalta Innovations GmbH, Rapporteur:
Filip Josephson

Orencia - abatacept -
EMEA/H/C/000701/II/0106/G
MAH: Bristol-Myers Squibb Pharma EEIG,
Rapporteur: Outi Mäki-Ikola

Privigen - human normal immunoglobulin -
EMEA/H/C/000831/II/0111

MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Retacrit - epoetin zeta - EMEA/H/C/000872/II/0075
MAH: Hospira UK Limited, Rapporteur: Martina Weise

Rivastigmine 1A Pharma - rivastigmine - EMEA/H/C/001181/II/0022/G
MAH: 1 A Pharma GmbH, Informed Consent of Exelon, Rapporteur: Pierre Demolis

Rivastigmine Hexal - rivastigmine - EMEA/H/C/001182/II/0023/G
MAH: Hexal AG, Informed Consent of Exelon, Rapporteur: Pierre Demolis

Rivastigmine Sandoz - rivastigmine - EMEA/H/C/001183/II/0024/G
MAH: Sandoz GmbH, Informed Consent of Exelon, Rapporteur: Pierre Demolis

RoActemra - tocilizumab - EMEA/H/C/000955/II/0067/G
MAH: Roche Registration Limited, Rapporteur: Jan Mueller-Berghaus

Silapo - epoetin zeta - EMEA/H/C/000760/II/0044
MAH: STADA Arzneimittel AG, Rapporteur: Martina Weise

Tenofovir disoproxil Zentiva - tenofovir disoproxil - EMEA/H/C/004120/II/0001
MAH: Zentiva k.s., Generic, Generic of Viread, Rapporteur: John Joseph Borg

Velphoro - mixture of polynuclear iron(III)-oxyhydroxide, sucrose and starches - EMEA/H/C/002705/II/0009/G
MAH: Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Johann Lodewijk Hillege

WS1068/G
Infanrix hexa-
EMEA/H/C/000296/WS1068/0216/G
MAH: GSK Biologicals SA, Lead Rapporteur: Bart Van der Schueren

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

Azarga - brinzolamide / timolol - EMEA/H/C/000960/II/0034

MAH: Alcon Laboratories (UK) Ltd, Rapporteur: Hanne Lomholt Larsen, “Update of sections 4.2, 4.4, 4.6 and 4.8 of the SmPC following a review of the safety profile taking into consideration data from clinical studies and post-marketing experience. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and Package Leaflet and to update the contact details for the local representative in Spain in the Package Leaflet.”

BeneFIX - nonacog alfa - EMEA/H/C/000139/II/0141

MAH: Pfizer Limited, Rapporteur: Jan Mueller-Berghaus, “Update of section 5.2 of the SmPC in order to update the information based on PK data from study B1821048.

This study reported PK from an extended collection time beyond the 72 hours previously used in all other BeneFIX studies, to 96 hours, after BeneFIX administration.”

Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0057/G

MAH: UCB Pharma S.A., Rapporteur: Kristina Dunder, “• B.II.e.6.a (Type IB) - to introduce an additional presentation which combines a Pre-filled Syringe (PFS) within a single-use, needle-safe Dose dispenser Cartridge (DDC) (functional secondary packaging), together with one new pack size,

• B.II.e.5.a).1 (Type IAin) - two additional pack sizes,

• C.I.4 (Type II) - amend the Product Information (PI) to add the Dose-dispenser Cartridge presentations.”

Descovy - emtricitabine / tenofovir alafenamide - EMEA/H/C/004094/II/0013

MAH: Gilead Sciences International Ltd, Rapporteur: Robert James Hemmings, “Submission of 96 week data from Study GS-US-311-1089 in order to support an update of the virological outcomes and measures of bone mineral density in Section 5.1 of the Summary of Product Characteristics (SmPC).”

Dynastat - parecoxib - EMEA/H/C/000381/II/0068/G

MAH: Pfizer Limited, Duplicate, Duplicate of

Xapit, Rapporteur: David Lyons, “C.I.4 - Update of section 4.4 of the SmPC in order to update the safety information related to cardiovascular risk information.
C.I.4 – Update of section 4.4 of the SmPC in order to update the safety information related to alcohol use and gastrointestinal (GI) risk.
C.I.4 - Update of section 4.6 of the SmPC in order to update the safety information related to oligohydramnios if the product is used during second or third trimester of pregnancy.
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, to bring the PI in line with the latest QRD template version 10.0 and to correct some mistakes.”

Giotrif - afatinib - EMEA/H/C/002280/II/0022

MAH: Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson, “Update of section 5.1 of the SmPC in order to update the information about the major mechanism of acquired resistance to afatinib. In addition, the Marketing authorisation holder (MAH) took the opportunity to add the side effects ‘itching’ and ‘dry skin’ with frequency very common to the package leaflet to bring it in line with the SmPC.”

GONAL-f - follitropin alfa - EMEA/H/C/000071/II/0136

MAH: Merck Serono Europe Limited, Rapporteur: Nithyanandan Nagercoil, “Update of the SmPC sections 4.4 and 4.8 to revise the frequency of thromboembolic events from 'very rare' to 'rare'. 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 10.0.”

Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/II/0046

MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson, “Submission of the final clinical study report of the study GS-US-337-1118: an Open-Label, Multicenter Study To Evaluate The Efficacy And Safety Of Sofosbuvir/Ledipasvir Fixed-Dose Combination

± Ribavirin For 12 or 24 Weeks In Chronic Genotype 1 HCV Infected Subjects Who Participated In A Prior Gilead-Sponsored HCV Treatment Study"

Jardiance - empagliflozin - EMEA/H/C/002677/II/0025

MAH: Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Dolores Montero Corominas, "Submission of the final results of non interventional study 1245.122 "Characteristics of patients initiating empagliflozin or other noninsulin glucose lowering drugs in the United Kingdom".
Consequently, the RMP (RMP 11.0) has been updated."

Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0018

MAH: GSK Biologicals SA, Rapporteur: Jan Mueller-Berghaus, "Submission of the final study report of study Malaria-057, a phase 2, open, randomised, controlled, multi-centre study to evaluate the safety and immunogenicity of 7 infant immunisation schedules of the RTS,S/AS01E candidate vaccine against P. falciparum in one study centre with 2 sites in Blantyre, Malawi. No changes to the product information or the RMP were proposed. The data is submitted to fulfil post-approval measure MEA 010."

Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0010

MAH: Orexigen Therapeutics Ireland Limited, Rapporteur: Hanne Lomholt Larsen, "Submission of study report NB-CVOT - Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Assessing the Occurrence of Major Adverse Cardiovascular Events (MACE) in Overweight and Obese Subjects with Cardiovascular Risk Factors Receiving Naltrexone SR/Bupropion SR. The product information remains unchanged."

Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0011

MAH: Orexigen Therapeutics Ireland Limited,

Rapporteur: Hanne Lomholt Larsen, "Submission of study report NaltrexBuprop-4001 - A Multicenter, Randomized, Double-blind, Placebo controlled, Phase 4 Study to Assess the Effect of Naltrexone Hydrochloride and Bupropion Hydrochloride Extended Release Combination on the Occurrence of Major Adverse Cardiovascular Events in Overweight and Obese Subjects with Cardiovascular Disease. The product information remains unchanged."

Noxafil - posaconazole - EMEA/H/C/000610/II/0048

MAH: Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, "Update of sections 4.4 and 4.5 of the SmPC in order to strengthen the current warning on interaction of posaconazole with vincristine. The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10."

Praluent - alirocumab - EMEA/H/C/003882/II/0018

MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Submission of study PDY13670 a Phase 1 study of the effects of subcutaneous doses of alirocumab on lipid and lipoprotein metabolism in adults with mildly elevated LDL-cholesterol."

Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0149

MAH: Pfizer Limited, Rapporteur: Kristina Dunder, "Submission of the final clinical study report (CSR) of study B1851018, a Phase 4 study evaluating the impact of 13vPnC in reducing AOM and NP colonisation caused by S pneumoniae in healthy children, in accordance with the Pharmacovigilance plan outlined in the EU RMP (version 11.0)."

Revestive - teduglutide - EMEA/H/C/002345/II/0037, Orphan

MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Sinan B. Sarac, "Update of section 4.2 of the SmPC in order to amend the recommendation that treatment effect should be evaluated after 12 months (instead of the

current recommended 6 months) based on literature references."

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."

Simponi - golimumab - EMEA/H/C/000992/II/0072

MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder, "Update of section 4.4 of the SmPC in order to include reports of Merkel cell carcinoma in patients treated with TNF blocking agents including Simponi. The frequency of this ADR has been reclassified from "not known" to "rare". Package Leaflet is updated accordingly."

Thalidomide Celgene - thalidomide - EMEA/H/C/000823/II/0050, Orphan

MAH: Celgene Europe Limited, Rapporteur: Pierre Demolis, "Submission of a final clinical study report for Study CC-2001-CP-001 together with the population pharmacokinetics (PK) meta-analysis CC-2001-MPK-001 and bioanalytical report CC-2001-CP-001-BA undertaken to evaluate thalidomide PK in multiple myeloma subjects in order to fulfil legally binding measure LEG 027.3."

Zaltrap - aflibercept - EMEA/H/C/002532/II/0035

MAH: Sanofi-Aventis Groupe, Rapporteur: Filip Josephson, "Update the Product Information (SmPC, section 5.1 Pharmacodynamic properties)to reflect the results of the biomarker programme encompassing the EFC10262,

EFC10668 and EFC11338 studies in order to fulfil the Annex II condition of Zaltrap, aflibercept 25 mg/ml, Concentrate for solution for infusion (EMEA/H/C/002532)."

Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/II/0002

MAH: AstraZeneca AB, Rapporteur: Robert James Hemmings, "Update of section 4.4 of the SmPC to revise the paragraph on limitations of clinical data for hospital acquired pneumonia (HAP) indication, section 4.8 of the SmPC to change the frequency from uncommon to common for thrombocytopia and puritis and section 5.1 of the SmPC to add a new section for HAP/VAP pathogens. The SmPC update is based on the availability of the final CSR for REPROVE (D4281C00001) an updated modelling and simulation report (CAZMS - 09). The Package Leaflet (section 4) is updated accordingly.
Study D4281C00001 is a PAES detailed in Annex II.D, therefore an update of Annex II.D is also proposed.
In addition, The MAH took the opportunity to add 'Dilute before use' to section 5 of the outer Packaging - Carton."

Zeffix - lamivudine - EMEA/H/C/000242/II/0068

MAH: Glaxo Group Ltd, Duplicate, Duplicate of Epivir, Rapporteur: Joseph Emmerich, "Update of sections 4.4 and 4.6 of the SmPC to reflect pregnancy clinical outcome data from the Antiretroviral Pregnancy Registry (APR). In addition, an introductory paragraph for pregnancy has been added to section 4.6 of the SmPC in line with Epivir (lamivudine for Human Immunodeficiency Virus Indication) (variation II/84)."

Zelboraf - vemurafenib - EMEA/H/C/002409/II/0039

MAH: Roche Registration Limited, Rapporteur: Filip Josephson, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to include the paediatric clinical data from the Zelboraf NO25390 (BRIM-P) after request during assessment as per procedure EMEA/H/C/002409/P46/033."

Zepatier - elbasvir / grazoprevir - EMEA/H/C/004126/II/0005

MAH: Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, “Update of section 4.5 of the SmPC in order to update information regarding drug-drug interaction (DDI) of elbasvir/grazoprevir when co-administrated with sunitinib (tyrosine kinase inhibitor). The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some editorial changes.”

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.”

WS1077/G
Aluvia-
EMEA/H/W/000764/WS1077/0101/G
Kaletra-
EMEA/H/C/000368/WS1077/0163/G
Norvir-
EMEA/H/C/000127/WS1077/0143/G
MAH: AbbVie Ltd., Lead Rapporteur: Joseph Emmerich, “Update of sections 4.3 and 4.5 of the SmPC in order to add information regarding the interaction of lopinavir/ritonavir and ritonavir with lurasidone and ranolazine. In addition, sections 4.4 and 4.5 of the SmPC are updated to add information regarding the interaction with injectable triamcinolone. The Labelling is updated accordingly.”

WS1091
Clopidogrel Zentiva-
EMEA/H/C/000975/WS1091/0056
Clopidogrel/Acetylsalicylic acid Zentiva-
EMEA/H/C/001144/WS1091/0048
DuoPlavin-
EMEA/H/C/001143/WS1091/0047
Iscover-
EMEA/H/C/000175/WS1091/0129

Plavix-EMEA/H/C/000174/WS1091/0125
MAH: Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, “Update of section 4.1 to clarify the indication and specify that clopidogrel is indication for the secondary prevention of atherothrombotic events.”

WS1092
Ebymect-
EMEA/H/C/004162/WS1092/0017
Edistride-
EMEA/H/C/004161/WS1092/0013
Forxiga-
EMEA/H/C/002322/WS1092/0032
Xigduo-EMEA/H/C/002672/WS1092/0028
MAH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder, , “Update of sections 4.4 and 5.1 of the SmPC in order to reflect the results of the Phase 3 study D5553C00003: 28-week safety and efficacy, randomised, double-blind comparison of simultaneous administration of exenatide once weekly 2 mg an dapagliflozin once daily 10 mg to exenatide once weekly 2 mg alone and dapagliflozin once daily 10 mg alone in patients with type 2 diabetes with inadequate glycaemic control on metformin.
The Package Leaflet is updated accordingly.
In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflets for Ebymect and Edistride and to introduce minor editorial changes throughout the Product Informations.”

WS1105
IntronA-
EMEA/H/C/000281/WS1105/0107
PegIntron-
EMEA/H/C/000280/WS1105/0128
ViraferonPeg-
EMEA/H/C/000329/WS1105/0121
MAH: Merck Sharp & Dohme Limited, Lead Rapporteur: Filip Josephson, “Update of sections 4.2 and 4.8 of the SmPC in order to update the safety information with information on HCV/HBV co-infection, and to add an ADR on hepatitis B reactivation in HCV/HBV co-infected patients as post marketing adverse experience respectively.
The Package Leaflet and Labelling are updated accordingly.
In addition, the Worksharing applicant (WSA) took the opportunity to bring the PI in line with

the latest QRD template version 10 including the implementation of the use of combined SmPCs and PLs for PegIntron and ViraferonPeg and the use of combined SmPCs for Intron A in multidose pen."	
WS1107/G **Prezista-** **EMEA/H/C/000707/WS1107/0085/G** **Rezolsta-** **EMEA/H/C/002819/WS1107/0017/G** MAH: Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.3 and 4.5 of the SmPC with contra-indication and information of drug-drug interactions of boosted darunavir with elbasvir/grazoprevir (Zepatier) and with lurasidone (Latuda). The PL was updated accordingly. Update of section 4.5 of the Prezista SmPC regarding the drug-drug interaction of boosted darunavir with corticosteroids in line with the PRAC Recommendation for Rezolsta. In addition, the MAH took the opportunity of this variation, for both products, to add information regarding alfuzosin in section 4.5 in line with section 3, to add inhibition of CYP2D6 for the alfa 1 adrenoreceptor antagonist and to correct the frequency of the adverse event osteonecrosis. Section 4.5 of Prezista was also updated to align information between the different formulations and with Rezolsta. An error was correct in section 5.2. The MAH also took the opportunity to update the Product Information with the lasts QRD templates version 9.1 and 10. The contact of the Dutch local representative in the PL was updated."	
WS1110 **Kinzalkomb-** **EMEA/H/C/000415/WS1110/0100** **MicardisPlus-** **EMEA/H/C/000413/WS1110/0102** **PritorPlus-** **EMEA/H/C/000414/WS1110/0110** MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Daniela Melchiorri, "Update of section 4.8 to align the hydrochlorothiazide component information with that of the originator. The Package Leaflet is	

updated accordingly.
In addition, Worksharing applicant (WSA) took the opportunity of this procedure to bring the PI in line with the latest QRD template, including combining the SmPC of the different strengths, as well as implement minor editorial changes and reformatting of some sections of the SmPC. The Portuguese local representative in the PL has been updated."

WS1114
Exviera-EMEA/H/C/003837/WS1114/0025
Viekirax-
EMEA/H/C/003839/WS1114/0030
MAH: AbbVie Ltd., Lead Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC to add that a treatment duration of 8 weeks may be considered in previously untreated genotype 1b-infected patients without advanced fibrosis or cirrhosis supported by the results of the study M15-684 (GARNET). Consequently the section 5.1 of the SmPC is updated to reflect the results of this study. The Package Leaflet is updated accordingly."

B.6.10. CHMP-PRAC assessed procedures

Adcetris - brentuximab vedotin -
EMEA/H/C/002455/II/0043, Orphan
MAH: Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "Update of sections 4.8 and 5.1 of the SmPC in order to add data from study C25007. The RMP (version 8.0) was updated accordingly. The submission of the clinical study report fulfils SOB 011 of the conditional marketing authorisation for Adcetris."

ELOCTA - efmoroctocog alfa -
EMEA/H/C/003964/II/0010
MAH: Swedish Orphan Biovitrum AB (publ), Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Rafe Suvarna, "Submission of the final Clinical Study Report of study 997HA307 (to investigate PK of rFVIIIFc at 2 vial strengths (1000 and 3000IU) and evaluate safety of rFVIIIFc.
Study 997HA307 is listed as an additional PhV activity (category 3 study, MEA 003) in the Risk Management Plan, therefore an updated RMP is included (ver. 1.5)."

Erivedge - vismodegib - EMEA/H/C/002602/II/0032

MAH: Roche Registration Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 5.3 of the SmPC in order to reflect non-clinical carcinogenicity studies (MEA 003):

- Study 13-0322 is a 26-Week Oral Gavage Carcinogenicity Study with Vismodegib in Hemizygous CByB6F1-Tg(HRAS)2Jic Mice.

- Study 13-0323 is a 104-Week and 52-Week with a 12-Week Recovery Phase Oral Gavage Carcinogenicity Study with Vismodegib in Sprague Dawley Rats.

The RMP (RMP 12.0) has been consequently updated. Furthermore, additional routine changes (including some resulting from the assessment of RMP version 11) have been introduced."

Increlex - mecasermin - EMEA/H/C/000704/II/0044/G, Orphan

MAH: Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "Update of section 4.4 of the SmPC in order to update the warning regarding antibody response to injected IGF-1.

Submission of an updated RMP version 9, including the educational materials, to update the instructions for antibody testing and improve wording and advices."

Jardiance - empagliflozin - EMEA/H/C/002677/II/0026

MAH: Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Dolores Montero Corominas, "Submission of the final results on non-clinical study "Effect of empagliflozin on blood ketone level at refeeding after a fasting period. Comparison between refeeding with glucose or fat."

Consequently, the RMP (RMP 11.0) has been updated."

Levemir - insulin detemir - EMEA/H/C/000528/II/0084

MAH: Novo Nordisk A/S, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Doris Stenver, “Submission of the summary analysis report on the incidence of neoplasms with the combination of liraglutide and insulin detemir from the cardiovascular outcome trial for Victoza®, trial EX2211-3748 (LEADER®). As a consequence the following important potential risk “Potential risk of malignant neoplasms following combination treatment with insulin detemir + liraglutide + metformin” is deleted from the updated RMP version 18.”

Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0017

MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Almath Spooner, “Update of sections 4.8 and 5.1 of the SmPC in order to reflect the long-term safety and efficacy data from Study VX12 809 105. Study VX12 809 105 is a Phase 3, rollover study to evaluate the safety and efficacy of long term treatment with LUM/IVA in subjects aged 12 years and older with cystic fibrosis, homozygous or heterozygous for the F508del CFTR mutation (MEA 001). A new version of the RMP (ver. 2.7) included in this submission has been updated to include the final data from Study 105.
In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.”

Perjeta - pertuzumab - EMEA/H/C/002547/II/0028

MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, “Final Clinical Study Report the TRYPHAENA study(BO22280) A randomised, multicentre, multinational Phase II study to evaluate pertuzumab in combination with trastuzumab, given either concomitantly or sequentially with standard anthracyclinebased chemotherapy or concomitantly with a nonanthracycline-based chemotherapy regimen, as neoadjuvant therapy for patients with locally advanced, inflammatory or early stage HER2-positive breast cancer.

The RMP (v 8) has been updated to reflect the completion of the study.”

Saxenda - liraglutide -
EMEA/H/C/003780/II/0011

MAH: Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Based on submission of the LEADER clinical study results (EX2211-3748: liraglutide effect on and action in diabetes, evaluation of cardiovascular outcome results), changes to sections 4.4, and 5.1 of the SmPC are being proposed in order to update the safety information and include a description of the clinical study outcomes. The Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement minor editorial changes throughout the product information.

The LEADER study was included in the liraglutide RMP as a required pharmacovigilance activity (category 3) to specifically address the important potential risk of cardiovascular disorders in patients with Type 2 Diabetes Mellitus. Updates to the liraglutide RMP based on the study results are also proposed: this variation application fulfils two post-approval commitments in relation to the cardiovascular outcomes trial (MEA 002), as well as to provide additional information on the breast cancer cases found in LEADER (MEA 005). RMP Version 27 was submitted with the application. These liraglutide RMP modifications are in line with the proposed updates to the Saxenda Product Information described above."

WS1101
Relvar Ellipta-
EMEA/H/C/002673/WS1101/0029
Revinty Ellipta-
EMEA/H/C/002745/WS1101/0025

MAH: Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, "Update of section 5.1 of the SmPC in order to update the safety information in relation to results of HZC115151 study (A 12-month, open label, randomised, effectiveness study to evaluate fluticasone furoate (FF, GW685698)/vilanterol (VI, GW642444) Inhalation Powder delivered once daily via a Novel Dry Powder Inhaler (NDPI) compared with the existing COPD maintenance therapy alone in subjects with Chronic

Obstructive Pulmonary Disease (COPD)(an Annex II condition) of the Relvar Ellipta and Revinty Ellipta (92/22mcg strength only). Consequently the RMP version 8.3 is updated."

B.6.11. PRAC assessed procedures

PRAC Led

Bydureon - exenatide - EMEA/H/C/002020/II/0042

MAH: AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, , "Submission of the updated RMP version 25 following closure and final summary of Exenatide Pregnancy Registry (a prospective, observational study conducted in the United States that actively collected information on exposure to antidiabetic medication during pregnancy and the associated pregnancy outcomes in patients with Type 2 diabetes mellitus). Moreover, the MAH included additional minor updates to the RMP."

PRAC Led

Herceptin - trastuzumab - EMEA/H/C/000278/II/0126

MAH: Roche Registration Limited, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, , "C.I.13. Submission of the final study report for the PrefHer study (MO22982); a category 3 study in the RMP to fulfill a required additional pharmacovigilance activity.
The PrefHer study is a Phase II, randomized, multicenter, open-label, two-cohort, two-arm, crossover study designed to investigate patient preference for Herceptin intravenous (IV) or Herceptin subcutaneous (SC) administered using the three-weekly (q3w) dosing regimen via the single-use injection device (SID) or from the vial via hand-held syringe, and to compare Health Care professional (HCP) satisfaction and perceived time savings with the two methods of administration in patients with HER2-positive early breast cancer (EBC) in the neoadjuvant/adjuvant setting.
The study also evaluated the safety and efficacy (event-free survival) of Herceptin SC and IV.
The crossover design of the study also allowed an evaluation of the safety and tolerability of switching between the Herceptin IV and the

Herceptin SC formulations, and vice versa."

PRAC Led

Mimpara - cinacalcet -

EMEA/H/C/000570/II/0056

MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, , "Submission of the final report for Study 20090686, a study designed to determine the efficacy of cinacalcet compared with vitamin D therapy for management of secondary HPT (hyperparathyroidism) in haemodialysis subjects.
This variation fulfils LEG 031."

PRAC Led

Remicade - infliximab -

EMEA/H/C/000240/II/0201/G

MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, , "Submission of the clinical study reports for C0168T45 and C0168T62 together with an overall summary and evaluation of the complete long term safety follow-up programs for Remicade (as per MEA 79).
Study C0168T45 (RESULTS: REMICADE Safety Under Long term Study) is a Multicenter International Observational Study of the Long-term Safety of Infliximab
Study C0168T62 (RESULTS UC: REMICADE Safety Under Long-term Study in Ulcerative Colitis) is a Multicenter International Study of the Long-term Safety of Infliximab in Ulcerative Colitis.
The RMP (RMP 14.0) has been updated to reflect the completion of these studies."

PRAC Led

Xeplion - paliperidone -

EMEA/H/C/002105/II/0031

MAH: Janssen-Cilag International NV, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, , "Submission of final study report "Post-Authorization Safety Study Using European Union Databases to Assess the Risk of Cardiovascular and Cerebrovascular Adverse Events in Elderly Patients Treated with Paliperidone Palmitate, Paliperidone Prolonged-Release, and Other Antipsychotics". No changes in the PI are proposed."

PRAC Led

Zaltrap - aflibercept -

EMEA/H/C/002532/II/0034
MAH: Sanofi-Aventis Groupe, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, , "Submission of the final results of the Drug Utilisation Study monitoring the use of Zaltrap in cancer patients including potential off-label use and evaluating the potential for intravitreal use. This fulfils the post authorisation commitment MEA 03."

PRAC Led
WS1088
Eucreas-
EMEA/H/C/000807/WS1088/0057
Galvus-EMEA/H/C/000771/WS1088/0048
Icandra-
EMEA/H/C/001050/WS1088/0058
Jalra-EMEA/H/C/001048/WS1088/0048
Xiliarx-EMEA/H/C/001051/WS1088/0047
Zomarist-
EMEA/H/C/001049/WS1088/0058
MAH: Novartis Europharm Ltd, Lead PRAC Rapporteur: Qun-Ying Yue, "Following the outcome of an Article 31 referral procedure for metformin and metformin-containing products (Procedure EMEA/H/A-31/1432), the Applicant was requested toupdate the Risk Management Plan (RMP) for galvus, Jalra, Xiliarx, Eucreas, Icandra and Zomarist to implement a targeted questionnaire for cases of lactic acidosis."

B.6.12. CHMP-CAT assessed procedures

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0008, ATMP
MAH: Amgen Europe B.V., Rapporteur: Olli Tenhunen,

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

WS0934/G
Suboxone-
EMEA/H/C/000697/WS0934/0034/G
MAH: Indivior UK Limited, Lead Rapporteur: Martina Weise

WS1030
ANORO-EMEA/H/C/002751/WS1030/0015
Incruse-
EMEA/H/C/002809/WS1030/0014
Laventair-
EMEA/H/C/003754/WS1030/0017
Relvar Ellipta-
EMEA/H/C/002673/WS1030/0028
Revinty Ellipta-
EMEA/H/C/002745/WS1030/0024
MAH: Glaxo Group Ltd, Lead Rapporteur: Nithyanandan Nagercoil"The MAH submitted a worksharing procedure in order to enhance patient safety: the MAH is proposing the addition of pictograms in the user instructions of the Umeclidinium Bromide/Vilanterol, Umeclidinium Bromide and Fluticasone Furoate/Vilanterol to inform the patient/prescriber what the contents of the carton are and that it contains a desiccant sachet which should be discarded when the tray containing the inhaler is first opened. Sections 4.2 of the SmPC and section 6 pf the Package leaflet are therefore amended.

In addition, the MAH took the opportunity to propose the following changes:
- to include a linguistic correction in the Slovakian translation of the section 4.5 of the SmPC of Anoro and Laventair.
- to include two updates related to QRDv10, in the Annex IIIA for outer packaging of Relvar
- to include an amendment to the Slovenian translation of the section 5.2 of the SmPC of high strength of Relvar and Revinty (EU/1/13/886/004, EU/1/13/886/005, EU/1/13/886/006 and EU/1/14/929/004, EU/1/14/929/005, EU/1/14/929/006)."

WS1046
Ambirix-
EMEA/H/C/000426/WS1046/0082
Twinrix Adult-
EMEA/H/C/000112/WS1046/0116
Twinrix Paediatric-
EMEA/H/C/000129/WS1046/0117
MAH: GSK Biologicals SA, Lead Rapporteur: Robert James Hemmings

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.”

WS1069/G
Infanrix hexa-
EMEA/H/C/000296/WS1069/0214/G
MAH: GSK Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1081
Hexacima-
EMEA/H/C/002702/WS1081/0055
Hexaxim-
EMEA/H/W/002495/WS1081/0062
Hexyon-
EMEA/H/C/002796/WS1081/0059
MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus

WS1085
Ceprotin-
EMEA/H/C/000334/WS1085/0098
HyQvia-EMEA/H/C/002491/WS1085/0034
Kiovig-EMEA/H/C/000628/WS1085/0076
MAH: Baxalta Innovations GmbH, Lead Rapporteur: Jan Mueller-Berghaus

WS1090/G
OFEV-
EMEA/H/C/003821/WS1090/0012/G
Vargatef-
EMEA/H/C/002569/WS1090/0014/G
MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Sinan B. Sarac

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 theopportunity 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.”	
WS1094/G **Eucreas-** **EMEA/H/C/000807/WS1094/0058/G** **Galvus-** **EMEA/H/C/000771/WS1094/0049/G** **Icandra-** **EMEA/H/C/001050/WS1094/0059/G** **Jalra-** **EMEA/H/C/001048/WS1094/0049/G** **Xiliarx-** **EMEA/H/C/001051/WS1094/0048/G** **Zomarist-** **EMEA/H/C/001049/WS1094/0059/G** MAH: Novartis Europharm Ltd, Lead Rapporteur: Kristina Dunder	
WS1098/G **Olazax-** **EMEA/H/C/001087/WS1098/0019/G** **Olazax Disperzi-** **EMEA/H/C/001088/WS1098/0020/G** MAH: Glenmark Pharmaceuticals s.r.o., Generic, Duplicate, Generic of Zyprexa, Zyprexa Velotab, Duplicate of Olanzapine Glenmark, Olanzapine Glenmark Europe, Lead Rapporteur: Pierre Demolis“B.II.e.5.a.2 – To add a new pack size of 56 tablets in blister (alu/alu) for the 5 mg strength. B.II.e.5.a.2 – To add a new pack size of 56 tablets in blister (alu/alu) for the 7.5 mg	

strength. B.II.e.5.a.2 – To add a new pack size of 56 tablets in blister (alu/alu) for the 10 mg strength. B.II.e.5.a.2 – To add a new pack size of 56 tablets in blister (alu/alu) for the 15 mg strength. B.II.e.5.a.2 – To add a new pack size of 56 tablets in blister (alu/alu) for the 20 mg strength. (Olazax EU/1/09/597/006-010 and Olazax Disperzi EU/1/09/592/006-010).”	
WS1104 **Epclusa-** **EMEA/H/C/004210/WS1104/0008** **Harvoni-** **EMEA/H/C/003850/WS1104/0047** **Sovaldi-EMEA/H/C/002798/WS1104/0039** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Filip Josephson	
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”	
WS1118/G **Helixate NexGen-** **EMEA/H/C/000276/WS1118/0185/G** **KOGENATE Bayer-** **EMEA/H/C/000275/WS1118/0193/G** MAH: Bayer Pharma AG, Duplicate, Duplicate of KOGENATE Bayer, Lead Rapporteur: Jan Mueller-Berghaus,	
WS1119/G **Iblias-** **EMEA/H/C/004147/WS1119/0004/G** **Kovaltry-** **EMEA/H/C/003825/WS1119/0007/G** MAH: Bayer Pharma AG, 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):

Qualification of Biomarkers:

HTA:

G.2. Ongoing procedures

G.3. PRIME

G.3.1. List of procedures concluding at 12-15 December 2016 CHMP plenary:

Oncology		
1.	(SME); Treatment of Malignant Pleural Mesothelioma	The CHMP denied eligibility to PRIME and adopted the critical summary report.
2.	Treatment of pediatric neuroblastoma patients with leptomeningeal metastasis	The CHMP denied eligibility to PRIME and adopted the critical summary report.
3.	**Autologous CD4+ and CD8+ T cells Expressing a CD19-Specific Chimeric Antigen Receptor (JCAR017**ATMP;Treatment of relapsed / refractory diffuse large B-cell Lymphoma (DLBCL)	The CHMP granted eligibility to PRIME and adopted the critical summary report.
4.	Treatment of patients with leptomeningeal carcinomatosis from solid tumours	The CHMP denied eligibility to PRIME and adopted the critical summary report.
5.	Treatment of Spinal Muscular Atrophy (SMA)	The CHMP denied eligibility to PRIME and adopted the critical summary report.
6.	Treatment of Alzheimer's disease	The CHMP denied eligibility to PRIME and adopted the critical summary report.
7.	Active immunisation for the prevention of disease caused by dengue virus	The CHMP denied eligibility to PRIME and adopted the critical summary report.

G.3.2. List of procedures starting in November 2016 for January 2017 CHMP adoption of outcomes

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