21 July 2017
EMA/CHMP/262210/2017 Corr[1]
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Minutes of the meeting on 15-18 May 2017

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

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

Note on access to documents

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

[1] Correction in section 16.

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

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1. Introduction

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

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) May 2017 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 15-18 May 2017 (to be published post June 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.

The CHMP welcomed the new alternate member Jorge Camarero Jiménez from Spain replacing Arantxa Sancho-Lopez and noted the new member Adriana Adameová from Slovakia.

1.2. Adoption of agenda

CHMP agenda for 15-18 May 2017

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 18-21 April 2017.

The CHMP adopted the CHMP minutes for 18-21 April 2017.

The Minutes of the May 2017 CHMP ORGAM meeting held on 8 May 2017, together with all decisions taken at that meeting, were adopted.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. iloperidone - EMEA/H/C/004149

treatment of schizophrenia

Scope: Oral explanation, SAG report

Action: Oral explanation to be held on 17 May 2017 at time 09:00

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 28.04.2016.

The CHMP noted the SAG report.

An oral explanation was held on 17 May 2017 at 09:00

See 3.2.

2.1.2. tivozanib hydrochloride monohydrate - EMEA/H/C/004131

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

Scope: Oral explanation

Action: Oral explanation to be held on 17 May 2017 at time 11:00

List of Outstanding Issues adopted on 26.01.2017. List of Questions adopted on 21.07.2016.

An oral explanation was held on 17 May 2017 at time 11:00. During the oral explanation the company presented the answers to the remaining clinical major objection

2.1.3. etirinotecan pegol - EMEA/H/C/003874

treatment of breast cancer with brain metastases

Scope: Oral explanation

Action: Oral explanation to be held on 16 May 2017 at time 14:00

List of Outstanding Issues adopted on 23.03.2017. List of Questions adopted on 10.11.2016.

See 3.2

An oral explanation was held on 16 May 2017 at 14:00.

2.1.4. Reagila - cariprazine - EMEA/H/C/002770

Gedeon Richter; treatment of schizophrenia

Scope: Oral explanation

Action: Oral explanation to be held on 16 May 2017 at time 11:00

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

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 21.07.2016.

See 3.1

Oral explanation to be held on 16 May 2017 at time 11:00 was cancelled. The CHMP agreed that an oral explanation was not needed.

2.1.5. Veltassa - patiromer sorbitex calcium - EMEA/H/C/004180

treatment of hyperkalaemia

Scope: Oral explanation to be held on 15 May 2017 at time 16:00

Action: For adoption

List of Outstanding Issues adopted on 21.04.2017, 23.02.2017. List of Questions adopted on 15.09.2016.

An oral explanation was held on 15 May 2017 at 16:00.

The presentation by the applicant focused on SmPC wording of the indication.

See 3.1

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. Adlumiz - anamorelin - EMEA/H/C/003847

Helsinn Birex Pharmaceuticals Ltd; treatment of anorexia, cachexia or unintended weight loss in adult patients with non-small cell lung cancer (NSCLC)

Scope: Opinion

Action: For adoption

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

Oral explanation was held on 19.04.2017.

List of Outstanding Issues adopted on 23.02.2017, 10.11.2016. List of Questions adopted on 25.02.2016.

The CHMP adopted a negative opinion by consensus, recommending the refusal of the marketing authorisation application. The CHMP adopted the assessment report.

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

The refusal question and answers document was circulated for information.

3.1.2. Blitzima - rituximab - EMEA/H/C/004723

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

Scope: Opinion

Action: For adoption

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

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 similarity assessment report.

3.1.3. Efavirenz/Emtricitabine/Tenofovir disoproxil Zentiva - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/004250

Zentiva k.s.; treatment of HIV-1 infection

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 23.03.2017. List of Questions 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 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.

3.1.4. Human IGG1 monoclonal antibody specific for human interleukin-1 alpha XBiotech - human IgG1 monoclonal antibody specific for human interleukin-1 alpha - EMEA/H/C/004388

XBiotech Germany GmbH; treatment of metastatic colorectal cancer

Scope: Opinion

Action: For adoption

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

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

The CHMP adopted a negative opinion by consensus recommending the refusal of the granting of the marketing authorisation together with the Assessment Report.

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

The refusal question and answers document was circulated for information.

The CHMP adopted the BWP report.

3.1.5. Insulin lispro Sanofi - insulin lispro - EMEA/H/C/004303

sanofi-aventis groupe; treatment of diabetes mellitus

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 21.04.2017. List of Questions adopted on 26.01.2017.

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.

The CHMP adopted the BWP report.

3.1.6. Kyntheum - brodalumab - EMEA/H/C/003959

LEO Pharma A/S; moderate to severe plaque psoriasis

Scope: Opinion

Action: For adoption

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

Oral explanation held on 26.01.2017. List of Outstanding Issues adopted on 21.04.2017, 26.01.2017, 10.11.2016, 15.09.2016. List of Questions adopted on 01.04.2016.

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.

Furthermore, the CHMP considered that brodalumab is a new active substance, as claimed by the applicant.

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 18.05.2017.

The summary of opinion was circulated for information.

3.1.7. Masipro - masitinib - Orphan - EMEA/H/C/004159

AB Science; treatment of mastocytosis

Scope: Opinion

Action: For adoption

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

Oral explanation was held on 20.04.2017.

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 15.09.2016.

The CHMP adopted a negative opinion by consensus recommending the refusal of the granting of the marketing authorisation together with the Assessment Report.

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

The refusal question and answers document was circulated for information.

3.1.8. Oxervate - cenegermin - Orphan - EMEA/H/C/004209

Accelerated assessment

Dompe farmaceutici S.p.A.; treatment of neurotrophic keratitis

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 19.04.2017. List of Questions adopted on 21.02.2017.

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.

Furthermore, the CHMP considered that cenegermin is a new active substance, as claimed by the applicant.

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 17.05.2017.

The summary of opinion was circulated for information.

The CHMP adopted the BWP report.

3.1.9. Reagila - cariprazine - EMEA/H/C/002770

Gedeon Richter Plc.; treatment of schizophrenia

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 21.07.2016.

See 2.1

Oral explanation to be held on 16 May 2017 at time 11:00 was cancelled. The CHMP agreed that oral explanation was not needed.

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.

Furthermore, the CHMP considered that cariprazine is a new active substance, as claimed by the applicant.

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.

3.1.10. Ritemvia - rituximab - EMEA/H/C/004725

Celltrion Healthcare Hungary Kft.; treatment of Non-Hodgkin's lymphoma (NHL), Granulomatosis with polyangiitis and microscopic polyangiitis

Scope: Opinion

Action: For adoption

Similar biological application (Article 10(4) 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.

3.1.11. Spherox spheroids of human autologous matrix-associated chondrocytes - ATMP - EMEA/H/C/002736

CO.DON AG; repair of symptomatic articular cartilage defects of the femoral condyle and the patella of the knee (International Cartilage Repair Society [ICRS] grade III or IV) with defect sizes up to 10 cm^2 in adults.

Scope: Report from CAT discussion/Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 17.02.2017. List of Questions adopted on 19.04.2013.

The CHMP noted the update from CAT discussion.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (23 positive out of 29 votes) together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that spheroids of human autologous matrix-associated chondrocytes is a new active substance, as claimed by the applicant.

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

The divergent position (Tuomo Lapvetelainen, Bruno Sepodes, Daniela Melchiorri, Johann Lodewijk Hillege, Ondrej Slanar, Romaldas Maciulaitis) were appended to the opinion.

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.

3.1.12. Trimbow - beclometasone dipropionate anhydrous / formoterol fumarate dihydrate / glycopyrronium bromide - EMEA/H/C/004257

Chiesi Farmaceutici S.p.A.; Maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who are not adequately treated by a combination of an inhaled corticosteroid and a long-acting beta2-agonist (for effects on symptoms control and prevention of exacerbations see section 5.1)

Scope: Opinion

Action: For adoption

Fixed combination application (Article 10b of Directive No 2001/83/EC)

List of Questions adopted on 23.02.2017.

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.

3.1.13. Tuxella - rituximab - EMEA/H/C/004724

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

Scope: Opinion

Action: For adoption

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

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 similarity assessment report.

3.1.14. Veltassa - patiromer sorbitex calcium - EMEA/H/C/004180

Vifor Fresenius Medical Care Renal Pharma France; treatment of hyperkalaemia

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 21.04.2017, 23.02.2017. List of Questions adopted on 15.09.2016.

See 2.1

An oral explanation was held on 15 May 2017 at 16:00.

The presentation by the applicant focused on SmPC wording of the indication.

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.

Furthermore, the CHMP considered that patiromer sorbitex calcium is a new active substance, as claimed by the applicant.

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.

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

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

Oasmia Pharmaceutical AB; treatment of ovarian cancer

Scope: Day 180 list of outstanding issue

Letter from the applicant dated 9 May 2017 requesting an extension of clock stop to respond to List of Outstanding Issues to be adopted on 18.05.2017.

Action: For adoption

List of Questions adopted on 23.06.2016.

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 for an extension to the clock stop to respond to the list of outstanding issues with a specific timetable.

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

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

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 26.01.2017.

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.

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

treatment of HIV-1 infection

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 15.12.2016.

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.

3.2.4. entecavir - EMEA/H/C/004377

treatment of chronic hepatitis B virus infection

Scope: Opinion

Action: Day 180 list of outstanding issue

List of Questions adopted on 15.12.2016.

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.

3.2.5. iloperidone - EMEA/H/C/004149

treatment of schizophrenia

Scope: Oral explanation, SAG report, List of Outstanding Issues

Action: Oral explanation to be held on 17 May 2017 at time 09:00

List of Outstanding Issues adopted on 23.02.2017. List of Questions adopted on 28.04.2016.

The CHMP noted the SAG report. According to the experts, the CYP2D6 genotyping might not be feasible in all contexts – as the availability of the test might vary and also in consideration of its cost and of the delay that it would impose on starting the treatment with

Iloperidone. The experts agreed that the CYP2D6 should not be considered mandatory prior to initiating treatment, but that it might be useful. The experts also questioned the validity of any conclusion on the cardiac safety of the use of Iloperidone solely made on the basis of the genotype for CYP2D6, as this – concurring to determine the extent of exposure – is only one of many elements of the causal chain of the relationship between administration of Iloperidone and risk of QT prolongation. The experts considered, that there is sequential ECGs as other viable options for the safe clinical use of Iloperidone, in case genotyping is not feasible or available. The experts were in the view that Iloperidone may not be appropriate for the treatment of acute exacerbation of schizophrenia due to the need for slow titration and the delayed onset of effect. The experts expressed the view that Iloperidone might only be of value in chronic, quite stable patients with mild positive symptoms of schizophrenia who need to discontinue their treatment due to debilitating adverse event – in particular EPS symptoms including akathisia. In selecting a patient population other elements of the safety profile of Iloperidone, including metabolic profile and hypotension, would need to be taken into account.

An oral explanation was held on 17 May 2017 at 09:00. The applicant presented data on short and long term efficacy as well as on safety and tolerability.

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

See 2.1

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

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

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 15.09.2016.

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.

3.2.7. trastuzumab - EMEA/H/C/004346

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

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 15.12.2016.

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.

3.2.8. etirinotecan pegol - EMEA/H/C/003874

treatment of breast cancer with brain metastases

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 23.03.2017. List of Questions adopted on 10.11.2016.

See 2.1

Oral explanation was held on 16 May 2017 at time 14:00. During the oral explanation, the Applicant presented the biological rationale for the use of product in the treatment of breast cancer with brain metastases (BCBM) and available data in support of their application.

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

The Committee agreed to consult a SAG.

Post meeting note: The list of questions to the SAG was adopted via written procedure on 24 May 2017.

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

3.3.1. peramivir - EMEA/H/C/004299

treatment of influenza

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.

3.3.2. metreleptin - Orphan - EMEA/H/C/004218

Aegerion Pharmaceuticals Limited; treatment of leptin deficiency (lipodystrophy)

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.

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

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

treatment of haemophilia A

Scope: Letter from the applicant dated 4 May 2017 requesting an extension of clock stop to respond to List of Outstanding Issues adopted on 21.04.2017.

Action: For adoption

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

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to List of Outstanding Issues adopted on 21.04.2017.

3.4.2. betrixaban - EMEA/H/C/004309

treatment of prophylaxis of venous thromboembolism (VTE)

Scope: Letter from the applicant dated 12 May 2017 requesting an extension of clock-stop to respond to the List of Questions adopted on 21 April 2017

Action: For adoption

List of Questions adopted on 21.04.2017

The CHMP agreed to the request by the applicant for an extension of clock-stop to respond to the List of Questions adopted on 21 April 2017

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

ACE Pharmaceuticals BV; treatment of Steroid Sensitive Nephrotic syndrome

Scope: Letter from the applicant dated 21 April 2017 requesting an extension of clock stop to respond to List of Questions adopted on 15.12.2016.

Action: For adoption

List of Questions adopted on 15.12.2016

The CHMP did not agree with an extension of clock stop to respond to List of Questions adopted on 15.12.2016.

3.4.4. eteplirsen - Orphan - EMEA/H/C/004355

AVI Biopharma International Ltd; treatment of Duchenne muscular dystrophy

Scope: Letter from the applicant dated 5 May 2017 requesting an extension of clock stop to respond to List of Questions adopted on 21.04.2017.

Action: For adoption

List of Questions adopted on 21.04.2017.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to List of Questions adopted on 21.04.2017.

3.4.5. cladribine - EMEA/H/C/004230

treatment of highly active relapsing-remitting multiple sclerosis (MS)

Scope: List of experts to the SAG

Action: For adoption

List of Outstanding Issues adopted on 21 April 2017, List of Questions adopted on 10.11.2016.

The CHMP adopted the list of experts to the SAG . Call for additional expertise for the SAG: Cancer Epidemiologist. Nominations should be sent.

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

AB Science; treatment of amyotrophic lateral sclerosis

Scope: Letter from the applicant dated 5 May 2017 requesting an extension of clock-stop to respond to the List of Questions adopted on 26 January 2017

Action: For adoption

List of Questions adopted on 26.01.2017

The CHMP noted the request by the applicant for an extension of clock-stop to respond to the List of Questions adopted on 26 January 2017. After discussion the CHMP adopted an extension of clock-stop.

3.4.7. ocrelizumab - EMEA/H/C/004043

treatment of multiple sclerosis

Scope: List of experts to the SAG

Action: For adoption

List of outstanding issues adopted on 23.03.2017, List of Questions adopted on 15.09.2016.

The CHMP adopted the list of experts to the SAG

3.4.8. tigecycline - EMEA/H/C/004419

Treatment of:
- complicated skin and soft tissue infections, excluding diabetic foot infections
- complicated intra-abdominal infections.

should be used only in situations where it is known or suspected that other alternatives are not suitable

Scope: Letter from the applicant dated 25 April 2017 requesting an extension of clock stop to respond to List of Questions adopted on 13.10.2016, adopted by written procedure on 27.04.2017.

Action: For information

List of Questions adopted on 13.10.2016.

The CHMP noted the clock stop extension adopted by written procedure on 27.04.2017.

3.4.9. padeliporfin - EMEA/H/C/004182

treatment of prostate cancer

Scope: Letter from Applicant dated 10 May 2017 requesting an extension of clock-stop to respond to the 2nd List of Outstanding Issues adopted on 28 April 2017

Action: For adoption

List of Outstanding Issues adopted on 28.04.2017, 15.12.2016. List of Questions adopted on 26.05.2016.

The CHMP agreed to the request by the applicant for an extension of clock-stop to respond to the 2nd List of Outstanding Issues adopted on 28 April 2017.

3.4.10. ngr-htnf – Orphan - EMEA/H/C/004455

MolMed SpA, treatment of advanced malignant pleural mesotheliom

Scope: Letter from Applicant dated 5 May 2017 requesting an extension of clock-stop to respond to the List of Questions adopted on 21.04.2017

Action: For adoption

List of Questions adopted on 21.04.2017.

The CHMP agreed to the request by the applicant for an extension of clock-stop to respond to the List of Questions adopted on 21.04.2017

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

Sunesis Europe Ltd; treatment acute myeloid leukaemia

Scope: Withdrawal of initial marketing authorisation application

Action: For information

Oral explanation was held 19.04.2017.

List of Outstanding Issues adopted on 15.12.2016. List of Questions adopted on 28.04.2016.

The CHMP noted the withdrawal of marketing authorisation application.

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. Isentress - raltegravir - EMEA/H/C/000860/X/0059

Merck Sharp & Dohme Limited

Rapporteur: Greg Markey, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Julie Williams

Scope: "Extension application to add a new strength of 600mg film coated tablets."

Action: For adoption

List of Questions adopted on 13.10.2016.

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.

4.1.2. Kuvan - sapropterin - Orphan - EMEA/H/C/000943/X/0047

BioMarin International Limited

Rapporteur: Patrick Salmon, PRAC Rapporteur: Almath Spooner

Scope: "Extension application to introduce a new pharmaceutical form associated with new strength (100 mg and 500 mg powder for oral solution)."

Action: For adoption

List of Outstanding Issues adopted on 21.04.2017. List of Questions adopted on 23.02.2017.

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.

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

Amgen Europe B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: “Extension application ”

Action: For adoption

List of Questions adopted on 26.01.2017.

The Committee discussed the issues identified in this application in relation to the proposed changes in the quality part of the dossier.

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

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

Amgen Europe B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: “Extension application ”

Action: For adoption

List of Questions adopted on 26.01.2017.

The Committee discussed the issues identified in this application in relation to the proposed changes in the quality part of the dossier.

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

No items

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

No items

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

No items

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

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

5.1.1. 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

Request for Supplementary Information adopted on 15.12.2016.

The Committee discussed the issues identified in this application, mainly relating to the appropriate dosing regimen.

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

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

Roche Registration Limited

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Patrick Batty

Scope: "Extension of Indication to include a new indication for Gazyvaro in combination with chemotherapy, followed by Gazyvaro maintenance therapy in patients achieving a response, for the treatment of patients with previously untreated advanced follicular lymphoma.

As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The

Package Leaflet and the RMP are updated in accordance. In addition, the due date for provision of the final clinical study report of study BO21223/GALLIUM listed in the Gazyvaro RMP as Category 3 has been updated.

Furthermore, the PI is brought in line with the missing information of QRD template version 9.1 regarding annex II C. In addition, clarification or editorial changes to the SmPC are proposed for accuracy and clarity.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 26.01.2017.

The Committee discussed the issues identified in this application. The members noted a delay in adverse event reporting. The Committee agreed to request further information on this issue and ask the MAH to provide the updated safety data and sensitivity analysis.

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

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

Novartis Europharm 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 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

Request for Supplementary Information adopted on 23.03.2017, 15.12.2016.

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.

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

AbbVie Ltd.

Rapporteur: Joseph Emmerich, PRAC Rapporteur: Caroline Laborde

Scope: "Extension of Indication to include children aged 14 days and older in the treatment

of HIV-1.

As a consequence, sections 4.1, 4.2, 4.3, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. The studies provided in support of the paediatric indication are part of the agreed PIP decision P/0144/2012.

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

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

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

Action: For adoption

Request for Supplementary Information adopted on 26.01.2017.

The Committee discussed the issues identified in this application, mainly in relation to the marketed pack sizes for the paediatric population, the level of excipients and the dosing regimen.

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

5.1.5. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0023/G

Merck Sharp & Dohme Limited

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

Scope: "Extension of Indication to add treatment of urothelial carcinoma in patients previously treated with chemotherapy based on the results from study KEYNOTE-045; a phase 3, randomized, active-controlled, multi-site, open-label trial evaluating pembrolizumab administered at 200 mg Q3W versus investigators' choice of paclitaxel, docetaxel, or vinflunine in patients previously treated with chemotherapy.

Extension of Indication to add treatment of urothelial carcinoma in patients ineligible for cisplatin (not previously treated) based on the results from study KEYNOTE-52; a phase 2, single-arm, multisite, open-label trial of pembrolizumab at 200 mg Q3W in the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy.

As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC have been updated and the Package Leaflet has been updated accordingly.

Further, the MAH is proposing a change to section 4.3 of the SmPC to add that only patients with severe hypersensitivity should be excluded from therapy, and a change to section 4.4 of the SmPC adding possible hypersensitivity and anaphylaxis as part of infusion reactions.

The application included an updated RMP version 7.0."

Action: For adoption

The Committee discussed the issues identified in this application. For the extension of

indication based on study KEYNOTE-045, clarification was considered required on the wording of the indication in relation to the previous chemotherapy treatment. Furthermore the members discussed the results from study KEYNOTE-52. The Committee considered additional efficacy data essential to better characterise the appropriate patient population.

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

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

Santhera Pharmaceuticals (Deutschland) GmbH

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

Scope: "Extension of indication to include treatment of patients with Duchenne muscular dystrophy in whom respiratory function has started to decline and who are currently not taking concomitant glucocorticoids. Can be used in patients previously treated with glucocorticoids or in patients in whom glucocorticoid treatment is not desired, not tolerated or is contraindicated."

Action: For adoption

Request for Supplementary Information adopted on 23.02.2017, 15.09.2016.

The Committee discussed the issues identified in this application, mainly relating to the clinical relevance of the study results and the appropriate patient population. The members were reminded about the legal framework of the marketing authorisation being under exceptional circumstances.

The Committee adopted a 3rd request for supplementary information with a specific timetable.

5.1.7. Renvela - sevelamer carbonate - EMEA/H/C/WS0965

Genzyme Europe BV

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

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

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

The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 26.01.2017, 15.09.2016.

The Committee discussed the issues identified in this application, which related to the formulation.

The CHMP agreed that the formulation could be updated through a variation after adoption of an opinion on the extension of indication.

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.

5.1.8. Sovaldi - sofosbuvir - EMEA/H/C/002798/II/0036

Gilead Sciences International Ltd

Rapporteur: Filip Josephson, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Julie Williams

Scope: "Extension of indication to add treatment of chronic hepatitis C in adolescents aged 12 to <18 years.

As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add information on posology, warnings, safety, efficacy and pharmacokinetics.

The Package Leaflet and Risk Management Plan (RMP version 5.0) are updated in accordance.

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

Furthermore, the Product Information is brought in line with the latest QRD template version 10."

Action: For adoption

Request for Supplementary Information adopted on 23.02.2017.

The Committee discussed the issues identified in this application. The main discussions focused on the pharmacokinetic data in relation to the proposed dosing.

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

5.1.9. Stivarga - regorafenib - EMEA/H/C/002573/II/0020

Bayer Pharma AG

Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus

Scope: "Extension of indication of Stivarga to include treatment of adult patients with hepatocellular carcinoma (HCC) who have been previously treated with one systemic therapy.

As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the EU SmPC are updated. The package leaflet and RMP (version 5.0) have been updated accordingly.

Furthermore, the PI is brought in line with the latest QRD template version 10.0."

Action: For adoption

Request for Supplementary Information adopted on 23.02.2017.

The Committee discussed the issues identified in this application. The discussion of the members related to the wording of the indication to better reflect the patient population from the pivotal study and in relation to other approved products.

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

5.1.10. Stribild - elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil - EMEA/H/C/002574/II/0079

Gilead Sciences International Ltd

Rapporteur: Robert James Hemmings, Co-Rapporteur: Joseph Emmerich, PRAC Rapporteur: Julie Williams

Scope: "Extension of Indication to include the treatment of HIV-1 infected adolescents, with NRTI resistance or toxicities precluding the use of first line agents, aged 12 to < 18 years and weighing ≥ 35 kg; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated based on pharmacokinetics, safety and efficacy data through 48 weeks of treatment with Stribild in Study GS-US-236-0112.

The Package Leaflet and Risk Management Plan (v.12) are updated in accordance.

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

In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor linguistic amendments"

Action: For adoption

The Committee discussed the issues identified in this application.

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

5.1.11. Truvada - emtricitabine / tenofovir disoproxil - EMEA/H/C/000594/II/0135

Gilead Sciences International Ltd

Rapporteur: Greg Markey, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Julie Williams

Scope: "Extension of Indication to include pre-exposure prophylaxis of HIV in adolescents aged 12 to < 18 years at high risk; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated based on extrapolation of data for emtricitabine, tenofovir disoproxil fumarate, and Truvada in HIV-infected and uninfected subjects.

The Package Leaflet and Risk Management Plan (v.15) are updated in accordance.

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

In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor linguistic amendments"

Action: For adoption

The Committee discussed the issues identified in this application. The members discussed the clinical data in particular from the viewpoint of adherence in the different age groups and from the safety perspective. The need for a high level of adherence was highlighted in order to achieve a benefit. In this context a possible age cut-off was discussed.

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

5.1.12. Victoza - liraglutide - EMEA/H/C/001026/II/0042

Novo Nordisk A/S

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of Indication to include a new indication/population in Section 4.1 of the SmPC for Victoza.

As a consequence, sections 4.2, 4.4, 4.7, 4.8, 5.1 and 6.5 of the SmPC are updated to add warnings and update the safety information based on the findings of the LEADER (EX2211-3748) clinical study results, which constitutes the data set for the application. The Package Leaflet and Labelling (sections 17 and 18) are updated in accordance.

Updates to the liraglutide RMP based on the LEADER study results are also proposed: RMP Version 27 was submitted with the application, showing the proposed RMP changes."

Action: For adoption

Request for Supplementary Information adopted on 23.02.2017.

The Committee discussed the issues identified in this application, related to the wording of the indication and particularly of the appropriate target population.

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

5.1.13. Vimpat - lacosamide - EMEA/H/C/000863/II/0065/G

UCB Pharma S.A.

Rapporteur: Filip Josephson, Co-Rapporteur: Luca Pani, PRAC Rapporteur: Qun-Ying Yue

Scope: "This is a group of variations including extension of Indication to include monotherapy and adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in children from 4 to less than 16 years old with epilepsy. For the treatment initiation pack it is proposed to extend only adjunctive treatment to adolescents weighting more than 50 kg (not suitable for monotherapy and children and adolescents weighting less than 50 kg). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to bring Annex

IIIA in line with the latest QRD template version 10 and to introduce combined SmPC for film coated tablets. Moreover, updated RMP version 12 has been submitted.

Furthermore, only for syrup presentation, in addition sections 6.3 and 6.5 of the SmPC are updated due to extension of shelf life of finished product after first opening from 4 weeks to 6 months and addition of a 10 mL dosing syringe for syrup, as additional dosing device for paediatric population."

Action: For adoption

Request for Supplementary Information adopted on 10.11.2016.

The Committee discussed the issues identified in this application. The members discussed the dosing recommendations in children and considered amendments to the proposed dosing regimen for monotherapy as well as for adjunctive therapy.

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

5.1.14. Zydelig - idelalisib - EMEA/H/C/003843/II/0032/G

Gilead Sciences International Ltd

Rapporteur: Filip Josephson, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Patrick Batty

Scope: "C.I.6. Extension of Indication: Extension of the approved chronic lymphocytic leukemia (CLL) indication for Zydelig to include its use in combination with bendamustine and rituximab based on the results of the primary analysis of pivotal Study GS-US-312-0115 "a Phase 3, randomized, double-blind, controlled study evaluating the efficacy and safety of idelalisib (GS-1101) in combination with bendamustine and rituximab for previously treated chronic lymphocytic leukemia" as a consequence, sections 4.1, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.

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

The RMP version 2.2 has also been submitted.

C.I.13: Submission of the final report from study 101-08, a phase 2, single-arm study evaluated idelalisib monotherapy and in combination with rituximab in elderly subjects with previously untreated CLL or small lymphocytic lymphoma. Inclusion of this report provides additional safety data to support the evaluation of the use of idelalisib in patients with CLL. Submission of this report is also made in fulfilment of PAM008.

C.I.13: Submission of the final report from study GS-US-312-0123, a phase 3 randomized study evaluated idelalisib in combination with bendamustine and rituximab in subjects with previously untreated CLL. Inclusion of this report is supportive of a complete safety evaluation concerning the use of this combination in patients with CLL."

Action: For adoption

The Committee discussed the issues identified in this application, concerning the efficacy and safety data in the triple combination. It was agreed to request updated overall survival data considering the low event rate.

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

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

Novartis Europharm Ltd

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Provision of an update for study A2303, listed in SOB004. Sections 4.8 and 5.1 of the SmPC are proposed to be updated to reflect the safety and efficacy findings of the study. The Package Leaflet and Labelling are updated accordingly.

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

Action: For adoption

Request for Supplementary Information adopted on 26.01.2017.

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.

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

Novartis Europharm Ltd

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "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 and 5.2 of the SmPC are updated to reflect the information based primarily on the supporting study, CLDK378A2301 (ASCEND-4). The Package Leaflet is updated in accordance.

The variation leads to amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan."

Action: For adoption

Request for Supplementary Information adopted on 23.03.2017.

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.

5.1.17. Onglyza – saxagliptin - EMEA/H/C/001039/WS1078, Komboglyze- saxagliptin / metformin hydrochloride - EMEA/H/C/002059/WS1078

AstraZeneca AB

Lead Rapporteur: Johann Lodewijk Hillege

Scope: "Extension of Indication to include the use of a triple combination therapy (saxagliptin, metformin and dapagliflozin) as adjunct to diet and exercise to improve glycaemic control in adult patients aged 18 years and older with type 2 diabetes mellitus, when metformin together with dapagliflozin, do not provide adequate glycaemic control. Editorial changes are made throughout the Summary Products Characteristics and Package Leaflets. Furthermore, the Product Information is brought in line with the latest QRD template version 10 for Onglyza."

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.

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

No items

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

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

6.1.1. recombinant human albumin solution - EMEA/H/D/004693

Facilitate gamete and embryo manipulation in vitro

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.

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. ivacaftor,tezacaftor - Orphan - H0004682

Vertex Pharmaceuticals (Europe) Ltd., The treatment of patients with CF aged 12 years and older who have at least one F508del mutation in the CFTR gene, and a second mutation that is responsive to tezacaftor/ivacaftor

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

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.

The CHMP discussed the combination pack request.

8.1.2. Emicizumab - H0004406

indicated for routine prophylaxis to prevent bleeding or reduce the frequency of bleeding episodes in patients with haemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors, can be used in all age groups.

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

The CHMP noted the list of applications received.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 12 recommendations for eligibility to PRIME: 5 were granted and 7 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. CHMP request for PRAC advice on Fluoropyrimidines (Capecitabine-Xeloda and 5-FU), EMEA/H/C/0316/LEG-033

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

Scope: Response from PGWP to questions from PRAC

Action: For adoption

The CHMP adopted the response from PGWP to questions from PRAC

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

treatment of moderate to severe active rheumatoid arthritis (RA)

Scope: Update on procedure

Action: For information

The CHMP was updated on the procedure, related to the risk of drug-induced thrombotic events. Risk minimisation measures were recommended, including a recommendation to include deep vein thrombosis (DVT)/pulmonary embolism (PE) as an important potential risk in the RMP and as a warning in the SmPC. The applicant was asked to submit a variation including the proposed measurements.

9.1.2. Opdivo - nivolumab - EMEA/H/C/003985/II/0032

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Variations that affect the PI

Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to add administration guidance and update the safety information based on final results from study…(include study CA209067 listed as a imposed PAES in the Annex II; this is an interventional randomized, double-blind study in subjects treated with nivolumab monotherapy, ipilimumab monotherapy and nivolumab combined with ipilimumab;

The Package Leaflet is updated accordingly.

The RMP version 5.8 has also been submitted.

This submission fulfils ANX 016 and Annex II is updated accordingly

In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial and formatting revisions in the PI."

Action: For discussion

The Committee discussed the issues identified in this application.

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

10. Referral procedures

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

No items

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: Opinion

Prescription status of desloratadine-containing products

Action: For adoption

The CHMP endorsed the PRAC advice.

PRAC generally agreed with the Safety Working Party's conclusion that the safety profile of desloratadine is expected to be similar to the safety profile of loratadine at standard clinical doses. In conclusion, based on currently available information, PRAC considered that it is not possible to perform a direct comparison between the safety profiles of desloratadine and loratadine. It was noted that the SmPCs differ between the two active substances, but the inherent limitations of clinical trials and spontaneous reporting data preclude firm conclusions in this regard. The PRAC will continue to regularly monitor the safety profile of both desloratadine and loratadine. The ongoing PASS is expected to clarify existing uncertainties in the safety profile of desloratadine. Based on the information currently available, it is not possible to draw a conclusion on whether differences in prescription status impact the risk associated with each product.

The CHMP discussed further whether desloratadine-containing products could be switched to non-prescription status.

The CHMP adopted a revised timetable:

CHMP discussion: May 2017 CHMP

CHMP discussion/opinion: June 2017 CHMP

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

10.4.1. Paracomb 500mg/150mg film coated tablets - Paracetamol/Ibuprofen 500 mg/150 mg Paracetamol and Ibuprofen - EMEA/H/1447

Vale Pharmaceutical Ltd

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Romaldas Maciulaitis

RMS: UK, CMS: AT, BE, DE, FR, HR, IE, LU, NL, PT, ES

Decentralised Procedure numbers: UK/H/6034-5/001/DC, UK/H/6176/001/DC

Scope: Opinion

Disagreement regarding justification for a fixed dose combination, the demonstration of an additional benefit and of an acceptable safety profile

Action: For adoption

The Committee adopted an opinion by majority (22 out of 26 votes) recommending that the marketing authorisation(s) should be granted together with the CHMP assessment report and translation timetable.

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

The divergent position (Alexandre Moreau, Johann Lodewijk Hillege, Concepcion Prieto Yerro, Sol Ruiz) was appended to the opinion.

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

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

Septodont group of companies and associated companies

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

Scope: Letter of intent from the MAH to initiate a referral under Article 30 of Directive 2001/83/EC, appointment of Rapporteurs

Action: For discussion

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

The CHMP noted the letter of intent from the MAH to initiate a referral under Article 30 and appointed Romaldas Maciulaitis as Rapporteur (interest level 2) and Fatima Ventura as Co-Rapporteur (interest level 2) for this procedure.

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

10.6.1. Vancomycin containing products – vancomycin - EMEA/H/A-31/1440

Rapporteur: Concepcion Prieto-Yerro, Co-rapporteur: Alar Irs,

Scope: Opinion

Action: For adoption

Review of the benefit-risk balance of vancomycin containing products following notification by the Spanish Agency of Medicines and Medical Devices of a referral under Article 31 of Directive 2001/83/EC.

The CHMP adopted an opinion by consensus recommending that the marketing authorisations for Vancomycin-containing medicinal products should be varied.

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

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)

10.11.1. Cardioxane - Dexrazoxane - EMEA/H/A-13/1453

Clinigen Group

Rapporteur: Alexandre Moreau, Co-Rapporteur: Greg Markey

RMS: FR, CMS: CZ, DE, ES, IT, NL, PL & UK

Decentralised Procedure numbers: FR/H/283/01/II/27G

Scope: Opinion

Article 13 triggered by the ANSM in France in January 2017 requesting the CHMP's opinion whether the proposed lifting of the contraindication for a subset of anthracycline treated children is justified.

Action: For adoption

The CHMP adopted an opinion by consensus recommending that the marketing authorisations for the above mentioned medicinal product should be varied.

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

11. Pharmacovigilance issue

11.1. Early Notification System

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

Action: For information

The CHMP noted the ENS.

11.2. Patient Registry Initiative: Update and Workshops on Cystic Fibrosis (CF) and Multiple Sclerosis (MS)

The Patient Registry Initiative published recently the workshop report held last October 2016 including some recommendations. Following these recommendations, one of the proposed activities is to organise two workshops, one on CF and another one on MS with the following objectives:

- To agree on implementable recommendations on core data elements to be collected, protocols, consents, governance supporting registry interoperability.
- Workplan for the further development and finalisation of recommendations to be used by registry holders and MAHs/MAAs.

The workshops are taking place on 14th June (CF) and 7th July (MS). PRAC (co-) Rapporteurs have been invited as being key to the success of the workshop.

Action: For discussion

The CHMP was updated on the patient registration initiative and the planned workshops. Rapporteurs were invited to send proposals of issues to be addressed at the planned workshops in the concerned therapeutic areas. It was agreed to have drafting group working on the initiative.

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

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. EU approval of biological generics

Action: For discussion

The CHMP discussed the approval of biological generics. First biological was approved under the generic legal basis Art 10(1) in February 2017: Lifmior (etanercept, Pfizer, reference medicine Enbrel (Pfizer)). The discussion was held, what should be the definition of 'Auto-biological' – should it be same active substance from same company and same manufacturing process. Further discussion on regulatory or legal and communication issues should be held. The CHMP agreed to have drafting groups.

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 2-5 May 2017

Action: For information

The CHMP noted the information.

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

Action: For adoption

The CHMP noted the information.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 10-12 May 2017
Action: For information

The CHMP noted the minutes.

14.2.3. Paediatric Committee (PDCO)

PIPs reaching D30 at May 2017 PDCO

Action: For information

Report from the PDCO meeting held on 17-19 May 2017

Action: For information

The CHMP noted the report.

14.2.4. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 10-12 May 2017

Action: For information

The CHMP noted the report.

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

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 15-17 May 2017

Action: For information

The CHMP noted the report.

List of questions to QWP on similarity of bortezomib versus ixazomib and assessment of starting materials of meropenem Coordination with EMA Working Parties/Working Groups/Drafting Groups

Action: For adoption

The CHMP agreed to the consultation of the QWP

14.2.6. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 2-5 May 2017. Table of conclusions

Action: For information

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

The CHMP noted the report.

14.2.7. Quality Working Party (QWP)

Chair: Jean-Luis Robert

Reflection paper on the pharmaceutical development of medicines for use in the older population

Action: For adoption for 6-month consultation

The CHMP adopted the reflection paper for 6-months public consultation.

Election of QWP Chair, the term of the current Chair ending in June 2017.

Nominations should be sent by 12 June 2017

Action: For information

The CHMP noted the information.

14.2.8. CHMP Guidelines Consistency Group (GCG)

Chair: Barbara van Zwieten-Boot

Election of GCG Chair, the term of the current Chair ending in May 2017.

Action: For adoption

The CHMP elected Barbara van Zwieten-Boot as chair of the Guideline Consistency Group.

14.3. Cooperation within the EU regulatory network

14.3.1. Revision of the Commission Regulation (EC) No 847/2000 of April 2000 laying down the provisions for implementation of the Criteria for designation of a medicinal product as an orphan medicinal product and definitions of the Concept 'similar medicinal product and 'clinical superiority'

Scope: Review of comments received from the public consultation. Endorsement of revised proposal

Action: For adoption

The CHMP adopted the revised proposal.

14.3.2. Generic applications referring to medicinal products authorised under exceptional circumstances

Scope: letter from the European Commission

Action: For discussion

The CHMP noted the letter.

14.4. Cooperation with International Regulators

14.4.1. EMA/FDA strategic document on Gaucher disease

Action: For adoption

Postponed to June.

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

No items

14.6. CHMP work plan

No items

14.7. Planning and reporting

No items

14.8. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Preparedness of the system and capacity increase

Action: For discussion

The CHMP noted the update and next steps.

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 15 – 18 May 2017 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	
Christophe Focke	Alternate	Belgium	No restrictions applicable to this meeting	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Katarina Vučić	Member	Croatia	No interests declared	
Selma Arapovic Dzakula	Alternate	Croatia	No interests declared	
Emilia Mavrokordatou	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	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Tuomo Lapveteläinen	Alternate	Finland	No interests declared	
Alexandre Moreau	Member	France	No interests declared	
Joseph Emmerich	Alternate	France	No interests declared	
Harald Enzmann	Member (Vice-Chair)	Germany	No interests declared	
Martina Weise	Alternate	Germany	No restrictions applicable to this meeting	
Eleftheria Nikolaidi	Member	Greece	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Agnes Gyurasics	Member	Hungary	No interests declared	
Kolbeinn Gudmundsson	Member	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	
Luca Pani	Alternate – by phone	Italy	No interests declared	
Juris Pokrotnieks	Member	Latvia	No restrictions applicable to this meeting	
Romaldas Mačiulaitis	Member	Lithuania	No participation in final deliberations and voting on:	3.4.7. Ocrelizumab - EMEA/H/C/004043 5.1.2. Gazyvaro - obinutuzumab - Orphan - EMEA/H/C/002799/II/0016 8.1.2. Emicizumab - Orphan - H0004406
Jacqueline Genoux-Hames	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	
Svein Rune Andersen	Member	Norway	No interests declared	
Bjorg Bolstad	Alternate	Norway	No restrictions applicable to this meeting	
Piotr Fiedor	Member	Poland	No interests declared	
Aldona Paluchowska	Alternate	Poland	No interests declared	
Bruno Sepodes	Member	Portugal	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meeting	
Nela Vilceanu	Member	Romania	No interests declared	
Eva Malikova	Alternate	Slovakia	No interests declared	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member	Spain	No interests declared	
Jorge Camarero Jiménez	Member	Spain	No participation in final deliberations and voting on:	3.4.7. Ocrelizumab - EMEA/H/C/004043 5.1.2. Gazyvaro - obinutuzumab - Orphan - EMEA/H/C/002799/II/0016 8.1.2. Emicizumab - Orphan - H0004406
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	
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	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Sabine Mayrhofer	Expert - via telephone*	Germany	No interests declared	
Patricia Diaz Ramos	Expert - in person*	Spain	No interests declared	
Anne Hasle Buur	Expert - in person*	Denmark	No interests declared	
Nicolas Nyssen	Expert - in person*	Belgium	No interests declared	
Sigrid Klaar	Expert - in person*	Sweden	No restrictions applicable to this meeting	
Michiel van den Heuvel	Expert - in person*	Netherlands	No restrictions applicable to this meeting	
Barbara Spruce	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Shirley Hopper	Expert - in person*	United Kingdom	No interests declared	
Pauliina Ikäheimo	Expert - in person*	Finland	No restrictions applicable to this meeting	
Arzu Günes Granberg	Expert - via telephone*	Sweden	No interests declared	
Eskild Colding-Jorgensen	Expert - via telephone*	Denmark	No restrictions applicable to this meeting	
Marcel Maliepaard	Expert - via telephone*	Netherlands	No interests declared	
Lennart Åkerblom	Expert - via telephone*	Sweden	No interests declared	
Paula Salmikangas	Expert - via telephone*	Finland	No interests declared	
Martina Schussler-Lenz	Expert - via telephone*	Germany	No interests declared	
Doris Johanna Hovgaard	Expert - via telephone*	Denmark	No interests declared	
Antonio Lopez Navas	Expert in	Spain	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
	person			
Mair Powell	Expert - via telephone*	United Kingdom	No interests declared	
Aghadiuno Olaperi	Expert - via telephone*	United Kingdom	No interests declared	
Jean-Michel Dogné	Expert - via telephone*	Belgium	No restrictions applicable to this meeting	
Didier Meulendijks	Expert - via telephone*	Netherlands	No restrictions applicable to this meeting	
João Manuel Lopes de Oliveira	Expert - via telephone*	Portugal	No interests declared	
Joao Freire	Expert - via telephone*	Portugal	No restrictions applicable to this meeting	
Adrien Inoubli	Expert - via telephone*	France	No interests declared	
Nele Steens	Expert - via Adobe*	Belgium	No interests declared	
Barbara Spruce	Expert - via Adobe*	United Kingdom	No restrictions applicable to this meeting	
Olga Kholmanskikh	Expert - via Adobe*	Belgium	No interests declared	
Marleen Laloup	Expert - via Adobe	Belgium	No restrictions applicable to this meeting	
Juha Vakkilainen	Expert - via Adobe*	Finland	No interests declared	
Arzu Günes Granberg	Expert - via Adobe*	Sweden	No interests declared	
Anna Nordmark	Expert - via Adobe*	Sweden	No interests declared	
Representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

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)*

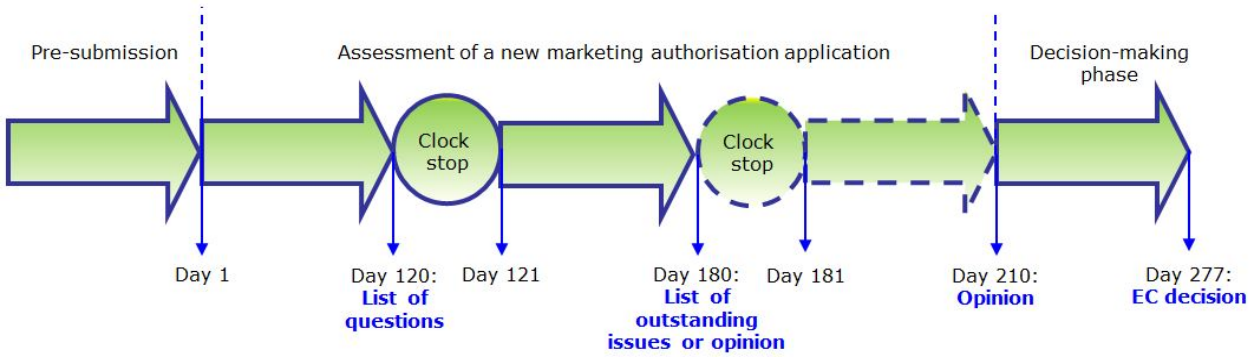
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

21 July 2017
EMA/CHMP/262209/2017

Annex to May 2017 CHMP Minutes

Pre submission and post authorisations issues

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

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A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for May 2017: **For adoption**	Adopted.

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

Final Outcome of Rapporteurship allocation for May 2017: **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

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Cuprymina - copper (64Cu) chloride - EMEA/H/C/002136/R/0014 MAH: Sparkle S.r.l., Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Patrick Batty Request for Supplementary Information adopted on 23.03.2017.	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

Betmiga - mirabegron - EMEA/H/C/002388/R/0026 MAH: Astellas Pharma Europe B.V., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Dolores Montero Corominas	Request for Supplementary Information adopted

Request for Supplementary Information adopted on 18.05.2017.	
Constella - linaclotide - EMEA/H/C/002490/R/0032 MAH: Allergan Pharmaceuticals International Limited, Rapporteur: Martina Weise, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Valerie Strassmann Request for Supplementary Information adopted on 18.05.2017.	Request for Supplementary Information adopted
Enurev Breezhaler - glycopyrronium bromide - EMEA/H/C/002691/R/0020 MAH: Novartis Europharm Ltd, Duplicate, Duplicate of Seebri Breezhaler, Rapporteur: Hanne Lomholt Larsen, Co-Rapporteur: David Lyons, PRAC Rapporteur: Torbjorn Callreus Request for Supplementary Information adopted on 23.03.2017.	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Eylea - aflibercept - EMEA/H/C/002392/R/0033 MAH: Bayer AG, Rapporteur: Alexandre Moreau, Co-Rapporteur: Nithyanandan Nagercoil, 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 the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Ibandronic acid Accord - ibandronic acid - EMEA/H/C/002638/R/0013 MAH: Accord Healthcare Ltd, Generic, Generic of Bondronat, Rapporteur: Alar Irs, PRAC Rapporteur: Doris Stenver Request for Supplementary Information adopted on 18.05.2017.	Request for Supplementary Information adopted
Memantine Merz - memantine hydrochloride - EMEA/H/C/002711/R/0012 MAH: Merz Pharmaceuticals GmbH, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Dolores Montero Corominas	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Picato - ingenol mebutate - EMEA/H/C/002275/R/0023	Positive Opinion adopted by consensus together with the CHMP assessment report and translation

MAH: LEO Laboratories Ltd, Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Julie Williams	timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Seebri Breezhaler - glycopyrronium - EMEA/H/C/002430/R/0020 MAH: Novartis Europharm Ltd, Rapporteur: Hanne Lomholt Larsen, Co-Rapporteur: David Lyons, PRAC Rapporteur: Torbjorn Callreus Request for Supplementary Information adopted on 23.03.2017.	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 the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
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 Request for Supplementary Information adopted on 23.03.2017.	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 the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Tovanor Breezhaler - glycopyrronium - EMEA/H/C/002690/R/0022 MAH: Novartis Europharm Ltd, Duplicate, Duplicate of Seebri Breezhaler, Rapporteur: Hanne Lomholt Larsen, Co-Rapporteur: David Lyons, PRAC Rapporteur: Torbjorn Callreus Request for Supplementary Information adopted on 23.03.2017.	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.

B.2.3. Renewals of Conditional Marketing Authorisations

Zalmoxis - allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - EMEA/H/C/002801/R/0003, Orphan, ATMP MAH: MolMed SpA, Rapporteur: Johannes Hendrikus Ovelgonne, PRAC Rapporteur: Brigitte	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional.

Keller-Stanislawski Request for Supplementary Information adopted on 12.04.2017.	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 2-5 May 2017 PRAC:	
Insulin glargine - Toujeo **EMEA/H/C/000309;** MAH: Sanofi-aventis Deutschland GmbH; Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, - Toujeo 300 units/ml solution for injection in a pre-filled pen (sanofi-aventis Deutschland GmbH) **Insulin human - Insuman** **EMEA/H/C/000201;** MAH: Sanofi-aventis Deutschland GmbH; Rapporteur: Bart Van der Schueren, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jean-Michel Dogné, - Insuman Implantable 400 IU/ml solution for infusion (sanofi-aventis Deutschland GmbH) **Insulin degludec - Tresiba** **EMEA/H/C/002498;** MAH: Novo Nordisk A/S; Rapporteur: Kristina Dunder, Co-Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Qun-Ying Yue - Tresiba 200 units/mL solution for injection in pre-filled pen (Novo Nordisk A/S) **Insulin degludec/Insulin aspart - Ryzodeg** **EMEA/H/C/002499;** MAH: Novo Nordisk A/S; Rapporteur: Kristina Dunder, Co-Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Qun-Ying Yue - Ryzodeg 100 units/mL solution for injection in pre-filled pen, Ryzodeg 100 units/mL solution for injection in cartridge (Novo Nordisk A/S) **Insulin degludec/Liraglutide- Xultophy** **EMEA/H/C/002647;** MAH: Novo Nordisk A/S; Rapporteur: Kristina Dunder, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Qun-Ying Yue - Xultophy 100 units/ml insulin degludec + 3.6 mg/mL liraglutide solution for injection in a pre-filled pen (Novo Nordisk A/S)	Adopted.

Signal of potential increased risk of medication error associated with pre-filled pens and cartridges presentations, leading to inadequate diabetes control: **For adoption**	
Adcetris - Brentuximab vedotin - EMEA/H/C/002455; MAH: Takeda Pharma A/S; Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus, Signal of Cytomegalovirus (CMV) reactivation: **For adoption**	Adopted.
PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its May 2017 meeting:	
EMEA/H/C/PSUSA/00000086/201609 (alglucosidase alfa) CAPS: **Myozyme** (EMEA/H/C/000636) (alglucosidase alfa), MAH: Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Caroline Laborde, "29-Sep-2013 TO 28-Sep-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 to add the adverse reactions infusion site swelling, infusion site induration and infusion site extravasation with a frequency not known. 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/00001205/201609 (eltrombopag) CAPS: **Revolade** (EMEA/H/C/001110) (eltrombopag / eltrombopag olamine), MAH: Novartis Europharm Ltd, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "01.10.2015-30.09.2016"	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, concerning the following changes: Update of the Annex II of the Product Information to remove the additional risk minimisation measures in relation to hepatotoxicity and thromboembolic events and accordingly the Annex related to Article 127a is recommended to be lifted. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

EMEA/H/C/PSUSA/00001988/201609 (mercaptopurine)
CAPS:
Xaluprine (EMEA/H/C/002022) (mercaptopurine), MAH: Nova Laboratories Limited, Rapporteur: Filip Josephson
NAPS:
Mercaptopurin-Medice 10 mg Tabletten 64742.00.00 DE - MEDICE ARZNEIMITTEL PÜTTER GMBH & CO. KG
Mercaptopurina Aspen 50 mg comprimidos 34565 ES - ASPEN PHARMA TRADING LIMITED
Mercaptopurine 50 mg tablets PL 39699/ 0047 UK - ASPEN PHARMA TRADING LIMITED
Puri-Nethol 50 mg 44/0228/99-S SK - ASPEN PHARMA TRADING LIMITED
Puri-Nethol 50 mg comprimate 5099/2005/01 RO - ASPEN PHARMA TRADING LIMITED
PURI-NETHOL 50 mg comprimés 2005038703 LU - ASPEN PHARMA TRADING LIMITED
PURI-NETHOL 50 mg comprimés BE058563 BE - ASPEN PHARMA TRADING LIMITED
PURI-NETHOL 50 mg tablete 5363-I-1339/12 SI - ASPEN PHARMA TRADING LIMITED
Puri-nethol 50 mg tabletes. 97-0466 LV - ASPEN PHARMA TRADING LIMITED
Puri-Nethol 50 mg tabletės LT/1/94/1051/001 LT - ASPEN PHARMA TRADING LIMITED
Puri-Nethol 50 mg Tablets PA 1691/009/001 IE - ASPEN PHARMA TRADING LIMITED
Puri-Nethol 50 mg Tablets PA 1691/9/1 MT - ASPEN PHARMA TRADING LIMITED
PURI-NETHOL 50 mg tabletten 2005038703 LU - ASPEN PHARMA TRADING LIMITED
Puri-Nethol 50 mg Tabletten 6102083.00.00 DE - ASPEN PHARMA TRADING LIMITED
PURI-NETHOL 50 mg tabletten BE058563 BE - ASPEN PHARMA TRADING LIMITED
Puri-Nethol 50 mg tabletten RVG 00859 NL - ASPEN PHARMA TRADING LIMITED
Puri-Nethol 50 mg tabletter 3973 NO - ASPEN PHARMA TRADING LIMITED
Puri-nethol 50 mg tabletter 5518 SE - ASPEN PHARMA TRADING LIMITED
Puri-nethol 50 mg töflur 660891 IS - ASPEN

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 authorisations for the medicinal products containing the above referred active substance(, concerning the following changes:

Update of sections 4.2 and 4.4 of the SmPC to include a new warning on the increased risk of severe toxicity in patients with inherited mutated NUDT15 gene treated with 6-mercaptopurine. Update of section 4.4 of the SmPC to include a new warning on the increased risk of infections (viral, fungal bacterial infections and viral reactivation). Update of section 4.8 to add 'bacterial and viral infections' and 'infections associated with neutropenia' as a new adverse drug reactions with an 'uncommon' frequency. The Package leaflet is updated accordingly.

The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

PHARMA TRADING LIMITED **PURI-NETHOL, 50 mg tabletid 101195 EE** - ASPEN PHARMA TRADING LIMITED **Puri-Nethol-50mg-Tabletten 8.931 AT** - ASPEN PHARMA TRADING LIMITED **Puri-Netol 50 mg tabletki 20020820 BG** - ASPEN PHARMA TRADING LIMITED **PURINETHOL 50 mg compresse 10344012 IT** - ASPEN PHARMA TRADING LIMITED **PURINETHOL 50 mg, comprimé sécable 308 819-4 FR** - ASPEN PHARMA TRADING LIMITED **PURINETHOL 50 mg, comprimé sécable 364 311-2 FR** - ASPEN PHARMA TRADING LIMITED , PRAC Rapporteur: Ulla Wändel Liminga, "14/09/2013-01/09/2016"	
EMEA/H/C/PSUSA/00010029/201610 (dapagliflozin) CAPS: **Edistride** (EMEA/H/C/004161) (dapagliflozin), MAH: AstraZeneca AB, Rapporteur: Kristina Dunder **Forxiga** (EMEA/H/C/002322) (dapagliflozin), MAH: AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "05 October 2015 to 04 October 2016"	Based on the PRAC review of data on safety and efficacy, the PRAC considers that the risk-benefit balance of medicinal products containing dapagliflozin remains unchanged but recommends that the terms of the marketing authorisation(s) should be varied as follows: Update of section 4.4 of the SmPC to update the existing warning of diabetic ketoacidosis (DKA) on the occurrence of fatal cases. The Package leaflet is updated accordingly. The PRAC considered that the RMP (version 14) is acceptable. In addition, minor revisions were recommended to be taken into account at the next RMP update. PSUR frequency and other changes to the EURD list 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/00010114/201610 (lurasidone) CAPS: **Latuda** (EMEA/H/C/002713) (lurasidone), MAH: Sunovion Pharmaceuticals Europe Ltd, Rapporteur: Filip Josephson, PRAC Rapporteur: Qun-Ying Yue, "28/10/2015 to 28/10/2016 Update of section 4.8 of the SmPC to add the adverse reaction hyponatremia with a frequency uncommon, to change the frequency of the adverse reaction hypersensitivity, rash and	Based on the PRAC review of data on safety and efficacy, the PRAC considers that the risk-benefit balance of medicinal products containing lurasidone remains unchanged but recommends that the terms of the marketing authorisation should be varied as follows: Update of section 4.8 of the SmPC to add the adverse reaction hyponatremia with a frequency uncommon to change the frequency of the adverse reaction hypersensitivity, rash and pruritus from not known to uncommon, and to change frequency of angioedema from not known

pruritus from not known to uncommon, and to change frequency of angioedema from not known to rare. Under the table, the footnote regarding hypersensitivity is deleted. The Package Leaflet is updated accordingly."	to rare. Under the table, the footnote regarding hypersensitivity is deleted. The Package leaflet is updated accordingly. In addition, the MAH should also address the following issues in the next PSUR: • Thromboembolic events and urinary retention should be reviewed in the next PSUR. 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/00010263/201610 (umeclidinium bromide) CAPS: **Incruse** (EMEA/H/C/002809) (umeclidinium bromide), MAH: Glaxo Group Ltd, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Carmela Macchiarulo, "16 April 2016 - 15 October 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 to add the adverse reaction "intraocular pressure increased" with a frequency "Not known" The Package leaflet should be updated accordingly.
EMEA/H/C/PSUSA/00010272/201609 (insulin degludec / liraglutide) CAPS: **Xultophy** (EMEA/H/C/002647) (insulin degludec / liraglutide), MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, "01-Apr-2016 - 30-Sep-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, concerning the following changes: Update of section 4.8 of the SmPC to add the adverse reactions 'cholecystitis' and 'cholelithiasis' with a frequency "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/00010319/201610 (nintedanib (respiratory indication)) CAPS: **OFEV** (EMEA/H/C/003821) (nintedanib), MAH: Boehringer Ingelheim International GmbH, Rapporteur: David Lyons, PRAC Rapporteur: Nikica Mirošević Skvrce, "16 Apr 2016 to 15 Oct 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 changes:

	Update of section 4.4 of the SmPC to amend the current warning on diarrhoea to add that it can lead to dehydration and electrolyte disturbances and update of section 4.8 of the SmPC to add 'dehydration' as a new ADR with an 'uncommon' frequency. Update of section 4.4 of the SmPC to amend the current warning on haemorrhage and update of section 4.8 to include a cross reference to section 4.4 of the SmPC for the ADR 'bleeding'. Update of section 4.4 of the SmPC to amend the current warning on gastrointestinal perforations. 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/00010387/201610 (edoxaban) CAPS: **Lixiana** (EMEA/H/C/002629) (edoxaban), MAH: Daiichi Sankyo Europe GmbH, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Julie Williams, "22 April 2016 to 21 October 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 to add the adverse reactions headache, abdominal pain and dizziness with a common frequency. 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/00010388/201610 (empagliflozin, empagliflozin / metformin) CAPS: **Jardiance** (EMEA/H/C/002677) (empagliflozin), MAH: Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege **Synjardy** (EMEA/H/C/003770) (empagliflozin / metformin), MAH: Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Dolores Montero Corominas, "18/04/2016 - 17/10/2016 Based on the PRAC Rapporteur review of data on safety and efficacy, the PRAC Rapporteur considers that the risk-benefit balance of medicinal products containing empaglifozin and empagliflozin/metformin remains unchanged but recommends that the terms of the marketing authorisation(s) should be varied as follows:	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 to add the adverse drug reactions angioedema with a frequency category not known, rash with a common frequency and urticaria with an uncommon frequency. Section 4.4 is also updated to reflect the occurrence of fatal cases of diabetic ketoacidosis. The Package Leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members

- Update section 4.8 of the SmPC to add the adverse drug reactions Angioedema and Rash. Regarding the frequencies, angioedema should be included with an unknown frequency and for rash, the MAH should calculate its frequency as requested in the Request for Supplementary Information detailed in section 5. The Package Leaflet should be updated accordingly. - Update the warning on Diabetic ketoacidosis of section 4.4 to reflect the occurrence of fatal cases of Diabetic ketoacidosis."	agree with the above-mentioned recommendation of the CHMP.

B.4. EPARs / WPARs

BESPONSA - inotuzumab ozogamicin - EMEA/H/C/004119, Orphan Applicant: Pfizer Limited, treatment B-cell precursor acute lymphoblastic leukaemia (ALL), Rapporteur: Robert James Hemmings, Co-Rapporteur: Filip Josephson, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Brineura - cerliponase alfa - EMEA/H/C/004065, Orphan Applicant: BioMarin International Limited, treatment of neuronal ceroid lipofuscinosis type 2, Rapporteur: Martina Weise, Co-Rapporteur: Concepcion Prieto YerroNew active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Cuprior - trientine - EMEA/H/C/004005, Orphan Applicant: GMP-Orphan SA, treatment of Wilson's disease, Rapporteur: David Lyons, Co-Rapporteur: Milena Stain,, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	adopted.
Erelzi - etanercept - EMEA/H/C/004192 Applicant: Sandoz GmbH, treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, axial spondyloarthritis, ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis, plaque psoriasis and paediatric plaque psoriasis, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Outi Mäki-Ikola,, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	Adopted by written procedure on 9 June 2017.
Febuxostat Mylan - febuxostat - EMEA/H/C/004374	adopted.

Applicant: Mylan S.A.S, treatment of hyperuricaemia, Generic, Generic of Adenuric, Rapporteur: Juris Pokrotnieks,, Generic application (Article 10(1) of Directive No 2001/83/EC)	
Kevzara - sarilumab - EMEA/H/C/004254 Applicant: sanofi-aventis groupe, treatment of active rheumatoid arthritis, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Daniela Melchiorri,, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Qinprezo - vosaroxin - EMEA/H/C/004118, Orphan Applicant: Sunesis Europe Ltd, treatment acute myeloid leukaemia, Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Paula Boudewina van Hennik, New active substance (Article 8(3) of Directive No 2001/83/EC) **WPAR**	adopted.
Rixathon - rituximab - EMEA/H/C/003903 Applicant: Sandoz GmbH, treatment of Non-Hodgkin's lymphoma (NHL), Chronic lymphocytic leukaemia (CLL), Rheumatoid arthritis and Granulomatosis with polyangiitis and microscopic polyangiitis, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Paula Boudewina van Hennik,, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	adopted.
Riximyo - rituximab - EMEA/H/C/004729 Applicant: Sandoz GmbH, treatment of Non-Hodgkin's lymphoma (NHL), Rheumatoid arthritis and Granulomatosis with polyangiitis and microscopic polyangiitis, Duplicate, Duplicate of Rixathon, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Paula Boudewina van Hennik, , Similar biological application (Article 10(4) of Directive No 2001/83/EC)	adopted.
Skilarence - dimethyl fumarate - EMEA/H/C/002157 Applicant: Almirall S.A, treatment of moderate to severe plaque psoriasis in adults in need of systemic drug therapy, treatment of plaque psoriasis, Rapporteur: Robert James Hemmings, Co-Rapporteur: Martina Weise,, Known active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.

Spinraza - nusinersen - EMEA/H/C/004312, Orphan Applicant: Biogen Idec Ltd, the treatment of Spinal Muscular Atrophy (SMA), Rapporteur: Bruno Sepodes, Co-Rapporteur: Greg Markey, , New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Ucedane - carglumic acid - EMEA/H/C/004019 Applicant: Lucane Pharma, treatment of hyperammonaemia, Generic, Generic of Carbaglu, Rapporteur: Eleftheria Nikolaidi, , Hybrid application (Article 10(3) of Directive No 2001/83/EC); Generic 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/0032 MAH: Seqirus S.r.l, Rapporteur: Daniela Melchiorri Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 06.04.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Armisarte - pemetrexed - EMEA/H/C/004109/II/0008/G MAH: Actavis Group PTC ehf, Rapporteur: Alar Irs Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 21.04.2017, 09.03.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Azopt - brinzolamide - EMEA/H/C/000267/II/0064/G MAH: Novartis Europharm Ltd, Rapporteur: Concepcion Prieto Yerro Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 06.04.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Bexsero - meningococcal group B vaccine (rDNA, component, adsorbed) - EMEA/H/C/002333/II/0051 MAH: GSK Vaccines S.r.l, Rapporteur: Kristina	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Dunder Opinion adopted on 18.05.2017.	
Biopoin - epoetin theta - EMEA/H/C/001036/II/0036/G MAH: TEVA GmbH, Rapporteur: Alexandre Moreau Opinion adopted on 05.05.2017. Request for Supplementary Information adopted on 23.03.2017, 19.01.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Darunavir Mylan - darunavir - EMEA/H/C/004068/II/0001/G MAH: Mylan S.A.S, Generic, Generic of Prezista, Rapporteur: John Joseph Borg Request for Supplementary Information adopted on 05.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Emtricitabine/Tenofovir disoproxil Zentiva - emtricitabine / tenofovir disoproxil - EMEA/H/C/004137/II/0001 MAH: Zentiva k.s., Generic, Generic of Truvada, Rapporteur: Alar Irs Opinion adopted on 27.04.2017. Request for Supplementary Information adopted on 23.02.2017.	Positive Opinion adopted by consensus on 27.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Enbrel - etanercept - EMEA/H/C/000262/II/0207/G MAH: Pfizer Limited, Rapporteur: Robert James Hemmings Opinion adopted on 05.05.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Eporatio - epoetin theta - EMEA/H/C/001033/II/0035/G MAH: ratiopharm GmbH, Rapporteur: Alexandre Moreau Opinion adopted on 05.05.2017. Request for Supplementary Information adopted on 23.03.2017, 19.01.2017.	Positive Opinion adopted by consensus on 05.05.2017. 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/0027 MAH: Seqirus S.r.l, Rapporteur: Daniela Melchiorri Opinion adopted on 22.06.2017. Request for Supplementary Information adopted on 18.05.2017, 06.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0075	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP

MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 05.05.2017. Request for Supplementary Information adopted on 23.03.2017.	Members were in agreement with the CHMP recommendation.
Imatinib Teva - imatinib - EMEA/H/C/002585/II/0026 MAH: Teva B.V., Generic, Generic of Glivec, Rapporteur: Jorge Camarero Jiménez Opinion adopted on 09.06.2017. Request for Supplementary Information adopted on 27.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Inflectra - infliximab - EMEA/H/C/002778/II/0050/G MAH: Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey Request for Supplementary Information adopted on 05.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Kalydeco - ivacaftor - EMEA/H/C/002494/II/0057, Orphan MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Concepcion Prieto Yerro Opinion adopted on 27.04.2017.	Positive Opinion adopted by consensus on 27.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
MabThera - rituximab - EMEA/H/C/000165/II/0129/G MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac Opinion adopted on 27.04.2017. Request for Supplementary Information adopted on 02.03.2017.	Positive Opinion adopted by consensus on 27.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
MabThera - rituximab - EMEA/H/C/000165/II/0130/G MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac Opinion adopted on 27.04.2017. Request for Supplementary Information adopted on 02.03.2017.	Positive Opinion adopted by consensus on 27.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Menveo - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/001095/II/0065 MAH: GSK Vaccines S.r.l, Rapporteur: Johann Lodewijk HillegeOpinion adopted on 22.06.2017. Request for Supplementary Information adopted on 27.04.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Nplate - romiplostim - EMEA/H/C/000942/II/0062/G, Orphan MAH: Amgen Europe B.V., Rapporteur:	Positive Opinion adopted by consensus on 27.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Concepcion Prieto Yerro Opinion adopted on 27.04.2017.	recommendation.
Nucala - mepolizumab - EMEA/H/C/003860/II/0007 MAH: GlaxoSmithKline Trading Services, Rapporteur: Nithyanandan Nagercoil Opinion adopted on 22.06.2017. Request for Supplementary Information adopted on 18.05.2017, 23.03.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Omnitrope - somatropin - EMEA/H/C/000607/II/0047 MAH: SANDOZ GmbH, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 11.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Praluent - alirocumab - EMEA/H/C/003882/II/0021/G MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 18.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Prezista - darunavir - EMEA/H/C/000707/II/0083/G MAH: Janssen-Cilag International NV, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 22.06.2017. Request for Supplementary Information adopted on 18.05.2017, 26.01.2017.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0114/G MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 11.05.2017.	Positive Opinion adopted by consensus on 11.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
ReFacto AF - moroctocog alfa - EMEA/H/C/000232/II/0139 MAH: Pfizer Limited, Rapporteur: Hanne Lomholt Larsen Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 23.03.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Remsima - infliximab - EMEA/H/C/002576/II/0042/G MAH: Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey Request for Supplementary Information adopted on 05.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

Siklos - hydroxycarbamide - EMEA/H/C/000689/II/0031/G, Orphan MAH: Addmedica, Rapporteur: Koenraad Norga Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 23.03.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Simponi - golimumab - EMEA/H/C/000992/II/0074/G MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 30.03.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Soliris - eculizumab - EMEA/H/C/000791/II/0093, Orphan MAH: Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez Opinion adopted on 18.05.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0116/G MAH: GSK Biologicals SA, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 18.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Tenofovir disoproxil Zentiva - tenofovir disoproxil - EMEA/H/C/004120/II/0001 MAH: Zentiva k.s., Generic, Generic of Viread, Rapporteur: John Joseph Borg Opinion adopted on 27.04.2017. Request for Supplementary Information adopted on 23.02.2017.	Positive Opinion adopted by consensus on 27.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Trisenox - arsenic trioxide - EMEA/H/C/000388/II/0063/G MAH: Teva B.V., Rapporteur: Alexandre Moreau Opinion adopted on 05.05.2017. Request for Supplementary Information adopted on 23.03.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Umbipro (TM) - chlorhexidine - EMEA/H/W/003799/II/0002/G MAH: GlaxoSmithKline Trading Services, Rapporteur: Patrick Salmon Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 23.03.2017, 26.01.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zevalin - ibritumomab tiuxetan - EMEA/H/C/000547/II/0046/G	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP

MAH: Spectrum Pharmaceuticals B.V., Rapporteur: Sinan B. Sarac Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 30.03.2017, 19.01.2017.	Members were in agreement with the CHMP recommendation.
WS1099/G **Neulasta-EMEA/H/C/000420/WS1099/0092/G** **Ristempa-EMEA/H/C/003910/WS1099/0009/G** MAH: Amgen Europe B.V., Lead Rapporteur: Robert James Hemmings Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 16.03.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1132 **Fiasp-EMEA/H/C/004046/WS1132/0002** **NovoMix-EMEA/H/C/000308/WS1132/0089** **NovoRapid-EMEA/H/C/000258/WS1132/0117** **Ryzodeg-EMEA/H/C/002499/WS1132/0022** MAH: Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder Opinion adopted on 05.05.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1143 **Aflunov-EMEA/H/C/002094/WS1143/0033** **Foclivia-EMEA/H/C/001208/WS1143/0028** MAH: Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 15.06.2017, 05.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
WS1145/G **Aflunov-EMEA/H/C/002094/WS1145/0034/G** **Foclivia-EMEA/H/C/001208/WS1145/0029/G** MAH: Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri Opinion adopted on 15.06.2017. Request for Supplementary Information adopted on 11.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
WS1155 **Abseamed-EMEA/H/C/000727/WS1155/0063**	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Binocrit-EMEA/H/C/000725/WS1155/0063 **Epoetin alfa** **Hexal-EMEA/H/C/000726/WS1155/0062** MAH: Medice Arzneimittel Pütter GmbH & Co. KG, Duplicate, Duplicate of Epoetin alfa Hexal, Lead Rapporteur: Alexandre Moreau Opinion adopted on 05.05.2017.	recommendation.

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

Aerinaze - desloratadine / pseudoephedrine sulphate - EMEA/H/C/000772/II/0033 MAH: Merck Sharp & Dohme Limited, Rapporteur: Koenraad Norga, "Update of sections 4.4 and 4.8 of the SmPC to include information on acute generalised exanthematous pustulosis (AGEP) based on literature reports for pseudoephedrine. In addition, the MAH took the opportunity to correct minor typographical errors in the SmPC and Package Leaflet and to align the annexes with the revised QRD template v10." Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 26.01.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cerdelga - eliglustat - EMEA/H/C/003724/II/0011, Orphan MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC in order to reflect the final study results from study GZGD00304 ("A Phase 2, Open-Label, Multi-Center Study Evaluating the Efficacy, Safety and Pharmacokinetics of Genz-112638 in Gaucher Type 1 Patients") listed as a category 3 study in the RMP (MEA 007). In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet." Opinion adopted on 11.05.2017.	Positive Opinion adopted by consensus on 11.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cinryze - C1-esterase inhibitor, human - EMEA/H/C/001207/II/0048 MAH: Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus, "To replace the term Unit (U) by International Unit (IU) for the product potency in the product information in line with World Health Organization (WHO) international C1-inhibitor concentrate standard (08/256) as well as in compliance with ICH guidelines (Q6B,	The Committee adopted a Request for Supplementary information together with a specific timetable.

2.2.1) analytical considerations, reference standards and reference materials and also to be consistent with Module 3 of the product dossier." Request for Supplementary Information adopted on 18.05.2017, 26.01.2017.	
Cyanokit - hydroxocobalamin - EMEA/H/C/000806/II/0031 MAH: SERB SA, Rapporteur: Alexandre Moreau, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning on renal disorders and to update the safety information on skin and subcutaneous tissue disorders, renal and urinary disorders following a safety signal on renal disorders. The package leaflet is updated accordingly." Request for Supplementary Information adopted on 18.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Docetaxel Winthrop - docetaxel - EMEA/H/C/000808/II/0051 MAH: Aventis Pharma S.A., Informed Consent of Taxotere, Rapporteur: Alexandre Moreau, "Update of section 4.8 of the SmPC to update the safety information related to electrolyte imbalance. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Bulgaria and introduce minor corrections in the Package Leaflet." Opinion adopted on 05.05.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Edurant - rilpivirine - EMEA/H/C/002264/II/0025 MAH: Janssen-Cilag International NV, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.5 of the SmPC in order to include Pharmacokinetics data of drug-drug interactions between simeprevir and rilpivirine, based on final result from study TMC435-TiDP16-C114; this is a Phase I, 2-panel, open-label, randomized, cross-over study in healthy subjects to investigate the potential drug-drug interaction between simeprevir and RPV. 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 on 11.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Elonva - corifollitropin alfa -	Positive Opinion adopted by consensus on

EMEA/H/C/001106/II/0033 MAH: Merck Sharp & Dohme Limited, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.8 of the SmPC to add the new ADR 'hypersensitivity reactions (both local and generalized, including rash)', identified through post-marketing surveillance, with frequency 'unknown' under the system organ class of 'immune system disorders'. The Package Leaflet has been updated accordingly." Opinion adopted on 18.05.2017.	18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0034 MAH: Merck Sharp & Dohme Limited, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.5 of the SmPC to add information pertaining to potential hCG cross-reactivity resulting in a false positive pregnancy test. In addition, the MAH is taking the opportunity to implement changes in the annexes in line with the QRD templates (versions 9.1 and 10) and to propose combined versions of the SmPCs and Package Leaflets for the different strengths." Request for Supplementary Information adopted on 18.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Eperzan - albiglutide - EMEA/H/C/002735/II/0032 MAH: GlaxoSmithKline Trading Services, Rapporteur: Kristina Dunder, "Submission of the final clinical study report of the study 201834: A randomized, double-blind, single-dose, placebo controlled, 2-way cross-over study evaluating effect of albiglutide on cholecystokinin-induced gallbladder emptying in fasting healthy subjects, listed as a category 3 study in the RMP." Opinion adopted on 05.05.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Epivir - lamivudine - EMEA/H/C/000107/II/0104 MAH: ViiV Healthcare UK Limited, Rapporteur: Joseph Emmerich, "Update of section 4.5 of the SmPC of both Epivir tablets and oral solution, and section 4.4 of the SmPC for Epivir Oral solution only, to add information regarding the potential for interaction between lamivudine and sorbitol based on the results of Study 204857. Further, a minor amendment has been implemented throughout the SmPC to update the clinical terminology for 'Pneumocystis carinii pneumonia'	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

to 'Pneumocystis jiroveci pneumonia'. In addition, the MAH has taken the opportunity to align the product information with the QRD template version 10, to make minor editorial changes in the annexes and to update the contact details of the local representative in Norway in the Package Leaflet." Request for Supplementary Information adopted on 05.05.2017.	
EVRA - ethinylestradiol / norelgestromin - EMEA/H/C/000410/II/0041 MAH: Janssen-Cilag International NV, Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.3, 4.4, and 4.5 of the SmPC in line with class labelling agreed by the CMDh, in order to add a contraindication against concomitant use of EVRA with direct-acting antiviral (DAA) agents that contain paritaprevir/ritonavir, ombitasvir, and/or dasabuvir, a warning and drug-drug interaction information, respectively. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representative in the Netherlands in the Package Leaflet." Opinion adopted on 05.05.2017. Request for Supplementary Information adopted on 16.03.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0098 MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.8 of the SmPC in order to add membranous glomerulonephritis as a new Adverse event with a not known frequency following periodic cumulative review of adverse event data from the MAH adverse event (AE) database which resulted in the decision to update the company core data sheet. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Portugal in the Package Leaflet." Request for Supplementary Information adopted on 18.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Galafold - migalastat - EMEA/H/C/004059/II/0009, Orphan MAH: Amicus Therapeutics UK Ltd, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1	Positive Opinion adopted by consensus on 11.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

of the SmPC to add new mutations in Table 2: Galafold (migalastat) amenability table and to Table 3: Mutations not amenable to Galafold (migalastat). In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some minor editorial changes to the tables and to update the list of local representatives in the Package Leaflet." Opinion adopted on 11.05.2017.	
Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/II/0049 MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to add angioedema with frequency 'unknown'. The Package Leaflet is updated accordingly." Opinion adopted on 11.05.2017.	Positive Opinion adopted by consensus on 11.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0031 MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, "To update the SmPC sections 4.4 and 4.8 to introduce a new warning and a detailed description regarding haemorrhage (not necessarily associated with thrombocytopenia) based on a safety review following the assessment of PSUR 4. The package leaflet is amended accordingly." Opinion adopted on 11.05.2017.	Positive Opinion adopted by consensus on 11.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kisplyx - lenvatinib - EMEA/H/C/004224/II/0004 MAH: Eisai Europe Ltd., Rapporteur: Bart Van der Schueren, "Submission of full report in regards to PD (secondary endpoint) from Study E7080-G000-205." Request for Supplementary Information adopted on 18.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Kuvan - sapropterin - EMEA/H/C/000943/II/0048/G, Orphan MAH: BioMarin International Limited, Rapporteur: Patrick Salmon, "Update of section 4.9 to add information regarding shortening of QT interval at high doses following review of data of study QTC-001. Submission of the clinical study report EMR700773-004 (pilot study assessing the effect of sapropterin on cognitive abilities, study prematurely terminated due to enrolment issues)	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

In addition, the MAH took the opportunity of this procedure to clarify the wording of section 4.2 and section 3 of the PL." Opinion adopted on 22.06.2017. Request for Supplementary Information adopted on 11.05.2017, 09.03.2017.	
Lixiana - edoxaban - EMEA/H/C/002629/II/0012 MAH: Daiichi Sankyo Europe GmbH, Rapporteur: Concepcion Prieto Yerro, "Update of sections 4.2 and 5.1 of the SmPC in order to add information deriving from new clinical data for the use of edoxaban as anticoagulant therapy for patients with non-valvular atrial fibrillation undergoing cardioversion (study ENSURE-AF). The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Portugal in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.0. In addition the MAH took the opportunity to introduce linguistic review in the Package Leaflet and to amend annex A as suggested during variation IA/05/G." Opinion adopted on 15.06.2017. Request for Supplementary Information adopted on 11.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Lumigan - bimatoprost - EMEA/H/C/000391/II/0052 MAH: Allergan Pharmaceuticals Ireland, Rapporteur: Hanne Lomholt Larsen, "Update of the Lumigan 0.1 mg/ml eye drops SmPC section 4.8 to add the adverse reactions Eye discharge, Lacrimation increased, Eye oedema and Foreign body sensation in eyes in line with the Company Core Data Sheet. The Package Leaflet has been updated accordingly. Section 3 of the PL was also amended to improve clarity of instructions. In addition, the MAH took the opportunity to update the Product Information in line with the QRD template version 10 and implement the unique identifier 2D barcode." Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 16.03.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
M-M-RVAXPRO - measles, mumps and rubella vaccine (live) - EMEA/H/C/000604/II/0080	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

MAH: MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC to correct the frequency of the adverse reaction 'Fever (38.5°C or higher)' to 'very common'. In addition, the MAH took the opportunity to make some other editorial changes in the product information and to make corrections in the Finnish, Hungarian, Italian, Norwegian, Slovakian and Swedish product information." Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 26.01.2017.	recommendation.
ProQuad - measles, mumps, rubella and varicella vaccine (live) - EMEA/H/C/000622/II/0114 MAH: MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC in order to change the frequency of the adverse reaction Henoch-Schönlein purpura from 'not known' to 'rare'. In addition, the MAH took the opportunity to make editorial changes in the product information and to make corrections in the Finnish and Swedish product information." Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 26.01.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pyramax - pyronaridine / artesunate - EMEA/H/W/002319/II/0015 MAH: Shin Poong Pharmaceutical Co., Ltd., Rapporteur: Joseph Emmerich, "Submission of the final report from study SP-C-013-11 listed as a category 3 study in the RMP. This is a phase IIIb/IV comparative, randomised, multi-centre, open label, parallel 3-arm clinical study to assess the safety and efficacy of repeated administration of pyronaridine-artesunate, dihydroartemisinin-piperaquine or artemether-lumefantrine or artesunate-amodiaquine over a 2-year period in children and adult patients with acute uncomplicated Plasmodium sp. malaria." Request for Supplementary Information adopted on 11.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
Revestive - teduglutide - EMEA/H/C/002345/II/0036/G, Orphan MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Sinan B. Sarac, "Submission of 7 non-clinical study reports comprising the in vitro	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

pharmacodynamic study 19498 and the pharmacokinetic studies 8248957, 8248958, TED-P10-007, P10-005, XGW00009, V7674M-SHP633; the final study report of the 2-year mouse carcinogenicity study P09-002/8214171 was also submitted at CHMP request." Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 26.01.2017.	
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." Request for Supplementary Information adopted on 18.05.2017, 23.02.2017.	The Committee adopted a Request for Supplementary information together with a specific timetable.
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 18) 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 opportunity to further update the RMP with the new due date for submission of the final study report for ROTA-085 PMS." Opinion adopted on 05.05.2017. Request for Supplementary Information adopted on 09.03.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
SIRTURO - bedaquiline - EMEA/H/C/002614/II/0021, Orphan MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, "Update of section 4.4 of the SmPC in order to add delamanid as an	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

example of a drug that prolongs the QT interval following the review of the global safety database for all serious cases received from 28 December 2012 to 30 September 2016. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 18.05.2017, 06.04.2017.	
Taxotere - docetaxel - EMEA/H/C/000073/II/0125 MAH: Aventis Pharma S.A., Rapporteur: Alexandre Moreau, "Update of section 4.8 of the SmPC to update the safety information related to electrolyte imbalance under the section metabolism and nutrition disorders. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Bulgaria and introduce minor corrections in the Package Leaflet. Minor linguistic amendments to the English PI were also made." Opinion adopted on 05.05.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tybost - cobicistat - EMEA/H/C/002572/II/0036 MAH: Gilead Sciences International Ltd, Rapporteur: Robert James Hemmings, "Submission of the integrated resistance analysis (PC-236-2016) of the genotypic changes in the protease gene for all HIV-1 infected subjects participating in Phase 3 clinical trials of Stribild (GS-US-236-0102, GS-US-236-0103, GS-US-236-0128, GS-US-264-0110, GS-US-236-0121 and GS-US-236-0123) listed as category 3 studies in the RMP." Opinion adopted on 05.05.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Uptravi - selexipag - EMEA/H/C/003774/II/0007 MAH: Actelion Registration Ltd., Rapporteur: Martina Weise, "Update of sections 4.3, 4.4 and 4.5 of the SmPC in order to add information on pharmacokinetic interactions with gemfibrozil and rifampicin in healthy subjects, based on the final clinical study report of the completed clinical pharmacology drug-drug interaction study AC-065-113. The Package Leaflet is updated	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update information on the hydrolysis of selexipag based on data from the previously submitted absolute bioavailability study AC-065-110, make minor amendments to sections 5.1 and 5.2 of the SmPC and to bring the PI in line with the latest QRD template version 10. An updated version of the RMP (version 5.3) was also submitted." Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 23.03.2017.	
Zeffix - lamivudine - EMEA/H/C/000242/II/0069 MAH: Glaxo Group Ltd, Duplicate, Duplicate of Epivir, Rapporteur: Joseph Emmerich, "Update of section 4.5 of the SmPC to add information regarding a potential interaction with sorbitol-containing medicines. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement a minor change in the labelling in line with the QRD template version 10." Request for Supplementary Information adopted on 05.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
WS1113 **Stribild-EMEA/H/C/002574/WS1113/0078** **Tybost-EMEA/H/C/002572/WS1113/0035** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings, "Submission of the final report from Study GS-US-236-0128 listed as a category 3 study in the RMP. This is a randomized, double-blind phase 3B study to evaluate the safety and efficacy of Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Disoproxil Fumarate versus Ritonavir-boosted Atazanavir plus Emtricitabine/Tenofovir Disoproxil Fumarate in HIV-1 infected, antiretroviral treatment-naive women." Opinion adopted on 11.05.2017. Request for Supplementary Information adopted on 16.03.2017.	Positive Opinion adopted by consensus on 11.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1136 **Descovy-EMEA/H/C/004094/WS1136/0017** **Genvoya-EMEA/H/C/004042/WS1136/003**	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

1 **Odefsey-EMEA/H/C/004156/WS1136/0013** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings, "Update of sections 4.4, 4.8. 5.1 and 5.2 of the SmPC in order to provide 48 weeks data from Study GS-US-292-1249; this is a Phase 3b open-label study of the efficacy and safety of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide single-tablet regimen in HIV-1/Hepatitis B co-infected adults. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to make minor administrative changes in the SmPC and the Package Leaflet." Request for Supplementary Information adopted on 05.05.2017.	
WS1137 **Lyrica-EMEA/H/C/000546/WS1137/0087** **Pregabalin** **Pfizer-EMEA/H/C/003880/WS1137/0017** MAH: Pfizer Limited, Lead Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect final results from paediatric study A0081041: "A Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study of the Efficacy and Safety of Pregabalin as Adjunctive Therapy in Children 4-16 Years of Age with Partial Onset Seizures"." Request for Supplementary Information adopted on 08.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
WS1144/G **Afinitor-EMEA/H/C/001038/WS1144/0052/G** **Votubia-EMEA/H/C/002311/WS1144/0042/G** MAH: Novartis Europharm Ltd, Lead Rapporteur: Harald Enzmann, "Update of sections 4.4 and 4.8 of the SmPC in order to include new safety information on stomatitis and its management based on final results from study CRAD001JUS226: a phase II, single arm study of the use of steroid-based mouthwash to prevent stomatitis in postmenopausal women with advanced or metastatic hormone receptor positive breast cancer being treated with everolimus plus exemestane Update of section 4.6 of the SmPC in order to add	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

new information on breast-feeding The Package Leaflets are updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to bring the Afinitor PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 27.04.2017.	
WS1152 **Descovy-EMEA/H/C/004094/WS1152/0016** **Genvoya-EMEA/H/C/004042/WS1152/0030** **Odefsey-EMEA/H/C/004156/WS1152/0012** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings, "Update of sections 4.8 and 5.1 of the SmPC in order to amend the information regarding undesirable effects and pharmacodynamic properties of Genvoya, Descovy and Odefsey following Week 144 efficacy and safety data from Study GS-US-292-0112, listed as a category 4 study in the RMP; this is a phase 3 open-label safety study of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide single-tablet regimen in HIV-1 positive patients with mild to moderate renal impairment. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity make administrative updated to the Genvoya SmPC." Opinion adopted on 05.05.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1156 **Combivir-EMEA/H/C/000190/WS1156/0090** **Kivexa-EMEA/H/C/000581/WS1156/0072** **Triumeq-EMEA/H/C/002754/WS1156/0042** **Trizivir-EMEA/H/C/000338/WS1156/0104** MAH: ViiV Healthcare UK Limited, Lead Rapporteur: Joseph Emmerich, "Update of section 4.5 of the SmPC to add information regarding the potential interaction between lamivudine and sorbitol based on the results of Study 204857. The Package Leaflet has been updated accordingly. Further, a minor amendment has been implemented throughout the SmPC in order to update the clinical	Weekly start timetable.

terminology of Pneumocystis carinii pneumonia to Pneumocystis jiroveci pneumonia. In addition, the MAH takes the opportunity to make minor editorial changes , to align the annexes with the QRD template version 10 and to update the contact details of the local representative in Norway in the Package Leaflet."	

B.5.3. 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." Request for Supplementary Information adopted on 18.05.2017, 23.02.2017.	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/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 18.05.2017, 15.12.2016.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Dificlir - fidaxomicin - EMEA/H/C/002087/II/0028 MAH: Astellas Pharma Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Qun-Ying Yue, "C.I.11: Submission of an updated RMP version 7	Weekly start timetable.

in order to remove the post-authorization measure (PAM) MEA003 (concerning clinical study 2819-CL-2001 in patients with Clostridium difficile Infection who will receive a second course offidaxomicin) due to the non-feasibility of the study." Request for Supplementary Information adopted on 05.05.2017.	
Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0064 MAH: AstraZeneca AB, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Jean-Michel Dogné, "C.I.13: Submission of the final Clinical Study Report for the study number MI-MA194: A Postmarketing Observational Evaluation of the Safety of Fluenz in Children and Adolescents with High-risk Conditions." Opinion adopted on 05.05.2017. Request for Supplementary Information adopted on 09.03.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Gilenya - fingolimod - EMEA/H/C/002202/II/0040 MAH: Novartis Europharm Ltd, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Claire Ferard, "Update of section 5.3 of the SmPC to include information about the dose correspondence between human and the species used for the preclinical tests of teratogenicity. RMP is updated (version 12.0). The MAH took the opportunity to make minor changes in sections 4.4, 4.5, 4.6 and 5.2 of the SmPC and also in Annex II." Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 26.01.2017, 13.10.2016.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0029, Orphan MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, "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	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

reflect this new safety information." Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 23.03.2017, 15.12.2016.	
Jinarc - tolvaptan - EMEA/H/C/002788/II/0006 MAH: Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, "Update of section 5.1 of the SmPC based on final results from study 156-08-271 (TEMPO 4:4) listed as a PAES in Annex II. This study is a Multicenter, Open-label, Extension Study (Extension of Trial 156-04-251) to Evaluate the Long-term Safety and Efficacy of Oral Tolvaptan Tablet Regimens in Patients With Autosomal Dominant Polycystic. It provides data for Jinarc treatment of autosomal dominant polcystic kidney disease (ADPKD) over 5 years. Reference to submission of this study is being deleted from Annex II. In addition, the Marketing authorisation holder (MAH) took the opportunity to add the current ATC code applicable for tolvaptan as it has been assigned by by WHO. The RMP version 13.1 has also been submitted to reflect the completion of the 156-08-271 study." Request for Supplementary Information adopted on 05.05.2017.	Weekly start timetable.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0025 MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus, "Update of sections 4.2, 4.4 and 4.8 of the SmPC to add a warning for the risk of severe skin reactions and to communicate that Stevens - Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), including fatal cases, have been reported in patients treated with pembrolizumab. The Package Leaflet has been updated accordingly. The application included an updated RMP version 8.0, and a proposed DHPC and communication plan." Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 21.04.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
NINLARO - ixazomib - EMEA/H/C/003844/II/0002, Orphan	Weekly start timetable.

MAH: Takeda Pharma A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.8 and 5.1 of the SmPC to reflect the final overall survival analysis of C16010 China continuation study, a phase III study comparing ixazomib plus lenalidomide and dexamethasone versus placebo plus lenalidomide in patients with relapsed and/or refractory multiple myeloma, in order to fulfil SOB (Specific Obligation) 002. Annex II.E and the RMP (version 2.0) are updated accordingly. In addition the Marketing Authorisation Holder (MAH) took the opportunity to make a small correction in sections 4.7 and 9 of the SmPC and to the German translations." Request for Supplementary Information adopted on 05.05.2017.	
OLYSIO - simeprevir - EMEA/H/C/002777/II/0031 MAH: Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Julie Williams, "Update of section 5.1 of the SmPC in order to update the efficacy information following results from study HPC3002 A Prospective 3-year Follow-up Study in Subjects Previously Treated in a Phase IIb or Phase III Study with a TMC435-containing Regimen for the Treatment of Hepatitis C Virus (HCV) Infection listed as a category 3 study in the RMP and in fulfilment of MEA005. The RMP version 4.0 has also been submitted which includes updates of changes already agreed in procedures EMEA/H/C/002777/II/0021,EMEA/H/C/002777/II/0027 and EMEA/H/A-20/1438/C/2777/0019." Request for Supplementary Information adopted on 18.05.2017.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Orencia - abatacept - EMEA/H/C/000701/II/0107 MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information following the MAH's initiative to update its clinical trials safety database to include all currently completed Orencia clinical trials for both the IV and SC formulations. The adverse reactions table in section 4.8, as well as the description of selected adverse reactions of special interest is being amended. Section 4.4 is	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

being brought in line with the updated section 4.8. The package leaflet is being revised accordingly. An updated Risk Management Plan (Version 22) is also being submitted within this variation." Opinion adopted on 05.05.2017. Request for Supplementary Information adopted on 09.03.2017.	
Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0017 MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Almath Spooner, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect the long-term safety and efficacy data from Study VX12 809 105. Study VX12 809 105 is a Phase 3, rollover study to evaluate the safety and efficacy of long term treatment with LUM/IVA in subjects aged 12 years and older with cystic fibrosis, homozygous or heterozygous for the F508del CFTR mutation (MEA 001). A new version of the RMP (ver. 2.7) included in this submission has been updated to include the final data from Study 105. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 18.05.2017, 23.02.2017.	The Committee adopted a Request for Supplementary information together with a specific timetable.
Pegasys - peginterferon alfa-2a - EMEA/H/C/000395/II/0092 MAH: Roche Registration Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Qun-Ying Yue, "Update of section 5.1 of the SmPC in order to add information on the predictive value of on-treatment biomarkers for final treatment response based on the final report from a systematic review and individual patient data meta-analysis of PEG-IFN studies. A cross-reference is added to section 4.2 of the SmPC accordingly." Opinion adopted on 05.05.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Rekovelle - follitropin delta - EMEA/H/C/003994/II/0003/G MAH: Ferring Pharmaceuticals A/S, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Menno van der Elst Opinion adopted on 18.05.2017. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 23.03.2017.	
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)." Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 23.02.2017, 15.12.2016.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0036/G MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "C.I.13: Submission of a Clinical Study Report for study 109HV321: A Randomized, Double-Blind, Phase 3b Study to Evaluate the Safety and Tolerability of BG00012 when Administered as 240 mg BID (twice daily) Dose Regimen with and without Aspirin Compared to Placebo or Following a Slow Titration (Category 3) C.I.13: Submission of a Clinical Study Report for study 109MS406 (ASSURE): A Phase 4, Randomized, Double-Blind Study with a Safety Extension Period to Evaluate the Effect of Aspirin on Flushing Events in Subjects with Relapsing-Remitting Multiple Sclerosis Treated with Tecfidera (Dimethyl Fumarate) Delayed-release Capsules (Category 4)" Request for Supplementary Information adopted on 05.05.2017.	Weekly start timetable.
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0037 MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "C.I.4: Submission of a Clinical Study Report for study	Weekly start timetable.

109MS307: An Open-Label Study to Assess the Immune Response to Vaccination in Tecfidera-Treated Versus Interferon-Treated Subjects With Relapsing Forms of Multiple Sclerosis (Category 3). Consequently, this variation includes an update to section 4.5 (Interaction with other medicinal products and other forms of interaction) of the Summary of Product Characteristics (SmPC) and section 2 of the package leaflet." Request for Supplementary Information adopted on 05.05.2017.	
Truxima - rituximab - EMEA/H/C/004112/II/0002/G MAH: Celltrion Healthcare Hungary Kft., Rapporteur: Sol Ruiz, PRAC Rapporteur: Doris Stenver Opinion adopted on 18.05.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xarelto - rivaroxaban - EMEA/H/C/000944/II/0052/G MAH: Bayer AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "Group of variations consisting of: 1) C.1.4. To add the authorised indications "Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults" to Xarelto 10 mg based on Einstein Choice trial (A randomised phase III clinical study to evaluate efficacy and safety of Reduced-dosed rivaroxaban and standard-dosed rivaroxaban versus ASA in the long-term prevention of recurrent symptomatic venous thromboembolism in patients with symptomatic deep-vein thrombosis and/or pulmonary embolism) in section 4.1 of the SmPC 10 mg. Consequently: - Changes in sections 4.2, 4.8 and 5.1 for Xarelto 10mg, 15mg and 20 mg are made in order to update the posology, efficacy and safety information. - Annex III is updated to include Xarelto 10 mg into Patient alert card to support management of bleeding when the 10 mg is treated for long-term prevention of recurrent VTE - RMP (version 10) is updated 2) B.II.e.5.a.1- to add a new pack size of 14 film coated tablets in blister (PP/alu) for Xarelto 10 mg 3) B.II.e.5.a.1- to add a new pack size of 28 film	The Committee adopted a Request for Supplementary information together with a specific timetable.

coated tablets in blister (PP/alu) for Xarelto 10 mg 4) B.II.e.5.a.1- to add a new pack size of 98 film coated tablets in blister (PP/alu) for Xarelto 10 mg 5) B.II.e.1.b.1 to change immediate packaging of the finished product for 10 mg film coated tablets to introduce HDPE bottle with screw cap including new presentation (pack containing 100 film coated tablets for 10 mg strength) 6) C.1.4 To add information on interactions with SSRIs and SNRIs in section 4.5 and a related warning in section 4.4 of the SmPC based on post-hoc analyses to investigate bleeding risk for rivaroxaban in patients with and without use of SSRI or SNRIs from the pivotal studies. In addition, MedDRA terminology is updated in the adverse drug reactions table in section 4.8 of the SmPC 7) C.1.11.z To delete from the summary of safety concerns: "Patients undergoing major orthopaedic surgery other than elective hip or knee replacement surgery" and "Remedial pro-coagulant therapy for excessive haemorrhage". Part II - Modules SVIII: Summary of the safety concerns, Part III, Section 1 Safety Concerns and overview of planned pharmacovigilance action were amended accordingly. In addition, Part II, Safety Specification, module SIV, Populations not studied in clinical trials: "Patients undergoing major orthopaedic surgery other than elective hip or knee replacement surgery" and "Remedial pro-coagulant therapy for excessive haemorrhage" was updated. Request for Supplementary Information adopted on 18.05.2017.	
Xtandi - enzalutamide - EMEA/H/C/002639/II/0034 MAH: Astellas Pharma Europe B.V., Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia, "Update of section 5.1 of the SmPC in order to reflect relevant information for physicians namely on the observed differences in treatment effect based on prior chemotherapy treatment history. In addition, the MAH took this opportunity to reflect the ATC code for enzalutamide. The RMP version 11.0 has also been submitted." Opinion adopted on 18.05.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Request for Supplementary Information adopted on 09.03.2017.	
Xultophy - insulin degludec / liraglutide - EMEA/H/C/002647/II/0017 MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, "Update of section 4.2 of the SmPC in order to update the information on use of Xultophy in patients with hepatic impairment, based on clinical trial NN2211-1328, the LEAD 1-6 meta-analysis as well as other liraglutide trials. In addition, 'fatigue' has been added to the tabulated list of adverse reactions in Section 4.8 of the SmPC. The Package Leaflet is updated accordingly. RMP version 6.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10. The requested variation proposed amendments to the Summary of Product Characteristics, Annex II, Labelling and Package Leaflet and to the Risk Management Plan (RMP)." Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 23.03.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Yervoy - ipilimumab - EMEA/H/C/002213/II/0042 MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "Update of sections 4.4, 4.8 and 5.1 of the SmPC to reflect the final results of study CA184-169, a randomized double-blind phase III study of ipilimumab administered at 3 mg/kg versus at 10 mg/kg in subjects previously treated or untreated with unresectable or metastatic melanoma, in order to fulfil ANX 014.1. The MAH also provided with this variation application efficacy and safety data from study CA184-169 in two subgroups: female ≥ 50 years of age and with brain metastases in order to fulfil MEA 015.1. Annex II.D and the RMP (version 14.0) are updated accordingly. In addition the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet, to include some editorial changes and correct some typos throughout the product information, and to	Weekly start timetable.

bring the product information in line with the latest QRD template version 10." Request for Supplementary Information adopted on 05.05.2017.	
Zinbryta - daclizumab - EMEA/H/C/003862/II/0007 MAH: Biogen Idec Ltd, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Eva A. Segovia, "Update of sections 4.4 and 4.8 of the SmPC in order to add autoimmune haemolytic anaemia with frequency 'uncommon' and to include a warning concerning symptoms of this adverse drug reaction. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder took the opportunity to implement minor editorial amendments throughout the Product Information. The RMP version 5.0 has also been submitted." Request for Supplementary Information adopted on 05.05.2017.	Weekly start timetable.
WS1086 **Stribild-EMEA/H/C/002574/WS1086/0077** **Tybost-EMEA/H/C/002572/WS1086/0034** MAH: Gilead Sciences International Ltd, Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Julie Williams, "Submission of the final report from Study GS-US-236-0140. This is a randomized, open-label, phase 4 study evaluating the renal effect of Elvitegravir/ Cobicistat/ Emtricitabine/Tenofovir DF or other Tenofovir DF-containing Regimens (Ritonavir-boosted Atazanavir plus Emtricitabine /Tenofovir DF or Efavirenz /Emtricitabine/Tenofovir DF) compared to Ritonavir-boosted Atazanavir plus Abacavir/ Lamivudine in Antiretroviral Treatment-naïve HIV-1 Infected Adults with eGFR ≥70 mL/min." Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 23.03.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1158/G **Humalog-EMEA/H/C/000088/WS1158/0154/G** **Liprolog-EMEA/H/C/000393/WS1158/0117/G** MAH: Eli Lilly Nederland B.V., Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Julie Williams	Weekly start timetable.

Request for Supplementary Information adopted on 05.05.2017.	
Lonsurf - trifluridine / tipiracil - EMEA/H/C/003897/II/0002/G MAH: Les Laboratoires Servier, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Ulla Wändel Liminga "1) C.I.4 (type II) - Update of sections 4.2, 4.4 and 5.2 of the SmPC following availability of the final clinical study report for the study TO-TAS-102-106, A phase I, open-label study evaluating the safety, tolerability, and pharmacokinetics of TAS-102 in patients with advanced solid tumours and varying degrees of hepatic impairment (requested in MEA 002). As a consequence of TO-TAS-102-106 study results, the RMP (ver. 5.0) is updated to remove the missing information "Use in patients with moderate to severe hepatic impairment". 2) C.I.4 (type II) - Update of sections 4.5 and 5.2 of the SmPC following availability of the results of the in vitro CYP induction study of tipiracil hydrochloride (TPI) using the appropriate concentration of TPI (requested in a recommendation). Section SVII.4 of the RMP is updated accordingly. 3) C.I.4 (type II) - Update of section 4.2 of the SmPC in order to correct inconsistencies in the dose calculation according to body surface area. The package leaflet is updated to add 'interstitial lung disease' in the serious side effects part of section 4. In addition, the MAH took the opportunity to update Annex IIIA in accordance with the latest QRD template." Corrected Opinion adopted on 23.03.2017. Request for Supplementary Information adopted on 26.01.2017.	Corrected positive Opinion adopted by consensus on 23.03.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.4. PRAC assessed procedures

PRAC Led **Avastin - bevacizumab - EMEA/H/C/000582/II/0095** MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 28.0 in order to remove the post-authorisation measure outlined in section III.4.3 of the RMP consisting of the submission of an extension protocol in order to	Weekly start timetable.

obtain additional long-term follow-up (LTFU) information from the paediatric population after patients complete the minimum 5.5 year follow-up period as defined in the BO20924 (BERNIE) paediatric study protocol and to amend the date of submission of the final report (addendum CSR) for the BO20924 (BERNIE) study." Request for Supplementary Information adopted on 05.05.2017.	
PRAC Led **Benlysta - belimumab - EMEA/H/C/002015/II/0049** MAH: Glaxo Group Ltd, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 23 in order to amend the CSR availability timeline, patient number and the primary and secondary endpoints listed in the EU Risk Management Plan, with regards to study HGS1006-C1121/BEL114054." Opinion adopted on 05.05.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Humira - adalimumab - EMEA/H/C/000481/II/0159** MAH: AbbVie Ltd., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of study P06-134: "A Long-Term Non-Interventional Registry to Assess Safety and Effectiveness of Humira in Subjects with Moderately to Severely Active Crohn's Disease" in fulfilment for MEA 056.9. The study includes also some paediatric patients and fulfils obligations according to article 46 of the paediatric Regulation (EC) No 1901/2006." Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 23.03.2017, 10.11.2016.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Humira - adalimumab - EMEA/H/C/000481/II/0162** MAH: AbbVie Ltd., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final national report for the Swedish biologics registry ARTIS (Anti-Rheumatic Treatment in Sweden) after	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

ending AbbVie's support by end 2015. This fulfils MEA 066.5." Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 26.01.2017.	
PRAC Led **Inovelon - rufinamide - EMEA/H/C/000660/II/0041, Orphan** MAH: Eisai Ltd, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Claire Ferard, PRAC-CHMP liaison Alexandre Moreau, "Submission of the final clinical study report for study E2080-E044-401, the European registry of anti-epileptic drug use in patients with Lennox-Gastaut Syndrome (LAG), listed as a category 3 study in the RMP, in order to fulfil MEA 002.1. This is a non-interventional EU registry study entering patients (aged ≥4 years) with LGS who required a modification in anti-epileptic therapy (either the addition of another AED or the change of one drug to another) to evaluate the long-term safety of rufinamide." Request for Supplementary Information adopted on 05.05.2017.	Weekly start timetable.
PRAC Led **Orencia - abatacept - EMEA/H/C/000701/II/0108/G** MAH: Bristol-Myers Squibb Pharma EEIG, PRAC Rapporteur: Kirsti Villikka, "This grouping of two type II variations (category C.I.13) covers the submission of the final clinical study reports from epidemiological studies IM101045A & IM101045B, listed as category 3 studies in the RMP. IM101045A & IM101045B are both observational studies, sharing overlapping safety objectives (e.g.: to assess the risk of infections, infusion-related reactions, autoimmune disorders, injection reactions and combination use)." Opinion adopted on 05.05.2017. Request for Supplementary Information adopted on 09.03.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Plenadren - hydrocortisone - EMEA/H/C/002185/II/0024, Orphan** MAH: Shire Services BVBA, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue,	Weekly start timetable.

PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP (version 3.1) in order to submit protocol amendments of SHP 617-400 (EU-AIR) study – A European multicentre, multi-country, post-authorisation, observation study (registry) of patients with chronic adrenal insufficiency (category 3). Additionally, the opportunity is being taken to implement a change agreed by the PRAC/CHMP as part of the assessment of MEA 005.3 in July 2016 and remove from the RMP reference to study SHP617-404 (SWE-DUS), a Category 3 study to monitor off-label use of Plenadren to evaluate physician prescribing patterns." Request for Supplementary Information adopted on 05.05.2017.	
PRAC Led **Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0100** MAH: Boehringer Ingelheim International GmbH, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Torbjorn Callreus, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final report for study 1160.144, which evaluated the potential off-label use of dabigatran etexilate in Europe: A drug utilisation study in Cegedim France, Denmark, and CPRD UK." Opinion adopted on 05.05.2017. Request for Supplementary Information adopted on 09.03.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS0960/G Komboglyze-EMEA/H/C/002059/WS0960/0033/G** **Onglyza-EMEA/H/C/001039/WS0960/0040/G** MAH: AstraZeneca AB, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Group of variations consisting of final epidemiological study results for: 1- study D1680R00011 2- study D1680R00012 3- study D1680R00013 4- study D1680R00014 5- study D1680R00015 6- update of the RMP to reflect the submission of the 5 epidemiological studies. As a consequence, the RMP (version 11) is updated accordingly. In	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

addition, routine changes are made in parts III (pharmacovigilance plan, overview of planned pharmacovigilance actions) and IV. A safety review based on literature has also been included to investigate acute kidney injury associated with saxagliptin/saxagliptin and metformin at the PRAC request." Opinion adopted on 18.05.2017. Request for Supplementary Information adopted on 26.01.2017, 15.09.2016.	
PRAC Led **WS1160** **Afinitor-EMEA/H/C/001038/WS1160/0053** **Votubia-EMEA/H/C/002311/WS1160/0043** MAH: Novartis Europharm Ltd, Lead Rapporteur: Harald Enzmann, Lead PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "To extend the due date of CRAD001Y2201 in the Oncology setting (Afinitor) from 3Q 2017 to 1Q 2018 in risk management plan and annex II and to for Study CRAD001MIC03 in the TSC setting (Votubia) from December 2017 to 2Q 2018. Furthermore the MAH align the RMP by introduced some administrative changes." Opinion adopted on 18.05.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1163** **Harvoni-EMEA/H/C/003850/WS1163/0051** **Sovaldi-EMEA/H/C/002798/WS1163/0041** MAH: Gilead Sciences International Ltd, Lead PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "To provide updated RMPs for Sovaldi and Harvoni following the CHMP opinion, endorsing a PRAC recommendation, issued on 15 December 2016 (EMA/CHMP/847450/2016) on the Article 20 procedure for Direct-acting antivirals (DAAs) indicated for the treatment of hepatitis C (interferon free). The PRAC requested `hepatitis B reactivation' to be considered as important identified risk for all direct-acting antivirals. In addition, `emergence of hepatocellular carcinoma' and `recurrence of hepatocellular carcinoma' have been included as important potential risks. `Patients with previous HCC' have been reflected as missing information in the RMP of the DAAs, since this population was excluded	The Committee adopted a Request for Supplementary information together with a specific timetable.

from existing clinical trials. The requested studies have also been reflected in the RMPs." Request for Supplementary Information adopted on 05.05.2017.	
PRAC Led **WS1169** **Exviera-EMEA/H/C/003837/WS1169/0028** **Viekirax-EMEA/H/C/003839/WS1169/0032** MAH: AbbVie Ltd., Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Dolores Montero Corominas, PRAC-CHMP liaison: Concepcion Prieto Yerro, "To provide updated RMPs for Exviera and Viekirax following the CHMP opinion, endorsing a PRAC recommendation, issued on 15 December 2016 (EMA/CHMP/847450/2016) on the Article 20 procedure for Direct-acting antivirals (DAAs) indicated for the treatment of hepatitis C (interferon free). The PRAC requested `hepatitis B reactivation' to be considered as important identified risk for all direct-acting antivirals. In addition, `emergence of hepatocellular carcinoma' and `recurrence of hepatocellular carcinoma' have been included as important potential risks. `Patients with previous HCC' have been reflected as missing information in the RMP of the DAAs, since this population was excluded from existing clinical trials. The requested studies have also been reflected in the RMPs." Request for Supplementary Information adopted on 05.05.2017.	The Committee adopted a Request for Supplementary information together with a specific timetable.

B.5.5. CHMP-CAT assessed procedures

Holoclar - ex vivo expanded autologous human corneal epithelial cells containing stem cells - EMEA/H/C/002450/II/0012/G, Orphan, ATMP MAH: Chiesi Farmaceutici S.p.A., Rapporteur: Egbert Flory Request for Supplementary Information adopted on 11.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

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

WS1115/G **Ambirix-EMEA/H/C/000426/WS1115/0084/G** **Twinrix Adult-EMEA/H/C/000112/WS1115/0118/G** **Twinrix Paediatric-EMEA/H/C/000129/WS1115/0119/G** MAH: GSK Biologicals SA, Lead Rapporteur: Robert James Hemmings Opinion adopted on 18.05.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1116 **Infanrix hexa-EMEA/H/C/000296/WS1116/0217** MAH: GSK Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 05.05.2017.	Positive Opinion adopted by consensus on 05.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1122/G **Hexacima-EMEA/H/C/002702/WS1122/0060/G** **Hexaxim-EMEA/H/W/002495/WS1122/0066/G** **Hexyon-EMEA/H/C/002796/WS1122/0064/G** MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 11.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.
WS1129/G **Hexacima-EMEA/H/C/002702/WS1129/0061/G** **Hexaxim-EMEA/H/W/002495/WS1129/0067/G** **Hexyon-EMEA/H/C/002796/WS1129/0065/G** MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 11.05.2017.	Positive Opinion adopted by consensus on 11.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1138 **Actos-EMEA/H/C/000285/WS1138/0077** **Competact-EMEA/H/C/000655/WS1138/0**	Positive Opinion adopted by consensus on 11.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

065 **Glubrava-EMEA/H/C/000893/WS1138/0051** **Glustin-EMEA/H/C/000286/WS1138/0076** **Tandemact-EMEA/H/C/000680/WS1138/0055** MAH: Takeda Pharma A/S, Lead Rapporteur: Patrick Salmon Opinion adopted on 11.05.2017.	recommendation.
WS1139/G **Rivastigmine 1A Pharma-EMEA/H/C/001181/WS1139/0023/G** **Rivastigmine Hexal-EMEA/H/C/001182/WS1139/0024/G** **Rivastigmine Sandoz-EMEA/H/C/001183/WS1139/0025/G** MAH: 1 A Pharma GmbH, Informed Consent of Exelon, Lead Rapporteur: Alexandre Moreau Opinion adopted on 27.04.2017.	Positive Opinion adopted by consensus on 27.04.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1157 **Relvar Ellipta-EMEA/H/C/002673/WS1157/0030** **Revinty Ellipta-EMEA/H/C/002745/WS1157/0026** MAH: Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro Opinion adopted on 18.05.2017.	Positive Opinion adopted by consensus on 18.05.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1165 **Aflunov-EMEA/H/C/002094/WS1165/0035** **Foclivia-EMEA/H/C/001208/WS1165/0030** MAH: Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 18.05.2017.	Weekly start timetable. The Committee adopted a Request for Supplementary information together with a specific timetable.

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

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

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

- viable t-cells - EMEA/H/C/002397, Orphan, ATMP
Applicant: Kiadis Pharma Netherlands B.V., adjunctive treatment in haematopoietic stem cell transplantation (HSCT) for a malignant disease

- doxorubicin hydrochloride - EMEA/H/C/004110
, treatment of breast and ovarian cancer

- efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/004274
, treatment of HIV-1 infection, Generic, Generic of Atripla

- adalimumab - EMEA/H/C/004429
, treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis

- adalimumab - EMEA/H/C/004320
, treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis

- imatinib - EMEA/H/C/004748
, treatment of newly diagnosed and chronic Philadelphia chromosome (bcr-abl) positive (Ph+) chronic myeloid leukaemia (CML), gastrointestinal stromal tumours (GIST), unresectable dermatofibrosarcoma protuberans (DFSP) and recurrent and/or metastatic DFSP,

- melatonin - EMEA/H/C/004425, PUMA
, treatment of insomnia in children with Autism Spectrum Disorders and neurogenetic diseases

- vestronidase alfa - EMEA/H/C/004438, Orphan
Applicant: Ultragenyx Germany GmbH, Mepsevii is indicated for the treatment of Mucopolysaccharidosis VII (MPS VII; Sly syndrome) for patients of all ages

- pegfilgrastim - EMEA/H/C/003961
, treatment of neutropenia

- prasugrel - EMEA/H/C/004644
, prevention of atherothrombotic events,

- infliximab - EMEA/H/C/004647
, treatment of rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, psoriasis and ulcerative colitis

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

Lynparza - olaparib - EMEA/H/C/003726/X/0016/G, Orphan
MAH: AstraZeneca AB, Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Carmela Macchiarulo, "Extension application to add a new pharmaceutical form (film-coated tablets) associated with new strength (100 mg and 150 mg) grouped with a variation C.I.4. to align the PI for the approved capsule presentation with the PI proposed for the tablet presentations."

Nuwiq - simoctocog alfa - EMEA/H/C/002813/X/0020
MAH: Octapharma AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga,"Extension application to add new strengths of 2500 IU, 3000 IU, 4000 IU for Nuwiq, powder and solvent for solution for injection."

Sprycel - dasatinib - EMEA/H/C/000709/X/0056/G
MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Fátima Ventura, PRAC Rapporteur: Doris Stenver"Extension application to introduce a new pharmaceutical form (powder for oral suspension) associated with a new strength (10 mg/ml)

2. C.I.6.a(type II) to include the treatment of children and adolescents aged 1 year to 18 years with Ph+ chronic phase CML for Sprycel. Sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, to add a warning on effects on growth and development in the paediatric population and to update the safety information. The Package Leaflet is updated in accordance."

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

- glibenclamide - EMEA/H/C/004379, Orphan
Applicant: Ammtek, treatment of neonatal diabetes
List of Questions adopted on 24.01.2017.

- avelumab - EMEA/H/C/004338, Orphan
Applicant: Merck Serono Europe Limited, treatment of Merkel cell carcinoma (MCC)
List of Questions adopted on 23.02.2017.

- belimumab - EMEA/H/C/002015/X/0046/G
List of Questions adopted on 23.02.2017.

- entecavir - EMEA/H/C/004458
, treatment of chronic hepatitis B virus infection, Generic,
List of Questions adopted on 15.12.2016.

- deferasirox - EMEA/H/C/000670/X/0054
List of Questions adopted on 23.02.2017.

- lacosamide - EMEA/H/C/004443
, treatment of epilepsy,
List of Questions adopted on 26.01.2017.

- miglustat - EMEA/H/C/004366
, treatment of Gaucher disease,
List of Questions adopted on 15.12.2016.

- sirukumab - EMEA/H/C/004165
, treatment of rheumatoid arthritis
List of Questions adopted on 26.01.2017.

- sulphur hexafluoride - EMEA/H/C/000303/X/0034/G
MAH: Bracco International B.V.,
List of Questions adopted on 26.01.2017.

- niraparib - EMEA/H/C/004249, Orphan
Treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer
List of Questions adopted on 23.02.2017.

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

Elaprase - idursulfase - EMEA/H/C/000700/S/0070
MAH: Shire Human Genetic Therapies AB,
Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty

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

Amyvid - florbetapir (18F) - EMEA/H/C/002422/R/0026
MAH: Eli Lilly Nederland B.V., Rapporteur: Harald Enzmann, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Valerie Strassmann,

Bexsero - meningococcal group B vaccine (rDNA, component, adsorbed) - EMEA/H/C/002333/R/0053
MAH: GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, Co-Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Qun-Ying Yue,

Imatinib Teva - imatinib - EMEA/H/C/002585/R/0028
MAH: Teva B.V., Generic, Generic of Glivec, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia,

Lyxumia - lixisenatide - EMEA/H/C/002445/R/0023
MAH: Sanofi-Aventis Groupe, Rapporteur: Kristina Dunder, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Qun-Ying Yue,

Prepandrix - A/Indonesia/05/2005 (H5N1) like strain used (PR8-IBCDC-RG2) - EMEA/H/C/000822/R/0071
MAH: GSK Biologicals SA, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams,

Ryzodeg - insulin degludec / insulin aspart - EMEA/H/C/002499/R/0024
MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, Co-Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Qun-Ying Yue

Tresiba - insulin degludec - EMEA/H/C/002498/R/0027
MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, Co-Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Qun-Ying Yue

Zaltrap - aflibercept - EMEA/H/C/002532/R/0037
MAH: sanofi-aventis groupe, Rapporteur: Filip Josephson, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Ulla Wändel Liminga

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

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

Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0048, Orphan MAH: Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus"Extension of indication to include the new indication "ADCETRIS is indicated for the treatment of adult patients with CD30+ cutaneous T-cell lymphoma (CTCL) who require systemic therapy", based on data from study C25001 (the 'ALCANZA' study): "A Phase 3 Trial of brentuximab vedotin(SGN-35) Versus Physician's Choice (Methotrexate or Bexarotene) in Patients With CD30-Positive Cutaneous T-Cell Lymphoma". 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. An updated RMP (version 10) has also been submitted."	
Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0142 MAH: Amgen Europe B.V., Rapporteur: Martina Weise, Co-Rapporteur: Koenraad Norga, PRAC Rapporteur: Valerie StrassmannExtension of Indication to include treatment of anaemia in adult patients with low transfusion demand in low or intermediate-1-risk myelodysplastic syndromes for Aranesp; as a consequence, sections 4.1, 4.2,4.8, 5.1 and 5.2 of the SmPC are updated in order to update the safety and efficacy information. The Package Leaflet is updated in accordance. Updated RMP version 8.0 has been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce QRD editorial changes in the SmPC, Annex IIIA and Annex IIIB."	
Faslodex - fulvestrant - EMEA/H/C/000540/II/0059 MAH: AstraZeneca UK Ltd, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga"Extension of Indication to include the use of faslodex in combination with palbociclib for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer in women who have received prior endocrine therapy (see section	

5.1). In pre- or perimenopausal women, the combination treatment with palbociclib should be combined with a luteinizing hormone releasing hormone (LHRH) agonist for Faslodex.

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

Kineret - anakinra - EMEA/H/C/000363/II/0056

MAH: Swedish Orphan Biovitrum AB (publ), Rapporteur: Sinan B. Sarac, Co-Rapporteur: Fátima Ventura, PRAC Rapporteur: Torbjorn Callreus,"Extension of indication to include a new indication for Kineret 100 mg/0.67 ml solution for injection in pre-filled syringe for the treatment of active Still's disease, including Systemic Juvenile Idiopathic Arthritis and Adult-Onset Still's Disease. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the marketing authorisation holder took the opportunity to make some editorial changes in the SmPC and Package leaflet."

Rapamune - sirolimus - EMEA/H/C/000273/II/0164

MAH: Pfizer Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel LimingaExtension of indication to include the treatment of patients with lymphangioleiomyomatosis. As a consequence section 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 6.0) are updated in accordance. In addition the MAH took the opportunity to make very minor formatting changes in the Labelling."

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

MAH: Pfizer Limited, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Carmela Macchiarulo, "Extension of Indication to include adjuvant treatment of patients at high risk of recurrent renal cell carcinoma (RCC) following nephrectomy for Sutent; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated based on the study A6181109 ("a randomized double-blind

phase 3 study of adjuvant sunitinib vs. placebo in subjects at high risk of recurrent RCC"). The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make minoreditorial changes to the SmPC and Package Leaflet and in addition, to fulfil PAM (FU2 22.5). Furthermore, the PI is brought in line with the latest QRD template version 10. Moreover, updated RMP version 16 has been submitted."

XGEVA - denosumab - EMEA/H/C/002173/II/0055

MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga, "Extension of Indication to include "Prevention of skeletal related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with multiple myeloma and in adults with bone metastases from solid tumours" for XGEVA; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance."

- abiraterone - EMEA/H/C/002321/II/0047

MAH: Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Eva A. SegoviaExtension of Indication to include "Treatment of newly diagnosed high risk metastatic hormone sensitive prostate cancer and in combination with androgen deprivation therapy" for Zytiga. 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.

In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0061/G

MAH: UCB Pharma S.A., Rapporteur: Kristina Dunder

Colobreathe - colistimethate sodium -

EMEA/H/C/001225/II/0031
MAH: Teva B.V., Rapporteur: Nithyanandan Nagercoil

Cosentyx - secukinumab - EMEA/H/C/003729/II/0024
MAH: Novartis Europharm Ltd, Rapporteur: Tuomo Lapveteläinen

Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0099/G
MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege

Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0019/G
MAH: MSD Vaccins, Rapporteur: Kristina Dunder

Imatinib Actavis - imatinib - EMEA/H/C/002594/II/0013
MAH: Actavis Group PTC ehf, Generic, Generic of Glivec, Rapporteur: Hrefna Gudmundsdottir,

IMVANEX - modified vaccinia Ankara virus - EMEA/H/C/002596/II/0027
MAH: Bavarian Nordic A/S, Rapporteur: Greg Markey,

Insuman - insulin human - EMEA/H/C/000201/II/0117/G
MAH: Sanofi-aventis Deutschland GmbH, Rapporteur: Bart Van der Schueren

Jakavi - ruxolitinib - EMEA/H/C/002464/II/0034
MAH: Novartis Europharm Ltd, Rapporteur: Filip Josephson,

Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0034
MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac

Keytruda - pembrolizumab - EMEA/H/C/003820/II/0030
MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri,

Keytruda - pembrolizumab - EMEA/H/C/003820/II/0031/G
MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri

NovoRapid - insulin aspart -

EMEA/H/C/000258/II/0118
MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder,

Pemetrexed Fresenius Kabi - pemetrexed - EMEA/H/C/003895/II/0002
MAH: Fresenius Kabi Oncology PLC, Generic, Generic of Alimta, Rapporteur: Bjorg Bolstad,

Perjeta - pertuzumab - EMEA/H/C/002547/II/0030
MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac,

Praluent - alirocumab - EMEA/H/C/003882/II/0024/G
MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege

Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0118
MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus,

Yervoy - ipilimumab - EMEA/H/C/002213/II/0048/G
MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik,

WS1150/G
Infanrix hexa-EMEA/H/C/000296/WS1150/0218/G
MAH: GSK Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1159
Neulasta-EMEA/H/C/000420/WS1159/0095
Ristempa-EMEA/H/C/003910/WS1159/0011
MAH: Amgen Europe B.V., Lead Rapporteur: Robert James Hemmings

WS1166
Infanrix hexa-EMEA/H/C/000296/WS1166/0219
MAH: GSK Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1186/G
Fertavid-EMEA/H/C/001042/WS1186/0036/G
Puregon-EMEA/H/C/000086/WS1186/0094/G

MAH: Merck Sharp & Dohme Limited, Lead Rapporteur: Nithyanandan Nagercoil

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

Bexsero - meningococcal group B vaccine (rDNA, component, adsorbed) - EMEA/H/C/002333/II/0054

MAH: GSK Vaccines S.r.l, Rapporteur: Kristina Dunder,"Update of section 4.8 of the SmPC in order to add the adverse reactions "injection site reactions (including extensive swelling of the vaccinated limb)" and "injection site nodule which may persist for more than one month" with a frequency not known. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template version 10.0."

Empliciti - elotuzumab - EMEA/H/C/003967/II/0006

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, "Update of section 5.2 of the SmPC to update the volume of distribution and elimination of elotuzumab based on an updated analysis of study HuLuc63-1701."

Esbriet - pirfenidone - EMEA/H/C/002154/II/0043, Orphan

MAH: Roche Registration Limited, Rapporteur: Greg Markey, "Update of sections 4.2 and 5.2 of the SmPC in order to update the existing safety information with revised recommendations for patients with moderate renal impairment based on the totality of data from clinical studies; the Package Leaflet is updated accordingly."

Galafold - migalastat - EMEA/H/C/004059/II/0010, Orphan

MAH: Amicus Therapeutics UK Ltd, Rapporteur: Johann Lodewijk Hillege,Submission of the final report from study AT1001-041: A phase 3 open label extension study to assess the safety and efficacy of 150 mg migalastat HCl QOD in subjects with Fabry disease who have completed Studies AT1001-011, AT1001- 012 or FAB-CL-205, listed as a category 3 study in the RMP."

Giotrif - afatinib -

EMEA/H/C/002280/II/0023
MAH: Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson,"Update of section 4.8 of the SmPC in order to add the adverse reaction nail disorders with a frequency common based on the results of study 1200.131 and supportive evidence from EGFR TKJ comparator studies. The package leaflet is updated accordingly."

Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/II/0053
MAH: Gilead Sciences International Ltd, Rapporteur: Filip Josephson,"Update of section 4.5 of the SmPC in order to revise information related to the Cytochrome P450 3A (CYP3A) mediated drug-drug interaction potential of ledipasvir based on final results from study GS-US-337-1887, listed as a category 3 study in the RMP"

IBRANCE - palbociclib - EMEA/H/C/003853/II/0006
MAH: Pfizer Limited, Rapporteur: Filip Josephson, "Update of sections 4.2, 4.8 and 5.1 in order to reflect the results of the study A5481008 (PALOMA-2) and of the Phase 2 portion of A5481010 single-arm study. The MAH took the opportunity to implement minor editorial changes to the PIL."

Imnovid - pomalidomide - EMEA/H/C/002682/II/0025, Orphan
MAH: Celgene Europe Limited, Rapporteur: Robert James Hemmings, Submission of a biomarker analysis report following a recommendation from CHMP in MAA procedure (EMEA/H/C/2682/0000) to present the biomarker analysis report based on clinical studies CC-4047-MM-008 and CC-4047-MM-010."

INTELENCE - etravirine - EMEA/H/C/000900/II/0050
MAH: Janssen-Cilag International NV, Rapporteur: Joseph Emmerich "Update of the Product Information (PI) of Etravirine (Intelence®). The PI for Intelence has been updated to include additions to the drug-drug interaction (DDI) information of Etravirine with hepatitis C virus (HCV) direct-acting antivirals (DAAs) and human immunodeficiency virus (HIV) protease inhibitors (PIs) (SmPC sections 4.3 and

4.5 and Patient Information Leafleft (PIL) section 2) and to include a change in the recommended treatment for Intelence overdose (SmPC section 4.9). Specifically, the product information of Intelence is updated with information about the drug-drug interactions of Etravirine with Elbasvir/Grazoprevir (Zepatier), Daclastavir and Simeprevir. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the PI of Intelence with: · Quality Review of Documents (QRD) template v9.1 o A combined SmPC for the 3 different strengths of Intelence (25-, 100- and 200 mg tablets) is provided within this submission o Although as a result of this update the content of the PI is not impacted, significant text formatting is introduced resulting in a rather complex track changes updated PI. Thus, for clarity purposes, the MAH refers the Agency to the submitted track version PI version within this procedure rather than listing all changes in current/proposed section of the Application form. · Quality Review of Documents (QRD) template v10.0 · For consistency with section 4.5 of the currently approved Intelence SmPC, guidance related to co-administration with anti-HIV medicines efavirenz, nevirapine, rilpivirine, indinavir, nelfinavir has been added to section 2 of the PIL. · The address of the Netherlands Local Operating Company (section 6, PIL) and · Minor editorial changes.”	
Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0033 MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, Procedure Manager: Jaime Oliva, EPL: Camille Vleminckx, “Submission of the final clinical study results from study TDM4788g/ BO22589 (MARIANNE) listed as a specific obligation in Annex II.D; this is an interventional randomised, 3-arm, phase III study to evaluate the efficacy and safety of trastuzumab emtansine combined with pertuzumab, or trastuzumab emtansine combined with pertuzumab-placebo versus trastuzumab plus taxane, as first line treatment in HER2-positive progressive or recurrent locally advanced breast cancer or	Timetable: Start: 15.05.2017 CHMP Rapporteur Assessment Report: 19.06.2017 CHMP members comments: 03.07.2017 Updated CHMP Rapporteur Assessment Report: 06.07.2017 Start of written procedure: 11.07.2017 Opinion: 13.07.2017

previously untreated metastatic breast cancer.

As a result of this submission, Annex II of the product information is affected."

Norvir - ritonavir - EMEA/H/C/000127/II/0146

MAH: AbbVie Ltd., Rapporteur: Johann Lodewijk Hillege, "Update of section 4.6 of the SmPC in order to update the safety information on pregnancy and lactation based on the company's core data sheet information."

Tafinlar - dabrafenib - EMEA/H/C/002604/II/0024

MAH: Novartis Europharm Ltd, Rapporteur: Filip Josephson"Update of section 4.5 of the SmPC in order to include some warning on a drug-drug interaction between dabrafenib and rifampicin (a CYP3A4/CYP2C8 inducer) and between dabrafenib and rabeprazole (a pH elevating agent), based on the final results of study 200072, a phase I open-label fixed sequence study to evaluate the effects of potent CYP3A4 inducer (rifampicin) and of a pH elevating agent (rabeprazole) on the repeat dose pharmacokinetics of dabrafenib in subjects with BRAFV60 mutation positive tumours, to fulfil MEA 005."

TAGRISSO - osimertinib - EMEA/H/C/004124/II/0014/G

MAH: AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez"Update of section 5.3 of the SmPC to include non-clinical data related to CNS distribution and in vivo intracranial tumour regression."

TAGRISSO - osimertinib - EMEA/H/C/004124/II/0015

MAH: AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, "Update of sections 5.1 and 5.2 of the SmPC to include data from studies performed to investigate human plasma protein binding (Study No. BS001265-53-AZD9291), the assessment of non-specific incubational binding in transporter inhibition assays (Study No. BS000760-92) and the implications on transporter DDI risk assessment. In addition, the MAH took the opportunity to update the address of the MAH and manufacturer in SmPC section 7, the labelling and the Package Leaflet."

Victrelis - boceprevir -

EMEA/H/C/002332/II/0042

MAH: Merck Sharp & Dohme Limited, Rapporteur: Joseph Emmerich"Update of sections 4.4 of the SmPC to add a warning regarding HBV reactivation observed in patients with HCV/HBV co-infection treated with some direct-acting antivirals not given in combination with peginterferon alfa and ribavirin. The Package Leaflet is updated accordingly.
In addition, the MAH took the opportunity to implement minor editorial updates in the Product Information."

Votubia - everolimus -
EMEA/H/C/002311/II/0044, Orphan

MAH: Novartis Europharm Ltd, Rapporteur: Harald Enzmann,"Update of sections 4.2, 4.4 and 4.8 of the SmPC for Votubia 2.5 mg, 5 mg and 10 mg tablets and 2 mg, 3 mg and 5 mg dispersible tablets in order to reflect on data from study CRAD001M230, in particular to revise dosing recommendations for patients with hepatic impairment, to update the warning related to infections, to include "sepsis" as an adverse drug reaction with the frequency "uncommon" and to revise frequencies of the following adverse drug reactions: "pharyngitis" ["common" to "very common"], "pneumonitis" ["uncommon" to "common"] and "rash" ["common" to "very common]". In addition, the subsection on Paediatric population in section 4.8 of the SmPC was updated based on results from study CRAD001M230.
Furthermore, sections 5.1 and 5.2 of the SmPC for Votubia 2 mg, 3 mg and 5 mg dispersible tablets was updated to add new information on pharmacodynamic and pharmacokinetic properties based on results from study CRAD001M230.
The Package Leaflet is updated accordingly."

Xofigo - radium-223 -
EMEA/H/C/002653/II/0025

MAH: Bayer AG, Rapporteur: Harald Enzmann, , "Update of sections 4.2, 5.1, 5.2, and 11 of the SmPC based on the update of the Xofigo Company Core Data Sheet (CCDS) to version 5.0. The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0 and to introduce non safety related editorial changes to

increase comprehensibility."

Zyclara - imiquimod - EMEA/H/C/002387/II/0013
MAH: Meda AB, Rapporteur: Nithyanandan Nagercoil, "Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to add data on the clinical experience gained with study X-03016-3284 (LEIDA 2) and a meta-analysis of X-03016-3271 and X-03016-3284. The MAH took the opportunity to update the details of local representatives in the PIL."

WS1181/G
Exviera-EMEA/H/C/003837/WS1181/0030/G
Viekirax-EMEA/H/C/003839/WS1181/0034/G
MAH: AbbVie Ltd., Lead Rapporteur: Filip Josephson"Submission of the final report for two phase IIIb studies (studies M13-774 and M13-862) to support the 3 direct-acting antiviral regimen administered with and without ribavirin for 12 weeks for hepatitis C virus genotype 1 infected, treatment-experienced and treatment-naïve subjects without cirrhosis, listed as category 3 studies in the RMP."

WS1189
ANORO-EMEA/H/C/002751/WS1189/0017
Laventair-EMEA/H/C/003754/WS1189/0019
MAH: Glaxo Group Ltd, Lead Rapporteur: Nithyanandan Nagercoil"Update of section 4.8 of the SmPC and relevant section of the PL to add "dysphonia" with rare frequency."

WS1191
Incruse-EMEA/H/C/002809/WS1191/0016
Rolufta-EMEA/H/C/004654/WS1191/0001
MAH: Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro"Update of section 4.8 of the SmPC and relevant section of the PL to add "Eye pain" with a rare frequency."

B.6.10. CHMP-PRAC assessed procedures

Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0045, Orphan
MAH: Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur:

Sabine Straus, , "Update of section 5.1 of the SmPC in order to add 5-year follow-up overall survival (OS) data from patients included in study SG035-0004, a phase 2 open-label study of brentuximab vedotin in the treatment of patients with relapsed or refractory systemic anaplastic large cell lymphoma (ALCL), in accordance with the specific obligation SOB 028. Annex II of the product information and the RMP (version 9.0) are updated accordingly."

Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0060

MAH: UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga"Update of section 4.6 of the SmPC in order to update the information on pregnancy and lactation based on two pharmacokinetics studies evaluation the transfer of Cimzia into breastmilk and via the placenta (UP0016 and UP0017). The Package Leaflet is updated accordingly. The RMP version 12 has also been submitted."

Glyxambi - empagliflozin / linagliptin - EMEA/H/C/003833/II/0005/G

MAH: Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Julie Williams, C.I.1.a. Update of section 4.4. of the SmPC to add a warning on the risk of lower limb amputations to align the PI wording with the parallel finalised Article 20 referral on the risk of lower limb amputation of SGLT2 inhibitors. The Package Leaflet is updated accordingly.

C.I.4.z.Update of sections 4.2., 4.4., 4.5., 4.8., 5.1., of the SmPC to update the PI with data from study 1245.25 Emp-Reg. This is a Phase III, multicentre, international, randomised, parallel group, double blind cardiovascular safety study of BI 10773 (10 mg and 25 mg administered orally once daily) compared to usual care in type 2 diabetes mellitus patients with increased cardiovascular risk. An RMP (v.2.0) has also been submitted."

Keytruda - pembrolizumab - EMEA/H/C/003820/II/0028

MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus"Update sections 4.4 and 4.8 of the SmPC to include the risk of

myocarditis that has been reported in patients treated with pembrolizumab. The Package Leaflet has been updated accordingly. An updated RMP version 10.0 was provided as part of the application."

Keytruda - pembrolizumab - EMEA/H/C/003820/II/0029

MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus"Submission of the final study report for non-clinical study "Anti-Murine PD-1 Antibody (muDX400 L-005571333): Exploratory Multiple-Dose Subcutaneous Immunotoxicity Study in Mice with Hepatitis B Vaccine (L-005552770). TT #15-1105". An updated RMP version 11.0 was provided as part of the application."

Latuda - lurasidone - EMEA/H/C/002713/II/0016

MAH: Sunovion Pharmaceuticals Europe Ltd, Rapporteur: Filip Josephson, PRAC Rapporteur: Qun-Ying Yue"Submission of the final CSR for Study D1001057, an extension of study of SM-13496 evaluating the long-term safety and efficacy of lurasidone (40 mg/day or 80 mg/day) in patients with schizophrenia.
The RMP is being updated (ver. 5.0) with information relative to this study and also information relative to Study D1050301, which has already been assessed in P46/006."

Mozobil - plerixafor - EMEA/H/C/001030/II/0032, Orphan

MAH: Genzyme Europe BV, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "Update of sections 4.2 and 5.2 of the SmPC in order to reflect the results of the completed study MSC12830 (MOZ11809), entitled "A Phase 4, Multicenter, Randomized, Comparator Trial Evaluating the Standard Weight-Based Dose (0.24 mg/kg) Compared to a Fixed Dose (20 mg) of Plerixafor Injection in Combination with G-CSF to Mobilize and Collect ≥5 x 106 CD34+ cells/kg in ≤4 Days and to Evaluate the Difference in Total Systemic Exposure in Patients with Non-Hodgkin's Lymphoma Weighing ≤70 kg" listed as a category 3 study in the RMP.

The Package Leaflet is updated accordingly. The

RMP version 9.0 has also been submitted.

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

Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0017

MAH: Orexigen Therapeutics Ireland Limited, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Martin Huber"Submission of the final report from phase I study NaltrexBuprop-1001 (TQT) to evaluate the potential effect of Naltrexone and Bupropion extended-release combination on cardiac repolarization in healthy subjects and updated RMP to include study NaltrexBuprop-1001 but also studies recently completed (NB-CVOT, NaltrexBuprop-4001, NaltrexBuprop-1004 and NB-404).
The MAH also took the opportunity to include throughout the RMP references to the PASS protocols currently under discussion at the PRAC."

Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0021

MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Almath Spooner"Update of section 4.8 of the SmPC in order to add information on respiratory events based on final results from study Study VX14-809-106 (Study 106), a Phase 3b, open-label study to evaluate safety and tolerability of lumacaftor and ivacaftor combination therapy in subjects 12 years and older with Cystic Fibrosis and advanced lung disease, homozygous for the F508del-CFTR Mutation. Efficacy was evaluated as a secondary objective. This study report is being submitted to fulfil MEA 002.
An updated RMP (version 3.2) has also been submitted."

Perjeta - pertuzumab - EMEA/H/C/002547/II/0029

MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver"Update of sections 4.2, 4.4, 4.8, 5.1 of the SmPC, annex II and relevant sections of the PL in order to update information on cardiac safety and reflect the results from study BERNICE (WO29217) listed as a specific obligation in the

Annex II; BERNICE is an ongoing Multicenter, Multinational, Phase II Study to Evaluate Perjeta in Combination with Herceptin and Standard Neoadjuvant Anthracycline-Based Chemotherapy in Patients with HER2- Positive, Locally Advanced, Inflammatory, or Early-Stage Breast Cancer.
The RMP v.9 has also been submitted."

Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0119

MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.2, 4.8 and 5.1 to implement the PATH (IgPro20_3003) study results (safety & efficacy study with chronic inflammatory demyelinating polyneuropathy (CIDP) patients). In addition, the MAH took the opportunity to implement a clarification on the hyperprolinemia types in section 4.3 and some editorial changes to section 5.2 of the SmPC. The Package leaflet was updated accordingly. The RMP is updated (version 5.0)"

Sivextro - tedizolid phosphate - EMEA/H/C/002846/II/0019

MAH: Merck Sharp & Dohme Limited, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Dolores Montero Corominas, "Update of section 4.8 of the SmPC of the concentrate for solution for infusion formulation, in order to add information from BAY119-2631/16121, a Phase 3 randomized, double-blind, multi-centre study comparing the efficacy and safety of intravenous to oral 6-day tedizolid phosphate and intravenous to oral 10 day linezolid for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and change the reported expected frequency of the adverse reaction "infusion site phlebitis" from "uncommon" to "common". The Package Leaflet is updated accordingly. An updated RMP (version 3.0) has also been submitted, proposing to collect safety information regarding tedizolid phosphate by conducting three investigator initiated studies and deleting the original proposed long term safety study. The MAH also took the opportunity to make minor editorial corrections throughout the product information."

SYLVANT - siltuximab - EMEA/H/C/003708/II/0023, Orphan

MAH: Janssen-Cilag International NV, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Brigitte Keller-Stanislawski, , "Submission of the final report from study CNTO328SMM2001 listed as a category 3 study in the RMP. This is a 'Phase 2, Randomized, Double-blind, Placebo-controlled, Multicenter Study of Siltuximab (Anti IL-6 Monoclonal Antibody) in Subjects with High-risk Smoldering Multiple Myeloma' to evaluate immunogenicity data. No changes to the PI are proposed. The RMP is being updated accordingly."

Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0117

MAH: GSK Biologicals SA, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to reflect the results from study10PN-PD-DIT-072, a phase III, open, controlled, multi-centric study to evaluate the immunogenicity, safety and reactogenicity of Synflorix in children at an increased risk of pneumococcal infection. The Package Leaflet is updated accordingly. An updated RMP version 16 has also been submitted. This submission fulfils the post-authorisation measure MEA 065."

TAGRISSO - osimertinib - EMEA/H/C/004124/II/0016

MAH: AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Sabine Straus"Provision of the final CSR for Study Aura 17; a phase II, open label, single-arm study to assess the safety and efficacy of AZD9291 in Asia pacific patients with locally advanced/metastatic non-small cell lung cancer whose disease has progressed with previous epidermal growth factor receptor tyrosine kinase inhibitor therapy and whose tumours harbour a T790M mutation within the epidermal growth factor receptor gene). An updated RMP version 7.0 was provided as part of the application."

Uptravi - selexipag - EMEA/H/C/003774/II/0009

MAH: Actelion Registration Ltd., Rapporteur: Martina Weise, PRAC Rapporteur: Julie Williams"Update of section 4.5 of the SmPC to add information on the effect of selexipag administration on the pharmacokinetics of

midazolam, its metabolite 1-hydroxymidazolam and the CYP3A4 metabolism, based on data from the completed clinical pharmacology study AC-065-114, a single-centre, open-label, randomized, two-treatment crossover Phase 1 study investigating the effect of selexipag on the pharmacokinetics of midazolam and its metabolite 1-hydroxymidazolam in healthy male subjects. An updated RMP (version 5.1) has also been submitted, to add the results of study AC-065-114, reclassify 'hyperthyroidism' as an important identified risk and update the PASS timelines and protocol versions in accordance with the current EXPOSURE protocol version 3 and the EDUCATE protocol version 2."	
XALKORI - crizotinib - EMEA/H/C/002489/II/0049/G MAH: Pfizer Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Caroline Laborde"Submission of the final results related of the Non_Interventional Post-Authorisation Safety Study (PASS) A8081049 "A cross-sectional study to evaluate the effectiveness of XALKORI (PF_02341066, also referred to as crizotinib) Therapeutic Management Guide among physicians prescribing XALKORI in Europe" and PASS A8081050 "A cross-sectional study to evaluate the effectiveness of XALKORI Patient Information Brochure among non-small cell lung cancer (NSCLC) patients receiving XALKORI treatment in Europe". In the light of the results from PASS study A8081049, the MAH is proposing to update Annex II to remove the XALKORI TMG from the Educational Materials. The MAH is also taking the opportunity to state "monotherapy" in section 4.1 of the SmPC as requested by CHMP and to bring the PI in line with the latest QRD template."	
Zykadia - ceritinib - EMEA/H/C/003819/II/0015 MAH: Novartis Europharm Ltd, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Ulla Wändel Liminga,"Update of sections 4.2, 4.4, 4.5, 4.8 and 5.2 of the SmPC in order to update the safety informatio based on based on the primary PK and preliminary safety results of the food effect study CLDK378A2112. The Package Leaflet is updated accordingly.	

The RMP version 9.0 has also been submitted."

WS1182
AMGEVITA-EMEA/H/C/004212/WS1182/0001
SOLYMBIC-EMEA/H/C/004373/WS1182/0001
MAH: Amgen Europe B.V., Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Ulla Wändel Liminga"Submission of the final report from study/studies 20130258, An open-label, single-arm extension study to evaluate the long-term safety and efficacy of ABP 501 in subjects with moderate to severe rheumatoid arthritis, listed as a category 3 study in the RMP (MEA002). No changes of the PI are proposed, the RMP is updated accordingly."

B.6.11. PRAC assessed procedures

PRAC Led
Aclasta - zoledronic acid - EMEA/H/C/000595/II/0069
MAH: Novartis Europharm Ltd, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina DunderSubmission of the final 5-year report from study (ZOL446H2422) listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study using health registries to compare safety of Aclasta against oral bisphosphonates and untreated population controls."

PRAC Led
NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0020
MAH: Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus"Submission of an amended protocol for PASS study NN7008-3553, category 3 study in the RMP.
Submission of an updated RMP version 3 to update the timelines of the milestones in order to integrate the required additional pharmacovigilance activities, which include a change in the Last Patient Last Visit (LPLV) date and a change in the Clinical Trial Report (CTR) finalisation date. In addition, the duration of the trial has been amended from 4 to 7 years."

PRAC Led

Rebif - interferon beta-1a - EMEA/H/C/000136/II/0129

MAH: Merck Serono Europe Limited, PRAC Rapporteur: Qun-Ying Yue, PRAC-CHMP liaison: Filip Josephson"Submission of an updated RMP version 9.0 in order to upgrade the important potential risk "Immunogenicity/safety risk associated with the formation of neutralizing antibodies" to important identified risk"

PRAC Led

Retacrit - epoetin zeta - EMEA/H/C/000872/II/0077

MAH: Hospira UK Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Valerie Strassmann, PRAC-CHMP liaison: Martina Weise"Submission of the final report from study (Registry based Health Care Database Study (HDBS-study) linked to PASCO (PMS-830-07-0043)) listed as a category 3 study in the RMP. This is an Observational Study on the Incidence of Thromboembolic Events in Patients with Renal Anemia Treated with Erythropoietin-Zeta as Compared with Erythropoietin-Alpha and other Erythropoiesis-Stimulating Agents."

PRAC Led

Silapo - epoetin zeta - EMEA/H/C/000760/II/0045

MAH: STADA Arzneimittel AG, Rapporteur: Martina Weise, PRAC Rapporteur: Valerie Strassmann, PRAC-CHMP liaison: Martina Weise"Submission of the final report from study (Registry based Health Care Database study – HDBS study linked to PASCO (PMS-830-07-0043)) listed as a category 3 study in the RMP. This is an Observational Study on the Incidence of Thromboembolic Events in Patients with Renal Anemia Treated with Erythropoietin-Zeta as Compared with Erythropoietin-Alpha and other Erythropoiesis-Stimulating Agents. In addition, an updated RMP (version 11) is submitted to reflect the outcome of the study."

PRAC Led

Yervoy - ipilimumab - EMEA/H/C/002213/II/0049

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, PRAC-CHMP liaison:

Johann Lodewijk Hillege"Submission of an updated RMP (version 17) in order to amend the study objectives and milestones for two studies: - study CA184332, a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab (Yervoy) as first line therapy in a community setting, a category 3 study in the RMP (MEA 029): to submit the final study report with 2-years of follow-up - study CA184338, a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab (Yervoy) as first line therapy, a category 3 study in the RMP (MEA 030): to submit the final study report with 4-years of follow-up."
PRAC Led **WS1188** **Humalog-EMEA/H/C/000088/WS1188/0157** **Liprolog-EMEA/H/C/000393/WS1188/0120** MAH: Eli Lilly Nederland B.V., Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Robert James Hemmings, "Submission of the final report of a non-interventional post-authorisation safety study EUPAS 13422. This study is aimed to evaluate the impact of additional risk minimisation measures on healthcare professionals and on patients' understanding and their behaviour regarding the risk of hypoglycaemia and/or hyperglycaemia due to medication errors associated with administration of Humalog 200 U/ml KwikPen."

B.6.12. CHMP-CAT assessed procedures

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

WS1153 **Hexacima-EMEA/H/C/002702/WS1153/0063** **Hexaxim-EMEA/H/W/002495/WS1153/00**

69
Hexyon-EMEA/H/C/002796/WS1153/006
7
MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus

WS1171
Jentadueto-EMEA/H/C/002279/WS1171/0
039
Synjardy-EMEA/H/C/003770/WS1171/00
27
MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege

WS1173
Glyxambi-EMEA/H/C/003833/WS1173/00
06
Jardiance-EMEA/H/C/002677/WS1173/00
32
Synjardy-EMEA/H/C/003770/WS1173/00
28
MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege

WS1175
Abseamed-EMEA/H/C/000727/WS1175/0
064
Binocrit-EMEA/H/C/000725/WS1175/006
4
Epoetin alfa
Hexal-EMEA/H/C/000726/WS1175/0063
MAH: SANDOZ GmbH, Lead Rapporteur: Alexandre Moreau

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

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

B.7.2. Monthly Line listing for Type I variations

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

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

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

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

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

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

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

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

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

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

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

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

G. ANNEX G

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

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

Qualification of Biomarkers:

HTA:

Post-Scientific Advice Issues:

G.2. Ongoing procedures

G.3. PRIME

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

G.3.1. List of procedures concluding at 15-18 May 2017 CHMP plenary:

Oncology	
1. **Asunercept,** Treatment of glioblastoma	The CHMP granted eligibility to PRIME and adopted the critical summary report.
2. Treatment of acute myeloid leukaemia	The CHMP denied eligibility to PRIME and adopted the critical summary report.
3. Treatment of pancreatic cancer	The CHMP denied eligibility to PRIME and adopted the critical summary report.
4. Treatment of metastatic uveal melanoma	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Immunology-Rheumatology-Transplantation	
Recombinant IgG degrading enzyme of Streptococcus pyogenes Prevention of graft rejection following solid organ transplantation	The CHMP granted eligibility to PRIME and adopted the critical summary report.
5. Treatment of diffuse cutaneous systemic sclerosis	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Infectious Diseases	
6. **Synthetic 47-amino-acid N-myristoylated lipopeptide, derived from the preS region of hepatitis B virus**Treatment of chronic	The CHMP granted eligibility to PRIME and adopted the critical summary report.

hepatitis D infection	
7. Treatment of cystic fibrosis exacerbations	The CHMP denied eligibility to PRIME and adopted the critical summary report.
8. **Olipudase alfa** Treatment of non-neurological manifestations of acid sphingomyelinase deficiency (ASMD)	The CHMP granted eligibility to PRIME and adopted the critical summary report.
Neonatology-Paediatric Intensive Care	
9. Prevention of necrotising enterocolitis	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Uro-nephrology	
10. Treatment of calciphylaxis	The CHMP denied eligibility to PRIME and adopted the critical summary report.
11. Rapastinel Adjunctive treatment of major depressive disorder	The CHMP granted eligibility to PRIME and adopted the critical summary report.

G.3.2. List of procedures starting in May 2017 for June 2017 CHMP adoption of outcomes

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