21 December 2017
EMA/829219/2017
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Minutes of the meeting on 06-09 November 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).

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

Table of contents

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) November 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 06-09 November 2017 (to be published post December 2017 CHMP meeting).

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

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

1.2. Adoption of agenda

CHMP agenda for 06-09 November 2017

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 9-12 October 2017

The CHMP adopted the CHMP minutes for 9-12 October 2017. The Minutes of the November 2017 CHMP ORGAM meeting held on 30 October 2017, together with all decisions taken at that meeting, were adopted.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. Adynovi - rurioctocog alfa pegol - EMEA/H/C/004195

Baxalta Innovations GmbH; treatment of haemophilia A

Scope: Oral explanation

Action: Oral explanation to be held 8 November 2017 at time 11:00

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

List of Outstanding Issues adopted on 12.10.2017, 21.04.2017, 15.12.2016. List of Questions adopted on 21.07.2016.

An oral explanation was held on 8 November 2017 at time 11:30.

See 3.1

2.1.2. plitidepsin - Orphan - EMEA/H/C/004354

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

Scope: Oral explanation

Action: Oral explanation to be held 7 November 2017 at time 11:00

List of Outstanding Issues adopted on 14.09.2017. List of Questions adopted on 23.02.2017.

An oral explanation was held on 7 November 2017 at time 11:45.

See 3.2

2.1.3. semaglutide - EMEA/H/C/004174

to improve glycaemic control in adults with type 2 diabetes and to prevent cardiovascular events

Scope: Oral explanation

Action: Oral explanation to be held 7 November 2017 at time 16:00

List of Outstanding Issues adopted on 14.09.2017. List of Questions adopted on 21.04.2017.

The CHMP agreed to cancel the oral explanation.

See 3.2

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

treatment of progressive multiple sclerosis (primary or secondary)

Scope: Oral explanation

Action: Oral explanation to be held on 8 November 2017 at time 14:00

List of Outstanding Issues adopted on 14.09.2017. List of Questions adopted on 15.12.2016.

An oral explanation was held on 8 November 2017 at time 14:00.

See 3.7

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

Clovis Oncology UK Ltd; treatment of ovarian cancer

Scope: Oral explanation/opinion

Action: Oral explanation to be held 8 November 2017 at time 09:00

List of Outstanding Issues adopted on 14.09.2017, List of Questions adopted on 23.03.2017.

An oral explanation was held 8 November 2017 at time 09:00.

See 3.2

2.2. Re-examination procedure oral explanations

2.2.1. Fanaptum - iloperidone - EMEA/H/C/004149

Vanda Pharmaceuticals Ltd.; treatment of schizophrenia

Scope: Oral explanation/opinion

Action: Oral explanation to be held 7 November 2017 at time 09:00

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

Opinion adopted on 20.07.2017

The Committee noted the report from Ad Hoc Expert Group meeting.

An oral explanation was held 7 November 2017 at time 09:00. The Company's presentation focussed on unmet medical need in schizophrenia and iloperidone's clinical position as 2nd line indicated medicine.

See 3.5

2.2.2. Onzeald - etirinotecan pegol - EMEA/H/C/003874

Nektar Therapeutics UK Limited; treatment of breast cancer with brain metastases

Scope: Oral explanation/opinion

Action: Oral explanation to be held 7 November 2017 at time 14:00

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

Opinion adopted on 20.07.2017

Oral explanation was held 7 November 2017 at time 14:45. During the oral explanation the company presented the grounds for re-examination.

See 3.5

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

Baxalta Innovations GmbH; treatment of haemophilia A

Scope: Opinion/Oral explanation

Action: For adoption

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

List of Outstanding Issues adopted on 12.10.2017, 21.04.2017, 15.12.2016. List of Questions adopted on 21.07.2016.

See 2.1

An oral explanation was held 8 November 2017 at time 11:30.

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 rurioctocog alfa pegol 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 summary of opinion was circulated for information.

3.1.2. Darunavir Krka - darunavir - EMEA/H/C/004273

KRKA, d.d., Novo mesto; treatment of HIV-1 infection

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 14.09.2017. List of Questions 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 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 noted the letter of recommendation dated 8 November 2017.

3.1.3. Darunavir Krka d.d. - darunavir - EMEA/H/C/004891

KRKA, d.d., Novo mesto; treatment of HIV-1 infection

Scope: Opinion

Action: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Prezista, Duplicate of Darunavir Krka

List of Outstanding Issues adopted on 14.09.2017.

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 noted the letter of recommendation dated 8 November 2017.

3.1.4. Fasenra benralizumab - EMEA/H/C/004433

AstraZeneca AB; treatment of severe asthma with an eosinophilic phenotype

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 14.09.2017. List of Questions adopted on 21.04.2017.

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 benralizumab 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 summary of opinion was circulated for information.

The CHMP noted the letter of recommendation dated 7 November 2017.

3.1.5. Fulvestrant Mylan - fulvestrant - EMEA/H/C/004649

Mylan S.A.S; treatment of breast cancer

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 14.09.2017. List of Questions adopted on 21.04.2017.

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.

3.1.6. Intrarosa - prasterone - EMEA/H/C/004138

Endoceutics Limited; treatment of vulvovaginal atrophy

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 14.09.2017, 22.06.2017, 26.01.2017, 13.10.2016. List of Questions adopted on 26.05.2016.

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

addressed.

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

Furthermore, the CHMP considered that prasterone is not 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.

3.1.7. Jorveza - budesonide - Orphan - EMEA/H/C/004655

Accelerated assessment

Dr. Falk Pharma GmbH; treatment of eosinophilic esophagitis (EoE)

Scope: Opinion

Action: For adoption

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

List of Questions adopted on 12.09.2017.

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.

3.1.8. Mvasi - bevacizumab - EMEA/H/C/004728

Amgen Europe B.V.; treatment of metastatic carcinoma of the colon or rectum ,metastatic breast cancer, unresectable advanced, metastatic or recurrent squamous and non-squamous non-small cell lung cancer, advanced and/or metastatic renal cell cancer, advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer and persistent, recurrent, or metastatic carcinoma of the cervix.

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 14.09.2017. List of Questions adopted on 21.04.2017.

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.

3.1.9. Ocrevus - ocrelizumab - EMEA/H/C/004043

Roche Registration Limited; treatment of multiple sclerosis

Scope: Opinion

Action: For adoption

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

Oral explanation held on 10.10.2017. Oral explanation held on 13.09.2017. List of Outstanding Issues adopted on 12.10.2017, 14.09.2017, 23.03.2017. List of Questions adopted on 15.09.2016.

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

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (27 out of 32 votes) together with the CHMP assessment report and translation timetable.

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

The Icelandic Member was in agreement with the CHMP recommendation. The Norwegian Member was not in agreement.

The divergent position (Hanne Lomholt Larsen, Alar Irs, Robert James Hemmings, Johann Lodewijk Hillege, Greg Markey, Svein Rune Andersen) was 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 noted the letter of recommendation dated 7 November 2017.

3.1.10. Prevymis - letermovir - Orphan - EMEA/H/C/004536

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

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 12.10.2017, 12.09.2017. List of Questions adopted on 18.07.2017.

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 letermovir 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 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. expanded human allogeneic mesenchymal adult stem cells extracted from adipose tissue - Orphan - ATMP - EMEA/H/C/004258

Tigenix, S.A.U.; treatment of complex perianal fistula(s)

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 17.02.2017. List of Questions adopted on 15.07.2016.

The CHMP was updated on discussions at the CAT during their November 2017 meeting.

The CHMP noted that the amended 2nd list of outstanding issues together with a specific timetable will be adopted by the CAT via written procedure.

3.2.2. plitidepsin - Orphan - EMEA/H/C/004354

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

Scope: Oral explanation

Action: Oral explanation to be held 7 November 2017 at time 11:00

List of Outstanding Issues adopted on 14.09.2017. List of Questions adopted on 23.02.2017.

An oral explanation was held on 7 November 2017 at time 11:45.

Post meeting note: The Committee adopted a 2nd list of outstanding issues with a specific timetable via written procedure on 16 November 2017.

3.2.3. trastuzumab - EMEA/H/C/002575

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 23.02.2017.

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.

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

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

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.

The CHMP agreed to a clock stop to respond to the list of outstanding issues with a specific timetable.

3.2.5. trastuzumab - EMEA/H/C/004361

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

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 20.07.2017.

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.

3.2.6. binimetinib - EMEA/H/C/004052

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

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.

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

3.2.7. semaglutide - EMEA/H/C/004174

to improve glycaemic control in adults with type 2 diabetes and to prevent cardiovascular events

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 14.09.2017. List of Questions adopted on 21.04.2017.

See 2.1

The CHMP agreed to cancel the oral explanation.

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

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

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

Clovis Oncology UK Ltd; treatment of ovarian cancer

Scope: Oral explanation/opinion

Action: For adoption

List of Outstanding Issues adopted on 14.09.2017, List of Questions adopted on 23.03.2017.

See 2.1

An oral explanation was held 8 November 2017 at time 09:00.

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

3.2.9. ertugliflozin / metformin hydrochloride - EMEA/H/C/004314

treatment of type 2 diabetes mellitus

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 22.06.2017.

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.

3.2.10. ertugliflozin - EMEA/H/C/004315

type 2 diabetes mellitus

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 22.06.2017.

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.

3.2.11. ertugliflozin / sitagliptin - EMEA/H/C/004313

type 2 diabetes mellitus

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 22.06.2017.

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.

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

3.3.1. glycopyrronium / formoterol fumarate dihydrate - EMEA/H/C/004245

indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD)

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. bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449

treatment of adults infected with human immunodeficiency virus-1 (HIV-1)

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

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

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

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.4. deferiprone - EMEA/H/C/004710

treatment of iron overload in thalassemia major

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

The CHMP agreed to the request by the applicant for a clock stop to respond to the list of questions.

3.3.5. lesinurad / allopurinol - EMEA/H/C/004412

gout

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.6. pacritinib - Orphan - EMEA/H/C/004793

CTI Life Sciences Limited; treatment of disease-related splenomegaly and control of symptoms in patients with primary myelofibrosis (PMF), post-polycythemia vera myelofibrosis (PPV-MF), or post-essential thrombocythemia myelofibrosis (PET-MF) who have thrombocytopenia (platelet counts ≤100,000 /µL).

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.

3.3.7. botulinum toxin type A - EMEA/H/C/004587

temporary improvement in the appearance of moderate to severe vertical lines between the eyebrows

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.

3.3.8. trastuzumab - EMEA/H/C/004463

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

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with

the list of questions.

3.3.9. meropenem / vaborbactam - EMEA/H/C/004669

treatment of infections

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

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

3.4.1. peramivir - EMEA/H/C/004299

treatment of influenza

Scope: Request for extension of clock stop to respond to List of outstanding issue adopted on 12.10.2017

Action: For adoption

List of outstanding issue adopted on 12.10.2017. List of Questions adopted on 18.05.2016.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to List of outstanding issue adopted on 12.10.2017 with a specific timetable.

3.4.2. brigatinib - EMEA/H/C/004248

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

Scope: Request for extension of clock stop to respond to List of outstanding issue adopted on 12.10.2017

Action: For adoption

List of outstanding issue adopted on 12.10.2017. List of Questions adopted on 22.06.2017.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to List of outstanding issue adopted on 12.10.2017, with a specific timetable.

3.4.3. betrixaban - EMEA/H/C/004309

treatment of prophylaxis of venous thromboembolism (VTE)

Scope: Draft list of questions and list of experts for the SAG meeting

Action: For adoption

List of Outstanding Issues adopted on 12.10.2017. List of Questions adopted on 21.04.2017.

The list of questions and list of experts for the SAG meeting will be adopted via written procedure after the CHMP plenary.

3.4.4. carmustine - EMEA/H/C/004326

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

Scope: Request for extension of clock stop to respond to List of outstanding issue adopted on 12.10.2017

Action: For adoption

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

The CHMP agreed to the request for an extension of clock stop to respond to List of outstanding issue adopted on 12.10.2017, with a specific timetable.

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

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

Scope: Draft list of questions and list of experts for the ad-hoc expert group meeting

Action: For adoption

List of Outstanding Issues adopted on 14.09.2017. List of Questions adopted on 26.01.2017.

The CHMP adopted the list of questions and list of experts for the ad-hoc expert group meeting .

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

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

Scope: List of questions to SAG

Action: For adoption

List of Outstanding Issues adopted on 20.07.2017. List of Questions adopted on 15.12.2016.

The CHMP adopted the list of questions to the SAG.

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

treatment of diabetes mellitus

Scope: Request for extension of clock stop to respond to List of outstanding issue adopted on 12.10.2017

Action: For adoption

List of outstanding issue adopted on 12.10.2017. List of Questions adopted on 23.02.2017.

The CHMP agreed to the request for an extension of clock stop to respond to List of outstanding issue adopted on 12.10.2017, with a specific timetable.

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

3.5.1. Fanaptum - iloperidone - EMEA/H/C/004149

Vanda Pharmaceuticals Ltd.; treatment of schizophrenia

Scope: Opinion/Oral explanation

Action: For adoption

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

Opinion adopted on 20.07.2017

See 2.2

The Committee noted the report from Ad Hoc Expert Group meeting. The experts were of 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 also 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.

An oral explanation was held 7 November 2017 at time 09:00. The Company's presentation focussed on unmet medical need in schizophrenia and iloperidone's clinical position as 2nd line indicated medicine.

The CHMP looked again at the data submitted by the company and the company's proposal to introduce several new measures to manage the risk of QT prolongation. The measures included restricting use to patients whose treatment with another antipsychotic did not work or was no longer tolerated, and prohibiting use in patients who cannot effectively break down the medicine or are taking certain other medicines.

However, the CHMP was still concerned about the risk of QT prolongation and considered that the measures proposed would not appropriately address this risk in clinical practice. In addition, the Committee was still concerned by the modest effectiveness of Fanaptum and

its delayed onset of action.

Therefore, the CHMP concluded that the benefits of Fanaptum did not outweigh its risks and maintained its previous recommendation that the medicine be refused marketing authorisation.

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.

3.5.2. Onzeald - etirinotecan pegol - EMEA/H/C/003874

Nektar Therapeutics UK Limited; treatment of breast cancer with brain metastases

Scope: Opinion/oral explanation

Action: For adoption

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

Opinion adopted on 20.07.2017

See 2.2

The Committee was reminded SAG discussions from the meeting 12 July 2017.

Oral explanation was held 7 November 2017 at time 14:45. During the oral explanation the company presented the grounds for re-examination. BEACON study results were presented more specifically. It was noted that conditional marketing authorisation was sought. In addition, ATTAIN study details were presented.

The CHMP considered that the benefit of Onzeald in the treatment of advanced breast cancer that had spread to the brain and other parts of the body had not been sufficiently demonstrated. The claim of effectiveness relied on data from a subgroup of patients from a main study which, overall, failed to convincingly show the effectiveness of Onzeald. The Committee considered that the data from this subgroup, which were not supported by additional studies, were not sufficient to prove the effectiveness of Onzeald, even when analysed by different methods.

Therefore, the CHMP was of the opinion that the study did not provide enough evidence on the benefits of Onzeald and recommended that the marketing authorisation be refused.

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

The Norwegian Member was in agreement with the CHMP recommendation. The Icelandic Member was not in agreement with the CHMP recommendation

The divergent position was appended to the opinion.

The refusal question and answers document was circulated for information.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. bevacizumab - EMEA/H/C/004360

treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer, unresectable advanced, metastatic or recurrent squamous and non-squamous non-small cell lung cancer, advanced and/or metastatic renal cell cancer, advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer and persistent, recurrent, or metastatic carcinoma of the cervix

Scope: Withdrawal of initial marketing authorisation application

Action: For information

List of Outstanding Issues adopted on 14.09.2017. List of Questions adopted on 21.04.2017.

The CHMP noted the withdrawal of the marketing authorisation application.

3.7.2. sirukumab - EMEA/H/C/004165

treatment of rheumatoid arthritis

Scope: Withdrawal of initial marketing authorisation application

Action: For information

List of Outstanding Issues adopted on 14.09.2017, 22.06.2017. List of Questions adopted on 26.01.2017.

The CHMP noted the withdrawal of the marketing authorisation application.

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

treatment of progressive multiple sclerosis (primary or secondary)

Scope: Oral explanation

Action: Oral explanation to be held on 8 November 2017 at time 14:00

List of Outstanding Issues adopted on 14.09.2017. List of Questions adopted on 15.12.2016.

See 2.1

An oral explanation was held on 8 November 2017 at time 14:00.

Post-meeting note: The applicant informed EMA about the withdrawal of the 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. Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/X/0020

Vertex Pharmaceuticals (Europe) Ltd.

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Almath Spooner

Scope: "Extension application to add a new strength of film-coated tablets (100 mg Lumacaftor / 125 mg Ivacaftor) for paediatric use (6 to 11 years). The RMP (version 3.1) is updated accordingly."

Action: For adoption

List of Questions adopted on 20.07.2017.

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 CHMP adopted the similarity CHMP Assessment Report for Orkambi.

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

No items

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

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

Novartis Europharm Limited

Rapporteur: Harald Enzmann, Co-Rapporteur: Greg Markey

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

Action: For adoption

The Committee discussed the issues identified in this application. The CHMP noted the lack of clinical data in the extension application and discussed the acceptability of a biowaiver for

the new strength.

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

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

No items

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

No items

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

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

5.1.1. Adcetris - brentuximab vedotin - Orphan - EMEA/H/C/002455/II/0048

Takeda Pharma A/S

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: "Extension of indication to include the new indication "ADCETRIS is indicated for the treatment of adult patients with CD30+ cutaneous T-cell lymphoma (CTCL) after at least 1 prior 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. Information on peripheral neuropathy was also updated in the SmPC. An updated RMP (version 10.1) has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 20.07.2017.

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.

5.1.2. Bosulif - bosutinib - Orphan - EMEA/H/C/002373/II/0025/G

Pfizer Limited

Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber

Scope: "Extension of Indication to include treatment of adult patients with newly diagnosed Philadelphia Chromosome positive (Ph+) Chronic Phase (CP) Chronic Myelogenous Leukaemia (CML) for Bosulif based on study AV001. In addition, the MAH updated SmPC with safety and efficacy data from studies B1871006 and B1871008. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated accordingly. Moreover, the updated RMP version 4.0 has been submitted, as part of this application. Furthermore, the Annex IIIA is brought in line with the latest QRD template version 10."

Action: For adoption

The Committee discussed the issues identified in this application. The Committee discussed the available data in support of this extension of indication and agreed that further clarification and data on PK and PD, but also some efficacy and safety aspects were required before concluding on the benefit/risk assessment.

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

The CHMP adopted the CHMP similarity Assessment Report for Bosulif.

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

UCB Pharma S.A.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of Indication to include plaque psoriasis in adult patients for Cimzia; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 13 has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application. It was noted that the proposed indication is too wide and not in accordance with the indications for recently approved monoclonal antibodies in psoriasis.

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

5.1.4. Genvoya - elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004042/II/0026

Gilead Sciences International Limited

Rapporteur: Robert James Hemmings, PRAC Rapporteur: Amelia Cupelli

Scope: “Extension of Indication to include paediatric patients from 6 of age to less than 12 years of age, with body weight of at least 25kg, infected with human immunodeficiency virus-1 (HIV-1) without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir, for Genvoya.

As a consequence, sections 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated based on the analysis of the paediatric study GS-US-292-0106 (Cohort 2) “A Phase 2/3, Open-Label Study of the Pharmacokinetics, Safety, and Antiviral Activity of the Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) Single Tablet Regimen (STR) in HIV-1 Infected Antiretroviral Treatment Naive Adolescents and Virologically Suppressed Children”.

The Package Leaflet and the Risk Management Plan (v. 3) are updated in accordance.”

Action: For adoption

Request for Supplementary Information adopted on 20.07.2017, 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.

5.1.5. Isentress - raltegravir - EMEA/H/C/000860/II/0064/G

Merck Sharp & Dohme Limited

Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams

Scope: “Extension of indication (for Isentress 100 mg granules for oral suspension) to include treatment of HIV-1 exposed full-term neonates (under the age of 4 weeks) based on safety and PK data from one pivotal Phase 1 study, IMPAACT P1110 (Protocol 080), in a total of 42 HIV-1 exposed full-term infants (defined as ≥37 weeks gestational age and ≥2000 g), who received either 2 single doses of oral suspension, within 48 hours of birth and Day 7-10 of age (Cohort I), or a multiple-dose regimen of raltegravir over the first 6 weeks of age (Cohort II). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly.
The provision of the study (IMPAACT P1110) addresses the final PIP measure, i.e. Study 4, conducted to generate PK, safety, and tolerability data in HIV exposed neonates and infants <6 weeks of age born to HIV infected mothers.
Further, the Applicant proposed to update the suspension volume from 5 mL to 10 mL for a final suspension concentration of 10 mg/mL to facilitate accurate measurement of the smaller doses required for neonates. As a consequence, there was a need to replace the 5 mL syringe supplied in the current commercial kit with 3 new oral dosing syringes, and sizes (1 mL, 3 mL, and 10 mL), from a different (new) supplier. As a consequence, sections 6.5 and 6.6 of the SmPC have been updated and the labelling and instructions for use in the Package Leaflet have been updated accordingly.
An updated RMP version 12.0 was submitted as part of the application.”

Action: For adoption

The Committee discussed the issues identified in this application. The remaining questions were related to clinical aspects - summary of the results of the simulations with other doses, reliability of the model to support dosing in pre-exposed infants, explanation related to dilution volume and other questions.

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

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

Swedish Orphan Biovitrum AB (publ)

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Fátima Ventura, PRAC Rapporteur: Doris Stenver

Scope: "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 and the RMP (version 4.0) are updated accordingly.
In addition, the marketing authorisation holder took the opportunity to make some editorial changes in the SmPC and Package leaflet."

Action: For adoption

Request for Supplementary Information adopted on 20.07.2017.

The Committee discussed the issues identified in this application. It was noted that further amendments are needed to restrict first-line therapy, to bring the indication in line with the current treatment guidelines, and also taking into account the increased risk of liver adverse events and infections.

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

5.1.7. Lenvima - lenvatinib - Orphan - EMEA/H/C/003727/II/0011/G

Eisai Europe Ltd.

Rapporteur: Bart Van der Schueren, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include treatment of hepatocellular carcinoma (HCC) based on pivotal Study 304. Consequently, sections 4.1, 4.2, 4.4, 4.8, 5.1, and 5.2 of the SmPC are being updated and the package leaflet is updated accordingly. In addition, section 4.2 of the SmPC is being updated to add that the product can be administered as a suspension in water or apple juice. In addition, the labelling is updated to include the unique identifier. An updated RMP version 10 was provided a part of the application."

Action: For adoption

The Committee discussed the issues identified in this application. The Committee noted that the target population of the currently proposed indication is considered too large as not reflecting the line of therapy and the characteristics of the enrolled study patient population.

Therefore, a positive benefit-risk should be further justified from an efficacy and safety point of view in the proposed patient population and in subpopulations of patients.

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

5.1.8. Nplate - romiplostim - Orphan - EMEA/H/C/000942/II/0060/G

Amgen Europe B.V.

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Eva A. Segovia

Scope: "C.I.6.a - Extension of Indication to include paediatric population for Nplate: to register Nplate for the use in the paediatric chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients: 1 year of age and older.

As a consequence Product information has been updated accordingly.
The RMP version 18.3 has also been submitted.
Furthermore, the PI is brought in line with the latest QRD templare version 10.

B.II.e.5.c – To add a low-dose romiplostim 125 microgram vial presentation for powder for solution for injection (4 vials pack).

B.II.e.5.a.1 – To add a 1 vial pack size of a low-dose romiplostim 125 microgram presentation."

Action: For adoption

Request for Supplementary Information adopted on 14.09.2017, 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.

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

Amgen Europe B.V.

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

Scope: "Extension of Indication to include "Treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at increased risk of fracture. Prevention of osteoporosis in women and men at increased risk of fracture who are starting or have recently started long-term glucocorticoid therapy." for Prolia; as a consequence, sections 4.1 and 5.1 of the SmPC are updated to reflect the new indications or are consequential to the analysis of the data from the pivotal study. The Package Leaflet is

updated in accordance.
The Risk Management Plan version 19.0 has also been updated to capture the new indications.
The variation proposed amendments to the Summary of Product Characteristics and Package Leaflet."

Report from ad hoc expert group meeting

Action: For adoption

Request for Supplementary Information adopted on 22.06.2017.

The CHMP noted the report from ad hoc expert group meeting. The experts gave advice on the identification of the optimal study population as well as on the study design of general studies for glucocorticoid induced osteoporosis (GIOP) treatment and of the provided studies in particular.

The Committee further discussed the issues identified in this application which mainly concerned the efficacy in patients initiating or being treated with glucocorticoids, and possible indication wordings.

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

5.1.10. RoActemra - tocilizumab - EMEA/H/C/000955/II/0072

Roche Registration Limited

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

Scope: "Extension of Indication to include "the treatment of juvenile idiopathic polyarthritis (pJIA; rheumatoid factor positive or negative and extended oligoarthritis) in patients 2 years of age and older, who have responded inadequately to previous therapy with methotrexate" for RoActemra; 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 is updated accordingly. The Risk Management Plan version 23.0 has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application. The remaining questions related to pharmacology, efficacy, safety and SmPC updates.

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

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

Pfizer Limited

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

Scope: "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 minor editorial 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."

Action: For adoption

Request for Supplementary Information adopted on 20.07.2017.

The Committee discussed the issues identified in this application, mainly relating to the efficacy and safety data. The members debated on the clinical trial reproducibility and the sensitivity analyses in light with the tolerability and safety profile.

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

5.1.12. Xgeva - denosumab - EMEA/H/C/002173/II/0055

Amgen Europe B.V.

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

Scope: "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."

Action: For adoption

Request for Supplementary Information adopted on 20.07.2017.

The Committee discussed the issues identified in this application. The members discussed the available data and raised questions relating to the add-on activity of zoledronic acid to modern myeloma therapy.

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

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

Gilead Sciences International Limited

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

Request for Supplementary Information adopted on 18.05.2017.

The Committee discussed the issues identified in this application, which were related to the effect of PFS. It was noted that maintenance therapy vs. placebo was part of the experimental regimen and progression on therapy had a different meaning to progression on placebo.

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

5.1.14. Relvar Ellipta - fluticasone furoate / vilanterol - EMEA/H/C/WS1208

Glaxo Group Ltd

Lead Rapporteur: Concepcion Prieto Yerro

Scope: "Extension of indication to include asthma adequately controlled on both inhaled corticosteroid and long-acting beta2-agonist for Relvar Ellipta and Revinty Ellipta. As a consequence, sections 4.1 and 5.1 of the SmPC are updated."

Action: For adoption

The Committee discussed the issues identified in this application. It was noted that further discussion and analyses across studies are requested related to this variation.

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

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

human assisted reproductive techniques including in-vitro fertilisation procedures

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 18.05.2017.

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.

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. tisagenlecleucel-T – ATMP - Orphan - H0004090

Novartis Europharm Ltd; Treatment of:

- Paediatric and young adult patients aged 3 to 25 years of age with relapsed or refractory B-cell acute lymphoblastic leukaemia (ALL).
- Adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who are ineligible for autologous stem cell transplant.

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

Action: For adoption

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

8.1.2. patisiran – Orphan - H0004699

Alnylam UK Limited; Treatment of polyneuropathy in patients with ATTR amyloidosis

Scope: Briefing note and the 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 9 recommendations for eligibility to PRIME: 3 were accepted and 6 were denied. In addition, 1 request was received but not started by EMA as it was deemed outside the scope of the scheme.

The individual outcomes are listed in PRIME Monthly Report on EMA website.

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Blincyto - blinatumomab - EMEA/H/C/003731/II/0011 & EMEA/H/C/003731/II/0018 Orphan

Amgen Europe B.V.

Rapporteur: Alexandre Moreau, Co-Rapporteur: Daniela Melchiorri

Scope: Draft list of experts for the SAG meeting

Action: For adoption

The CHMP adopted the list of experts for the SAG meeting.

9.1.2. IDflu - influenza vaccine (split Virion inactivated) - EMEA/H/C/000966

Sanofi Pasteur SA

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Dolores Montero Corominas

Scope: Withdrawal of IDflu 15 microgram marketing authorisation

Action: For information

The CHMP noted the withdrawal of the marketing authorisation

9.1.3. Opdivo - nivolumab - EMEA/H/C/003985/II/30

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Paula Boudewina van Hennik

Scope: Draft list of questions and list of experts for the SAG meeting

Action: For adoption

The CHMP adopted a list of questions and list of experts for the SAG meeting

9.1.4. Tarceva - erlotinib - EMEA/H/C/000618/II/0051

Roche Registration Limited

Rapporteur: Sinan B. Sarac

Scope: "Update of section 4.1 of the SmPC in relation to the treatment of patients with locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen based on a review of relevant literature, Real World Data Reports (BIOMARQUEURS FRANCE CSR and ESCAP-2011-CPHG CSR) and a new CSR Addendum of the previously submitted relevant pivotal study BR.21, as requested by the CHMP following assessment of variation EMEA/H/C/000618/II/0043"

Action: For adoption

Request for Supplementary Information adopted on 15.06.2017.

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.

9.1.5. Zelboraf - vemurafenib - EMEA/H/C/002409/II/0043

Roche Registration Limited

Rapporteur: Filip Josephson

Scope: "Update of section 4.8 of the SmPC in order to update the safety information following results from pooled safety analysis of the final results from pivotal phase II (NP22657 BRIM-2) and pivotal phase III (NO25026 BRIM-3) trials. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to review the SmPC and Package Leaflet in order to improve clarity and consistency across sections."

Action: For adoption

The Committee discussed the issues identified in this application. During the discussion of the variation the comment was made that the approved monotherapy does not reflect the current status of standard of care anymore. The CHMP agreed to recommend to the MAH to consider an update of the SmPC, particularly in sections 4.1 and 5.1.

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 of Regulation (EC) No 726/2004

10.1.1. Zinbryta - daclizumab – EMEA/H/A-20/1456

Biogen Idec Ltd

Rapporteurs for the Article 20 referral: PRAC Rapporteur: Eva Segovia; PRAC Co-rapporteur: Marcia Sofia Sanches de Castro Lopes Silva,

Rapporteurs for Zinbryta: CHMP Rapporteur: Bruno Sepodes, CHMP Co-rapporteur: Greg MarkeyPRAC Rapporteur: Eva Segovia; PRAC Co-rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

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

SAG report

Action: For adoption

The CHMP noted the report from the SAG Neurology.

The CHMP adopted an opinion by consensus based on the PRAC recommendation.

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

The CHMP agreed the wording of a DHPC and communication plan.

The CHMP noted the EMA public health communication

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

No items

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

No items

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

No items

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

No items

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

10.6.1. Gadolinium-containing contrast agents (GdCA): Gadobenate dimeglumine; gadobutrol; gadodiamide; gadopentetic acid dimeglumine, gadoteric acid (intra articular formulation); gadoteric acid (intrvenous and intravascular formulations); gadoteridol; gadoxetic acid disodium (NAP)

Lead Rapporteur: Patrick Batty,

Scope: Annual cumulative reviews on NSF cases submission as a post-authorisation measure resulting from the 2010 Article 20 and Article 31 referral procedures for gadolinium-containing contrast agents

Action: For adoption

The CHMP adopted the annual cumulative reviews.

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

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

D&A Pharma

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

Scope: Final opinion documents

Action: For information

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

Re-examination opinion adopted on 12 October 2017, Opinion adopted on 22 June 2017

The CHMP noted the final documents.

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

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

Action: For information

The CHMP noted the November 2017 ENS.

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

No items

13.2. Innovation Task Force briefing meetings

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

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. Election of co-opted member

Election of co-opted member with area of expertise “Quality, safety and efficacy of biological medicinal products, including advanced therapies and vaccines”

Action: For adoption

The CHMP re-elected Jan Mueller-Berghaus as co-opted member of the CHMP for a 3-year mandate.

14.1.2. Area of expertise of co-opted member

Jean-Louis Robert will step down as CHMP co-opted member by end of the year 2017 (expertise in Quality (non-biologicals)).

Scope: Discussion on area of expertise

The CHMP noted the timetable. Agreement on the area of expertise: December 2017

Action: For discussion

The discussion and agreement on the area of expertise is planned for the December 2017 Plenary. Proposals should be sent by 11 December 2017.

14.1.3. User manual – CxMP/WP/SAG members and experts representing CxMP or EMA at external meetings

Action: For discussion

Follow-up from November ORGAM

Postponed to December ORGAM meeting.

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 23-26 October 2017

Action: For information

The CHMP noted the Summary of recommendations and advice.

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

Action: For adoption

The CHMP noted the information.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 30-31 October 2017
Action: For information

The CHMP noted the draft minutes.

14.2.3. Paediatric Committee (PDCO)

PIPs reaching D30 at November 2017 PDCO

Action: For information

The CHMP noted the information.

Report from the PDCO meeting held on 7-10 November 2017

Action: For information

The CHMP noted the report.

Joint CHMP/PDCO session

Agenda for joint session

Action: For discussion

The CHMP and PDCO joint discussion was held.

14.2.4. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 30-31 October 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 6-8 November 2017

Action: For information

The CHMP noted the report.

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

14.3.1. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 23-26 October 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.

14.3.2. Infectious Diseases Working Party (IDWP)

Vice Chair: María Jesús Fernández Cortizo

Election of IDWP Chair

Action: For adoption

The CHMP elected María Jesús Fernández Cortizo (ES) as IDWP chair.

14.3.3. Radiopharmaceutical Drafting Group (RadDG)

Chair: Anabel Cortes

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

Action: For adoption

The CHMP appointed Riccardo Schiavo (IT) and Tomás Arroyo Pérez (ES) as new core members.

Furthermore the CHMP offered Christof Krummeich (DE), Jean-Noël Talbot (FR) and Joao Correia (PT) to participate at the RadDG as additional assessors.

Guideline on core SmPC and Package Leaflet for sodium iodide (131I) therapy capsule

Action: For adoption

The CHMP adopted the guideline. The guideline describes the information to be included in the Summary of Products Characteristics (SmPC) and package leaflet for sodium iodide (131I) therapy capsule.

Guideline on core SmPC and Package Leaflet for fluorodopa (18F)

Action: For adoption

The CHMP noted the update. The adoption was postponed to allow for further discussion.

Guideline on core SmPC and Package Leaflet for (99Mo/99mTc) generator

Action: For adoption

The CHMP adopted the guideline. The guideline describes the information to be included in the Summary of Products Characteristics (SmPC) and Package Leaflet for (99Mo/99mTc) generator.

14.3.4. Respiratory Drafting Group (RDG)

Chair: Karolina Törneke

Appointment of new core member

Action: For adoption

The CHMP appointed Helga Haugom Olsen (NO) as new core member. Furthermore the CHMP offered Agnieszka Przybyszewska (IE) to participate at the RDG as additional assessor.

14.3.5. Safety Working Party (SWP)

Chair: Jan Willem Van der Laan

SWP Answers to CHMP List of Questions on Estragole (EMA/CHMP/SWP/620432/2017)

Action: For adoption

The Committee discussed the SWP answers. A limit should be proposed to apply for all uses of estragole-containing substances, be it as excipient or as active ingredient. For that reason, a strict PDE approach has been applied. Clearly, for an active ingredient, a benefit-risk assessment should be applied and the risks associated with estragole would be evaluated in a risk assessment going beyond the definition of a PDE. It has been identified that in the food area the addition of pure estragole as flavouring agent has been banned. Given the type of products in the pharmaceutical area where pure estragole as a flavour is used, a similar approach for pharmaceuticals could be considered, and for remaining products a standard benefit/risk assessment can be conducted.

The CHMP adopted the SWP answers.

14.3.5. Biostatistics Working Party (BSWP)

Chair: Anja Schiel/Thomas Lang

Call for nominations for BSWP Vice Chair:

Nominations should be sent by **15th January 2018**. Elections will take place at the January CHMP Plenary meeting.

Action: For information

The CHMP noted the information.

14.3.6. Central Nervous System Working Party (CNSWP)

Chair: Karl Broich/André Elferink

Guideline on the clinical development of medicinal products for the treatment of Autism Spectrum Disorder (ASD) EMA/CHMP/598082/2013

Rapporteurs: Greg Markey, Sabine Lenton, Violeta Stoyanova

Action: For adoption

The CHMP adopted the guideline. The guideline provides guidance on the design of clinical trials intended to establish the efficacy and safety of treatments for the core symptoms of ASD. Specific age-category issues (childhood versus adulthood) and the need for comparative studies are also considered in this document.

14.3.7. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP November 2017 meeting to CHMP for adoption:

- 12 reports on products in scientific advice and protocol assistance

- 11 reports on products in pre-authorisation procedures
- 04 reports on products in plasma master file

Action: For adoption

The CHMP adopted the BWP reports.

14.3.8. Cardiovascular Working Party (CVSWP)

Chair: Pieter de Graeff/Kristina Dunder

Call for nomination for CVSWP Chair. Nominations should be sent by 7th December 2017
Action: For information

The CHMP noted the information.

14.4. Cooperation within the EU regulatory network

None

14.5. Cooperation with International Regulators

None

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

None

14.7. CHMP work plan

None

14.8. Planning and reporting

None

14.9. Others

None

15. Any other business

15.1. AOB topic

15.1.1. Preparedness of the system and capacity increase

Action: For information

Postponed

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 6 – 9 November 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	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Katarina Vučić	Member	Croatia	No interests declared	
Emilia Mavrokordatou	Member	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Tomas Boran	Alternate	Czech Republic	No interests declared	
Sinan B. Sarac	Member	Denmark	No interests declared	
Hanne Lomholt Larsen	Alternate	Denmark	No interests declared	
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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	
Agnes Gyurasics	Member	Hungary	No interests declared	
Hrefna Gudmundsdottir	Alternate	Iceland	No interests declared	
Jayne Crowe	Member	Ireland	No interests declared	
Peter Kiely	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No restrictions applicable to this meeting	
Juris Pokrotnieks	Member	Latvia	No participation in final deliberations and voting on:	3.1.7. Jorveza - budesonide - Orphan - EMEA/H/C/004655
Natalja Karpova	Alternate	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No participation in final deliberations and voting on:	3.1.9. Ocrevus - ocrelizumab - EMEA/H/C/004043 5.1.10. RoActemra - tocilizumab - EMEA/H/C/000955/II/0072 9.1.6. Tarceva - erlotinib - EMEA/H/C/000618/II/0051 9.1.7. Zelboraf - vemurafenib -

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				EMEA/H/C/002409/II/0043
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	
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Aldona Paluchowska	Alternate	Poland	No interests declared	
Bruno Sepodes	Member	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No participation in final deliberations and voting on:	2.1.4., 3.7.3- d-biotin - EMEA/H/C/004153
Simona Badoi	Member	Romania	No interests declared	
Francisek Drafi	Member	Slovakia	No interests declared	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member	Spain	No interests declared	
Jorge Camarero Jiménez	Alternate	Spain	No participation in final deliberations and voting on:	3.1.9. Ocrevus - ocrelizumab - EMEA/H/C/004043 5.1.10. RoActemra - tocilizumab - EMEA/H/C/000955/II/0072 9.1.6. Tarceva - erlotinib - EMEA/H/C/000618/II/0051 9.1.7. Zelboraf - vemurafenib -

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				EMEA/H/C/002409/II/0043
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 participation in final deliberations and voting on:	5.1.14. Relvar Ellipta - fluticasone furoate / vilanterol - EMEA/H/C/WS1208
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	
Theis Moeslund Jensen	Expert - in person*	Denmark	No restrictions applicable to this meeting	
Valerie Lescrainier	Expert - in person*	Belgium	No interests declared	
Olga Kholmanskikh	Expert - in person*	Belgium	No interests declared	
Noan-Minh Chau	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Tove Lill Stendal	Expert - via telephone*	Norway	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Per Harald Fuglerud	Expert - in person*	Norway	No restrictions applicable to this meeting	
Anna Maria Urbaniak	Expert - via phone*	Norway	No restrictions applicable to this meeting	
Ingrid Lund	Expert - via telephone*	Norway	No interests declared	
Jacqueline Wiesner	Expert - via telephone*	Germany	No interests declared	
Cecilia Chisholm	Expert - via telephone*	United Kingdom	No interests declared	
Eva Segovia	Expert - via telephone*	Spain	No interests declared	
Karri Penttilä	Expert - via telephone*	Finland	No interests declared	
Helgi Helgason	Expert - via telephone*	Iceland	No restrictions applicable to this meeting	
Catarina Eriksson	Expert - via telephone*	Sweden	No interests declared	
Ulla Wändel Liminga	Expert - via telephone*	Sweden	No interests declared	
Carl Henrik Alm	Expert - via telephone*	Sweden	No restrictions applicable to this meeting	
Olive Smyth	Expert - via telephone*	Ireland	No interests declared	
Brigitte Mueller	Expert - via telephone*	Austria	No interests declared	
Katja Valent	Expert - via telephone*	Austria	No interests declared	
Klaudia Hettinger	Expert - via telephone*	Austria	No interests declared	
Serena Marchetti	Expert - via telephone*	Netherlands	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Regine Lehnert	Expert - via Adobe*	Germany	No interests declared	
Elmer Schabel	Expert - via Adobe*	Germany	No interests declared	
Daniela Gildemeister	Expert - via Adobe*	Germany	No interests declared	
Gerd Maack	Expert - via Adobe*	Germany	No interests declared	
Zane Neikena	Expert - via Adobe*	Latvia	No interests declared	
Representatives from MEB (Netherlands) attended the meeting as observers				
Representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

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

17. Explanatory notes

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

Oral explanations *(section 2)*

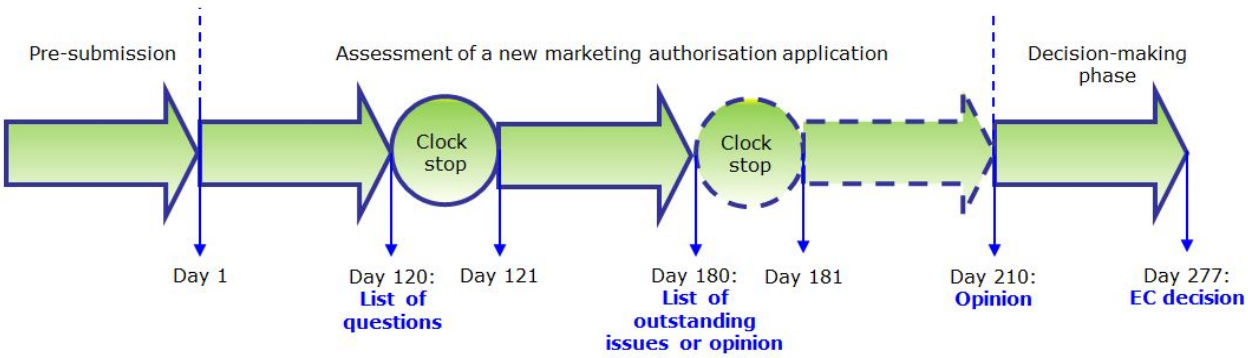
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

Initial applications *(section 3)*

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

Re-examination procedures *(section5.3)*

This section lists applications for type II variations (including extension of indication applications) for which the applicant has requested re-examination of the opinion previously issued by the CHMP.

Withdrawal of application *(section 3.7)*

Applicants may decide to withdraw applications at any stage during the assessment and a CHMP opinion will therefore not be issued. Withdrawals are included in the agenda for information or discussion, as necessary.

Procedure under article 83(1) of regulation (EC) 726/2004 (compassionate use) *(section 7)*

Compassionate use is a way of making available to patients with an unmet medical need a promising medicine which has not yet been authorised (licensed) for their condition. Upon request, the CHMP provides recommendations to all EU Member States on how to administer, distribute and use certain medicines for compassionate use.

Pre-submission issues *(section 8)*

In some cases the CHMP may discuss a medicine before a formal application for marketing authorisation is submitted. These cases generally refer to requests for an accelerated assessment for medicines that are of major interest for public health or can be considered a therapeutic innovation. In case of an accelerated assessment the assessment timetable is reduced from 210 to 150 days.

Post-authorisation issues *(section 9)*

This section lists other issues concerning authorised medicines that are not covered elsewhere in the agenda. Issues include supply shortages, quality defects, some annual reassessments or renewals or type II variations to marketing authorisations that would require specific discussion at the plenary.

Referral procedures *(section 10)*

This section lists referrals that are ongoing or due to be started at the plenary meeting. A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a

particular medicine or class of medicines on behalf of the EU. Further information on such procedures can be found here.

Pharmacovigilance issues *(section 11)*

This section lists issues that have been discussed at the previous meeting of the PRAC, the EMA's committee responsible for evaluating and monitoring safety issues for medicines. Feedback is provided by the PRAC. This section also refers to the early notification system, a system used to notify the European regulatory network on proposed EMA communication on safety of medicines.

Inspections Issues *(section 12)*

This section lists inspections that are undertaken for some medicinal products. Inspections are carried out by regulatory agencies to ensure that marketing authorisation holders comply with their obligations. Inspection can relate to good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP) or good pharmacovigilance practice (GVP).

Innovation task force *(section 13)*

The Innovation Task Force (ITF) is a body set up to encourage early dialogue with applicants developing innovative medicines. Minutes from the last ITF meeting as well as any related issue that requires discussion with the CHMP are listed in this section of the agenda. Further information on the ITF can be found here.

Scientific advice working party (SAWP) *(section 14.3.1)*

This section refers to the monthly report from the CHMP's Scientific Advice Working Party (SAWP) on scientific advice given to companies during the development of medicines. Further general information on SAWP can be found here.

Satellite groups / other committees *(section 14.2)*

This section refers to the reports from groups and committees making decisions relating to human medicines: the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), the Committee for Orphan Medicinal Products (COMP), the Committee for Herbal Medicinal Products (HMPC), Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT) and the Pharmamacovigilance Risk Assessment Committee (PRAC).

Invented name issues *(section 14.3)*

This section list issues related to invented names proposed by applicants for new medicines. The CHMP has established the Name Review Group (NRG) to perform reviews of the invented names. The group's main role is to consider whether the proposed names could create a public-health concern or potential safety risk. Further information can be found here.

More detailed information on the above terms can be found on the EMA website: www.ema.europa.eu/

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

21 December 2017
EMA/840992/2017

Annex to 06-09 November 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

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

Final Outcome of Rapporteurship allocation for November 2017: **For adoption**	Adopted.

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

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

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

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

Atriance - nelarabine - EMEA/H/C/000752/S/0038, MAH: Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver	Positive Opinion adopted by consensus together with the CHMP assessment report. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.
Evoltra - clofarabine - EMEA/H/C/000613/S/0055 MAH: Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni,	Positive Opinion adopted by consensus together with the CHMP assessment report. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.
Imvanex - modified vaccinia ankara virus - EMEA/H/C/002596/S/0029 MAH: Bavarian Nordic A/S, Rapporteur: Greg Markey, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Julie Williams	Positive Opinion adopted by consensus together with the CHMP assessment report. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.
Lojuxta - lomitapide - EMEA/H/C/002578/S/0026	Request for Supplementary Information adopted

MAH: Aegerion Pharmaceuticals Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 09.11.2017.	
Naglazyme - galsulfase - EMEA/H/C/000640/S/0067 MAH: BioMarin Europe Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty	Positive Opinion adopted by consensus together with the CHMP assessment report. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Pradaxa - dabigatran etexilate - EMEA/H/C/000829/R/0105 MAH: Boehringer Ingelheim International GmbH, Rapporteur: Hanne Lomholt Larsen, Co-Rapporteur: Joseph Emmerich, PRAC Rapporteur: Doris Stenver Request for Supplementary Information adopted on 14.09.2017.	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 Opinion.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Adasuve - loxapine - EMEA/H/C/002400/R/0024 MAH: Ferrer Internacional s.a., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus Request for Supplementary Information adopted on 14.09.2017.	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.
Hexacima - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and Haemophilus type B conjugate vaccine (adsorbed) - EMEA/H/C/002702/R/0068 MAH: Sanofi Pasteur SA, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Brigitte Keller-Stanislawski	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.

Request for Supplementary Information adopted on 12.10.2017.	
Hexyon - diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and Haemophilus influenzae type b (Hib) conjugate vaccine (adsorbed) - EMEA/H/C/002796/R/0072 MAH: Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Brigitte Keller-Stanislawski Request for Supplementary Information adopted on 12.10.2017.	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.
HyQvia - human normal immunoglobulin - EMEA/H/C/002491/R/0037 MAH: Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski	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.
Imatinib Actavis - imatinib - EMEA/H/C/002594/R/0015 MAH: Actavis Group PTC ehf, Generic, Generic of Glivec, Rapporteur: Hrefna Gudmundsdottir, PRAC Rapporteur: Eva A. Segovia Request for Supplementary Information adopted on 12.10.2017.	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.
Memantine LEK - memantine hydrochloride - EMEA/H/C/002630/R/0009 MAH: Pharmathen S.A., Generic, Generic of Ebixa, Rapporteur: Martina Weise, PRAC Rapporteur: Dolores Montero Corominas	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.
Memantine Mylan - memantine - EMEA/H/C/002660/R/0010 MAH: Generics UK Limited, Generic, Generic of Ebixa, Rapporteur: Concepcion Prieto Yerro,	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.

PRAC Rapporteur: Dolores Montero Corominas	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.
Nemdatine - memantine - EMEA/H/C/002680/R/0008 MAH: Actavis Group PTC ehf, Generic, Generic of Ebixa, Rapporteur: Milena Stain, PRAC Rapporteur: Dolores Montero Corominas	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.
Stayveer - bosentan - EMEA/H/C/002644/R/0021 MAH: Marklas Nederlands BV, Rapporteur: Alexandre Moreau, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Caroline Laborde	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.
Tolucombi - telmisartan / hydrochlorothiazide - EMEA/H/C/002549/R/0020 MAH: KRKA, d.d., Novo mesto, Generic, Generic of MicardisPlus, Rapporteur: Alar Irs, PRAC Rapporteur: Carmela Macchiarulo Request for Supplementary Information adopted on 12.10.2017.	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.
Votrient - pazopanib - EMEA/H/C/001141/R/0042 MAH: Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Doris Stenver	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.

B.2.3. Renewals of Conditional Marketing Authorisations

Caprelsa - vandetanib - EMEA/H/C/002315/R/0027 MAH: Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni Request for Supplementary Information adopted on 09.11.2017.	Request for Supplementary Information adopted
Cometriq - cabozantinib - EMEA/H/C/002640/R/0027, Orphan MAH: Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Sabine Straus	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. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Sirturo - bedaquiline - EMEA/H/C/002614/R/0024, Orphan MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Qun-Ying Yue Request for Supplementary Information adopted on 09.11.2017.	Request for Supplementary Information adopted

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection PRAC recommendations on signals adopted at the PRAC meeting held on 23-26 October 2017 PRAC:	Noted
PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its November 2017 meeting:	
EMEA/H/C/PSUSA/00000624/201703 (certolizumab) CAPS: **Cimzia** (EMEA/H/C/001037) (certolizumab pegol), MAH: UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "7 March 2014 to 6 March 2017"	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 "worsening of symptoms of dermatomyositis" and to add the TNF-antagonist class adverse reactions: "Stevens-Johnson syndrome" and "erythema multiforme » with a frequency "rare". 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/00001801/201703 (japanese encephalitis virus (inactivated)) CAPS: **Ixiaro** (EMEA/H/C/000963) (japanese encephalitis vaccine (inactivated, adsorbed)), MAH: Valneva Austria GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "April 1, 2016 to March 31, 2017"	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 4.8 of the SmPC to add the adverse reaction 'Syncope' with a frequency 'rare'. 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/00003152/201703 (zonisamide) CAPS: **Zonegran** (EMEA/H/C/000577) (zonisamide), MAH: Eisai Ltd, Rapporteur: Peter Kiely, PRAC Rapporteur: Almath Spooner, "1 April 2016 to 31 March 2017"	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 and 4.6 to add information from a registry study on the risk of low birth weight and small for gestational age in infants exposed to zonisamide in utero and to update information regarding the need to counsel women of child-bearing potential on the risk of anti-epileptic drugs in pregnancy. 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/00009200/201703 (ipilimumab) CAPS: **Yervoy** (EMEA/H/C/002213) (ipilimumab),	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

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "25 March 2016 - 24 March 2017"	report as appended, recommends by consensus, the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change: Update of section 4.4 of the SmPC to add a warning on histiocytosis haematophagic and of section 4.8 of the SmPC to add 'pemphigoid' and 'histiocytosis haematophagic' as new adverse drug reactions with a 'not known' frequency. The Package leaflet is updated accordingly. In addition the MAH took the opportunity to include in section 4 of the Package Leaflet the standard statement about contacting your doctor in case of side effects to ensure consistency with the other frequency categories. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010388/201704 (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, "18/10/2016 - 17/04/2017"	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 4.4 of the SmPC to add a warning on pyelonephritis and urosepsis and of section 4.8 to add the following adverse reactions pyelonephritis and urosepsis under the SOC "Infections and infestations with a frequency *common*. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010541/201704 (olaratumab) CAPS: **Lartruvo** (EMEA/H/C/004216) (olaratumab), MAH: Eli Lilly Nederland B.V., Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Sabine Straus, "19 Oct 2016 - 19 Apr 2017"	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 Summary of Products Characteristics to add a clarification

	that infusion-related reactions may include anaphylactic reactions/anaphylactic following relevant cases reported in the post-marketing setting. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

B.4. EPARs / WPARs

Kyomarc - bevacizumab - EMEA/H/C/004360 Applicant: Amgen Europe B.V., treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer, unresectable advanced, metastatic or recurrent squamous and non-squamous non-small cell lung cancer, advanced and/or metastatic renal cell cancer, advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer and persistent, recurrent, or metastatic carcinoma of the cervix, Similar biological application (Article 10(4) of Directive No 2001/83/EC) **WPAR**	adopted.
Tacforius - tacrolimus - EMEA/H/C/004435 Applicant: Teva B.V., prophylaxis of transplant rejection and treatment of allograft rejection, Generic, Generic of Advagraf, Generic application (Article 10(1) of Directive No 2001/83/EC)	adopted.
Zafiride - NGR-hTNF - EMEA/H/C/004455, Orphan Applicant: MolMed SpA, treatment of advanced malignant pleural mesothelioma, New active substance (Article 8(3) of Directive No 2001/83/EC) **WPAR**	adopted.

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Atripla - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/000797/II/0125/G MAH: Bristol-Myers Squibb and Gilead Sciences	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Ltd., Rapporteur: Martina Weise Opinion adopted on 26.10.2017.	recommendation.
BeneFIX - nonacog alfa - EMEA/H/C/000139/II/0146 MAH: Pfizer Limited, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 26.10.2017. Request for Supplementary Information adopted on 14.09.2017.	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Benepali - etanercept - EMEA/H/C/004007/II/0026 MAH: Samsung Bioepis UK Limited, Rapporteur: Andrea Laslop Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 14.09.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Bortezomib Hospira - bortezomib - EMEA/H/C/004207/II/0006/G MAH: Hospira UK Limited, Generic, Generic of VELCADE, Rapporteur: Milena Stain Opinion adopted on 26.10.2017. Request for Supplementary Information adopted on 21.09.2017.	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cerezyme - imiglucerase - EMEA/H/C/000157/II/0105 MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 02.11.2017.	Positive Opinion adopted by consensus on 02.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Daptomycin Hospira - daptomycin - EMEA/H/C/004310/II/0003 MAH: Hospira UK Limited, Generic, Generic of Cubicin, Rapporteur: Kolbeinn Gudmundsson Request for Supplementary Information adopted on 19.10.2017.	Request for Supplementary Information adopted
Darunavir Mylan - darunavir - EMEA/H/C/004068/II/0001/G MAH: Mylan S.A.S, Generic, Generic of Prezista, Rapporteur: John Joseph Borg Opinion adopted on 26.10.2017. Request for Supplementary Information adopted on 14.09.2017, 05.05.2017.	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Elaprase - idursulfase - EMEA/H/C/000700/II/0071/G MAH: Shire Human Genetic Therapies AB, Rapporteur: Greg Markey Request for Supplementary Information adopted	Request for Supplementary Information adopted

on 26.10.2017.	
Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0037/G MAH: Merck Sharp & Dohme Limited, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 19.10.2017.	Request for Supplementary Information adopted
Erbitux - cetuximab - EMEA/H/C/000558/II/0078/G MAH: Merck KGaA, Rapporteur: Filip Josephson Opinion adopted on 09.11.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Flixabi - infliximab - EMEA/H/C/004020/II/0013/G MAH: Samsung Bioepis UK Limited, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 19.10.2017. Request for Supplementary Information adopted on 01.06.2017.	Positive Opinion adopted by consensus on 19.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Foscan - temoporfin - EMEA/H/C/000318/II/0042 MAH: biolitec Pharma Ltd, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 26.10.2017. Request for Supplementary Information adopted on 14.09.2017.	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0086 MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 19.10.2017. Request for Supplementary Information adopted on 14.09.2017.	Positive Opinion adopted by consensus on 19.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Natpar - parathyroid hormone - EMEA/H/C/003861/II/0004/G, Orphan MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Bart Van der Schueren Request for Supplementary Information adopted on 02.11.2017.	Request for Supplementary Information adopted
Omnitrope - somatropin - EMEA/H/C/000607/II/0047 MAH: Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 19.10.2017. Request for Supplementary Information adopted on 11.05.2017.	Positive Opinion adopted by consensus on 19.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opatanol - olopatadine - EMEA/H/C/000407/II/0035/G MAH: Novartis Europharm Limited, Rapporteur: Peter Kiely Request for Supplementary Information adopted on 19.10.2017.	Request for Supplementary Information adopted
Plavix - clopidogrel - EMEA/H/C/000174/II/0127/G MAH: Sanofi Clir SNC, Rapporteur: Bruno Sepodes Request for Supplementary Information adopted on 26.10.2017, 20.07.2017.	Request for Supplementary Information adopted
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0126 MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 09.11.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Strensiq - asfotase alfa - EMEA/H/C/003794/II/0023, Orphan MAH: Alexion Europe SAS, Rapporteur: Greg Markey Opinion adopted on 19.10.2017.	Positive Opinion adopted by consensus on 19.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Trulicity - dulaglutide - EMEA/H/C/002825/II/0021 MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey Request for Supplementary Information adopted on 19.10.2017.	Request for Supplementary Information adopted
Vaniqa - eflornithine - EMEA/H/C/000325/II/0051 MAH: Almirall S.A, Rapporteur: Peter Kiely Request for Supplementary Information adopted on 26.10.2017.	Request for Supplementary Information adopted
Vyndaqel - tafamidis - EMEA/H/C/002294/II/0041/G, Orphan MAH: Pfizer Limited, Rapporteur: Joseph Emmerich Request for Supplementary Information adopted on 19.10.2017.	Request for Supplementary Information adopted
Xadago - safinamide - EMEA/H/C/002396/II/0020 MAH: Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 19.10.2017.	Request for Supplementary Information adopted
WS1206/G	Positive Opinion adopted by consensus on

Exelon- **EMEA/H/C/000169/WS1206/0114/G** **Prometax-** **EMEA/H/C/000255/WS1206/0114/G** MAH: Novartis Europharm Limited, Lead Rapporteur: Alexandre Moreau Opinion adopted on 19.10.2017.	19.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1254/G **Hirobriz Breezhaler-** **EMEA/H/C/001211/WS1254/0042/G** **Onbrez Breezhaler-** **EMEA/H/C/001114/WS1254/0041/G** **Oslif Breezhaler-** **EMEA/H/C/001210/WS1254/0041/G** **Ultibro Breezhaler-** **EMEA/H/C/002679/WS1254/0017/G** **Ulunar Breezhaler-** **EMEA/H/C/003875/WS1254/0017/G** **Xoterna Breezhaler-** **EMEA/H/C/003755/WS1254/0020/G** MAH: Novartis Europharm Limited, Lead Rapporteur: Hanne Lomholt Larsen Request for Supplementary Information adopted on 19.10.2017.	Request for Supplementary Information adopted

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

Abilify - aripiprazole - **EMEA/H/C/000471/II/0127** MAH: Otsuka Pharmaceutical Europe Ltd, Rapporteur: Bruno Sepodes, "Update of sections 4.4 and 4.8 of the SmPC with further information about the risk of impulse control disorders, and section 4.8 of the SmPC to include the new ADRs 'impulse control disorders', 'binge eating', 'compulsive shopping' and 'poriomania' and to delete the ADR 'hyperglycaemia'. The Package Leaflet has been updated accordingly. Further, the MAH has implemented minor editorial changes in section 6.1 of the SmPC, section 6 of the Package leaflet and module 3.2.P.1 to include lactose as one of the components of the excipient vanilla flavour for Abilify orodispersible tablets. In addition, the MAH took the opportunity to align the annexes with the product information of Abilify Maintena and the latest QRD template." Opinion adopted on 26.10.2017.	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Abilify Maintena - aripiprazole -	Positive Opinion adopted by consensus on

EMEA/H/C/002755/II/0023 MAH: Otsuka Pharmaceutical Europe Ltd, Rapporteur: Bruno Sepodes, "Update of sections 4.4 and 4.8 of the SmPC with further information about the risk of impulse control disorders, and section 4.8 of the SmPC to include the new ADRs 'impulse control disorders', 'binge eating', 'compulsive shopping' and 'poriomania'. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes and align the annexes with the latest QRD template." Opinion adopted on 26.10.2017.	26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0027/G MAH: Biofrontera Bioscience GmbH, Rapporteur: Harald Enzmann, "C.I.4 Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the posology and method of administration of Ameluz for the treatment of actinic keratosis (AK) and field cancerization in combination with daylight and to update the safety information, based on the clinical study results from ALA-AK-CT009; this is a phase III, randomised, interventional, observer-blinded study aimed to compare the efficacy and safety of Ameluz in the treatment of mild to moderate AK with Metvix in combination with daylight photodynamic therapy. Section 5.2 of the SmPC has included a minor editorial change. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. C.I.5.b Change in the legal status of Ameluz from "medicinal product subject to restricted medical prescription" to "medicinal product subject to medical prescription"." Request for Supplementary Information adopted on 09.11.2017, 12.10.2017.	Request for Supplementary Information adopted
Eliquis - apixaban - EMEA/H/C/002148/II/0047 MAH: Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.5 of the SmPC to include clarithromycin as one of the active substances	Positive Opinion adopted by consensus on 19.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

which are not considered strong inhibitors of both CYP3A4 and P-gp and which are expected to increase apixaban plasma concentration to a lesser extent based on the final results from study CV185547. The final study report of study CV185547 (an open-label, non-randomised, single-sequence, crossover study in healthy subjects to determine the effect of multiple-dose clarithromycin on the single-dose pharmacokinetics of apixaban) is also submitted. In addition, the MAH took the opportunity to make some corrections in the SmPC and to update the labelling in line with the latest QRD template version 10.0." Opinion adopted on 19.10.2017.	
Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0038 MAH: Merck Sharp & Dohme Limited, Rapporteur: Paula Boudewina van Hennik, "Update of section 5.1 of the SmPC to include updated information regarding congenital malformations reported in infants born after a frozen_thawed embryo transfer (FTET) cycle." Opinion adopted on 02.11.2017.	Positive Opinion adopted by consensus on 02.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Enbrel - etanercept - EMEA/H/C/000262/II/0213 MAH: Pfizer Limited, Rapporteur: Robert James Hemmings, "Update of section 4.8 of the SmPC to update the frequency category of 7 ADRs currently listed and to split one ADR into 2, following a re-analysis of the frequencies of all listed ADRs based on clinical trial experience in controlled clinical studies as proposed by the MAH in LEG 0168 in follow-up to a PRAC request in etanercept PSUSA/00001295/201602. The description of the ADRs 'interstitial lung disease and 'autoimmune hepatitis' has also been amended as a consequence. The Marketing authorisation holder (MAH) also took the opportunity to reformat the ADR listing in section 4.8 of the SmPC. Section 4.4 of the SmPC and the Package Leaflet are updated accordingly. In addition, the MAH took the opportunity to combine the 25 mg and 50 mg pre-filled syringe (PFS) SmPCs and Package Leaflets." Opinion adopted on 26.10.2017.	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Esbriet - pirfenidone - EMEA/H/C/002154/II/0043, Orphan	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP

MAH: Roche Registration Limited, Rapporteur: Greg Markey, "Update of sections 4.2 and 5.2 of the SmPC in order to update dosing recommendations and pharmacokinetic information for patients with renal impairment based on the totality of data from clinical studies; the Package Leaflet is updated accordingly." Opinion adopted on 26.10.2017. Request for Supplementary Information adopted on 14.09.2017, 29.06.2017.	Members were in agreement with the CHMP recommendation.
Forsteo - teriparatide - EMEA/H/C/000425/II/0046 MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey, "Update of section 5.1 of the SmPC of the SmPC based on the results of study B3D-EW-GHDW (VERO), a phase 4 multi-centre, prospective, randomized, parallel, double-blind, double-dummy, active controlled study comparing the effect of teriparatide for injection versus risedronate on the incidence of fractures and low bone mass. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct the formatting throughout the Product Information and to bring Annex II in line with the latest QRD template version 10." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 14.09.2017, 20.07.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Galafold - migalastat - EMEA/H/C/004059/II/0010, Orphan MAH: Amicus Therapeutics UK Ltd, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC to reflect the final results 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." Opinion adopted on 26.10.2017. Request for Supplementary Information adopted on 21.09.2017, 13.07.2017.	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0020, Orphan MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, "Update of section 4.4 of the SmPC to revise the safety information on	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

delayed hypersensitivity reactions based on a review of relevant cases by the Marketing authorisation holder (MAH). In addition, the MAH took the opportunity to introduce editorial changes to the SmPC and package leaflet." Opinion adopted on 26.10.2017.	
Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/II/0053 MAH: Gilead Sciences International Limited, 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" Opinion adopted on 19.10.2017. Request for Supplementary Information adopted on 13.07.2017.	Positive Opinion adopted by consensus on 19.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Praluent - alirocumab - EMEA/H/C/003882/II/0029 MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Submission of the final report from study R727-CL-1032 (study title: A Phase 2, Open-Label Extension of Study R727-CL-1003 to Evaluate the Long-Term Safety and Efficacy of REGN727 Administered by Subcutaneous Injection in Patients with Heterozygous Familial Hypercholesterolemia), listed as a category 3 study in the RMP (MEA013)." Opinion adopted on 09.11.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
ReFacto AF - moroctocog alfa - EMEA/H/C/000232/II/0140 MAH: Pfizer Limited, Rapporteur: Hanne Lomholt Larsen, "Submission of the report 'The Immunogenicity of ReFacto AF in UK PUPs Who Started Treatment from 2010' prepared by the United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO). This report is being submitted in the context of a post-approval commitment, MEA 115.1 ('The MAH commits to submit the CSR for "A Postauthorization Safety Surveillance Registry or ReFacto AF in Previously Untreated Patients (PUPs) in Usual Care Settings – study number 4435" and to initiate the registry'), as supporting evidence of the ongoing safety evaluation of ReFacto AF in PUPs with	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

haemophilia A and with a specific focus on the development of inhibitors." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 14.09.2017.	
Revatio - sildenafil - EMEA/H/C/000638/II/0077 MAH: Pfizer Limited, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.6 of the SmPC in order to revise the statement concerning the detection of sildenafil and its active metabolite in human milk and the potential for impact on the breastfed infant. 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." Opinion adopted on 26.10.2017. Request for Supplementary Information adopted on 14.09.2017.	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Spinraza - nusinersen - EMEA/H/C/004312/II/0002/G, Orphan MAH: Biogen Idec Ltd, Rapporteur: Bruno Sepodes, "Update of sections 4.8 and 5.1 of the SmPC to reflect efficacy and immunogenicity data from the final clinical study reports for study CS4 and CS12 and the final update to the CS2-12 longitudinal analysis." Opinion adopted on 02.11.2017.	Positive Opinion adopted by consensus on 02.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Stivarga - regorafenib - EMEA/H/C/002573/II/0024/G MAH: Bayer AG, Rapporteur: Paula Boudewina van Hennik, "Submission of final results from two non-clinical pharmacokinetic studies (study investigating the substrate characteristics and the inhibitory potential of major human plasma metabolites towards OATP1B1 and OATP1B3; study investigating the hepatobiliary disposition of regorafenib and its metabolites in human hepatocytes and the inhibitory potential of regorafenib and metabolites M-2 and M-5 towards BSEP) and study 16671 using physiologically-based pharmacokinetic (PBPK) modelling investigating CYP3A4, UGT1A9 and P-gp inhibition." Opinion adopted on 09.11.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Strensiq - asfotase alfa - EMEA/H/C/003794/II/0019/G, Orphan	Request for Supplementary Information adopted

MAH: Alexion Europe SAS, Rapporteur: Greg Markey, "Update of section 5.1 of the SmPC in order to update information following final results from studies ENB-006-09 [A Randomized, Open-Label, Multicenter, Multinational, Dose-Ranging, Historical Control Study of the Safety,Efficacy, Pharmacokinetics, and Pharmacodynamics of Asfotase Alfa (Human Recombinant Tissue-Nonspecific Alkaline Phosphatase Fusion Protein) in Children with Hypophosphatasia (HPP)] (and its extension ENB-008-10 [Extension Study of Protocol ENB-006-09 Evaluating the Long-Term Safety and Efficacy of Asfotase Alfa (Human Recombinant Tissue-Nonspecific Alkaline Phosphatase Fusion Protein) in Children with Hypophosphatasia (HPP)]) and ENB-009-10 [A Randomized, Open-Label, Multicenter, Multinational, Dose-Ranging, Concurrent Control Study of the Safety, Efficacy, and Pharmacokinetics of ENB-0040 (Human Recombinant Tissue-Nonspecific Alkaline Phosphatase Fusion Protein) in Adolescents and Adults with Hypophosphatasia (HPP)] listed as an obligation in the Annex II (ANX002). In addition, the Marketing authorisation holder (MAH) took the opportunity to propose editorial changes for section 4.5 to better clarify the information provided." Request for Supplementary Information adopted on 09.11.2017, 14.09.2017.	
Tarceva - erlotinib - EMEA/H/C/000618/II/0051 MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, "Update of section 4.1 of the SmPC in relation to the treatment of patients with locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen based on a review of relevant literature, Real World Data Reports (BIOMARQUEURS FRANCE CSR and ESCAP-2011-CPHG CSR) and a new CSR Addendum of the previously submitted relevant pivotal study BR.21, as requested by the CHMP following assessment of variation EMEA/H/C/000618/II/0043." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 15.06.2017..	See agenda 9.1
Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0041	Request for Supplementary Information adopted

MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Update of sections 4.4 and 4.8 of the SmPC in order to add anaphylactic reaction as a warning and as an adverse reaction with unknown frequency, based on post-marketing experience. The Package Leaflet is updated accordingly. In addition, the Biogen Idec Ltd took the opportunity to bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 09.11.2017, 14.09.2017.	
Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0042 MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update the safety and efficacy information in the paediatric population based on the clinical study results from study 109MS202, listed as a category 3 study in the RMP; this is an open-label, multicentre, multidose study designed to assess the effect of Tecfidera on magnetic resonance imaging lesions and pharmacokinetics, safety and tolerability in paediatric population with relapsing-remitting multiple sclerosis. There are no updates proposed in the package leaflet or RMP." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 14.09.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Toujeo - insulin glargine - EMEA/H/C/000309/II/0100 MAH: Sanofi-Aventis Deutschland GmbH, Duplicate, Duplicate of Lantus, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4 and 6.6 of the SmPC in order to add a warning on the risk for medication error associated with pre-filled pens and cartridges presentations following the evaluation of a signal (EPITT 18893) .The Package Leaflet is updated accordingly." Opinion adopted on 26.10.2017.	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/II/0047 MAH: ViiV Healthcare UK Limited, Rapporteur: Kristina Dunder, "Update of section 4.5 of the SmPC with new transporter data available for	Request for Supplementary Information adopted

abacavir and lamivudine. In addition, the MAH took the opportunity to implement some minor editorial changes in the SmPC." Request for Supplementary Information adopted on 09.11.2017.	
Xalkori - crizotinib - EMEA/H/C/002489/II/0051 MAH: Pfizer Limited, Rapporteur: Alexandre Moreau, "Update of section 4.5 and 5.2 of the SmPC based on the results from the crizotinib-itraconazole drug-drug interaction (DDI) substudy of Study A8081001 (to determine the effect of the coadministration of a strong cytochrome P450 (CYP) 3A inhibitior, itraconazole, on the multiple-dose plasma pharmacokinetic of crizotinib) and the assessment of potential DDIs between crizotinib and weak and moderate CYP3A inhibitors. The labelling is also updated in line with the QRD template." Request for Supplementary Information adopted on 09.11.2017.	Request for Supplementary Information adopted
Xeplion - paliperidone - EMEA/H/C/002105/II/0035 MAH: Janssen-Cilag International NV, Rapporteur: Kristina Dunder, "Update of section 4.2 of the SmPC in order to add a dosage conversion table to provide guidance for healthcare professionals when switching patients from paliperidone ER tablets to paliperidone palmitate long acting injection (PP1M). The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 09.11.2017, 14.09.2017, 20.07.2017.	Request for Supplementary Information adopted
Zelboraf - vemurafenib - EMEA/H/C/002409/II/0043 MAH: Roche Registration Limited, Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to update the safety information following results from pooled safety analysis of the final results from pivotal phase II (NP22657 BRIM-2) and pivotal phase III (NO25026 BRIM-3) trials. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to review the SmPC and Package Leaflet in order to improve clarity and consistency across sections."	Request for Supplementary Information adopted

Request for Supplementary Information adopted on 09.11.2017.	
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." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 14.09.2017, 22.06.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zykadia - ceritinib - EMEA/H/C/003819/II/0016 MAH: Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.2, 4.4, 4.8 and 5.2 of the SmPC in order to include amendments to the posology in hepatically impaired patients and update the safety information, respectively. The updates are based on the results from the hepatic function Study CLDK378A2110 which evaluated the PK, safety and tolerability of a single oral dose of ceritinib in subjects with varying degrees of impaired hepatic function and results from physiology-based pharmacokinetic (PBPK) modeling at steady-state. Submission of the Report for Study A2110 fulfils MEA 001 for Zykadia." Request for Supplementary Information adopted on 09.11.2017, 14.09.2017.	Request for Supplementary Information adopted
WS1193 Evotaz-EMEA/H/C/003904/WS1193/0018 Reyataz-EMEA/H/C/000494/WS1193/0113 MAH: Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Caroline Laborde, "To update sections 4.3 and 4.5 of the SmPC to include information on the contraindicated co-administration with grazoprevir-containing products, including elbasvir/grazoprevir fixed dose combination (used to treat chronic hepatitis C infection) reflecting the results of interaction studies. The Package Leaflets are updated accordingly. The RMP versions 13.2 and	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

5.0, for Reyataz and Evotaz respectively have been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to make some editorial changes and typographical corrections in the REYATAZ and EVOTAZ Product Information." Opinion adopted on 26.10.2017. Request for Supplementary Information adopted on 28.09.2017.	
WS1251 **Eviplera-** **EMEA/H/C/002312/WS1251/0086** **Odefsey-** **EMEA/H/C/004156/WS1251/0019** MAH: Gilead Sciences International Limited, Lead Rapporteur: Johann Lodewijk Hillege, "Updates to the Summary of Product Characteristics (SmPC) sections 4.2, 4.4 , 4.6, 5.1 and 5.2 for Eviplera and Odefsey with data from Study TMC114HIV3015, a Category 4 additional pharmacovigilance activity in the pharmacovigilance plan for both the Eviplera and Odefsey. This is a single-arm, open-label study to assess the pharmacokinetics of Darunavir and Ritonavir, Darunavir and Cobicistat, Etravirine, and Rilpivirine in HIV-1 infected pregnant women results for the Rilpivirine arm. The Labelling and Package Leaflet are updated accordingly. In addition, the Worksharing Applicant (WSA) has taken the opportunity to introduce some minor administrative amendments and to implement some minor linguistic amendments (MLAs) to the translations of the product information annexes." Opinion adopted on 19.10.2017.	Positive Opinion adopted by consensus on 19.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1267 **Docetaxel Winthrop-** **EMEA/H/C/000808/WS1267/0054** **Taxotere-** **EMEA/H/C/000073/WS1267/0129** MAH: Aventis Pharma S.A., Lead Rapporteur: Alexandre Moreau, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning of enterocolitis in patients with neutropenia and to update the safety information on enterocolitis to reflect fatal outcomes based on the review of the MAH global pharmacovigilance data base,	Request for Supplementary Information adopted

worldwide scientific literature and main pharmacovigilance textbooks; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 09.11.2017.	

B.5.3. CHMP-PRAC assessed procedures

Cabometyx - cabozantinib - EMEA/H/C/004163/II/0002/G MAH: Ipsen Pharma, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Sabine Straus, "1) C.I.4 (type II) Update of section 5.1 of the SmPC to reflect the final study results from clinical study XL184-308: A Phase 3, Randomized, Controlled Study of Cabozantinib (XL184) vs Everolimus in Subjects with Metastatic Renal Cell Carcinoma that has Progressed after Prior VEGFR Tyrosine Kinase Inhibitor Therapy, to fulfil the condition to the marketing authorisation listed as a PAES in the Annex II. The RMP version 2.0 has also been submitted. 2) C.I.4 (type II) Update of section 5.3 of the SmPC to reflect the final study results from non-clinical study XL184-NC-036: 104-Week Oral Gavage Carcinogenicity and Toxicokinetic Study with Cabozantinib (XL184) in Rats. The RMP version 2.0 has also been submitted. 3) C.I.3.z (type IB) Update of section 4.5 of the SmPC to implement the wording agreed by the PRAC following the outcome of the PSUR procedure EMEA/H/C/PSUSA/10180/201603." In addition, the MAH took the opportunity to update the list of local representatives." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 14.09.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
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	Request for Supplementary Information adopted

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." Request for Supplementary Information adopted on 09.11.2017, 14.09.2017, 22.06.2017.	
Defitelio - defibrotide - EMEA/H/C/002393/II/0027, Orphan MAH: Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, "Submission of an updated RMP version 4.0 in order to re-classify the imposed non-interventional PASS listed as a category 2 study in the RMP (specific obligation) to a study listed as a category 3 in the RMP (required additional pharmacovigilance activities). This study is an observational registry (DF-VOD2013-03-REG) which aims to record safety and outcome data in patients diagnosed with severe VOD following HSCT treated or not with defitelio. The Annex II of the product information is updated accordingly." Request for Supplementary Information adopted on 09.11.2017.	Request for Supplementary Information adopted
Galafold - migalastat - EMEA/H/C/004059/II/0011, Orphan MAH: Amicus Therapeutics UK Ltd, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Qun-Ying Yue, "Update of section 4.2 of the SmPC to provide further information on missing doses and to improve wording on the administration with food. No new data is submitted to support these changes. In addition, the MAH took this opportunity to include the ATC code and to update the local representatives in the Package Leaflet. Consequently changes are proposed in Annex I, IIIA and IIIB. The RMP version 2.0 has also been submitted" Opinion adopted on 26.10.2017. Request for Supplementary Information adopted on 28.09.2017.	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Olumiant - baricitinib - EMEA/H/C/004085/II/0002 MAH: Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Patrick Batty, "Update of sections 4.5 and 5.2 of the SmPC based on the final study report of an	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

in vitro study to investigate the inhibitory effect of baricitinib on the organic anion transporter 2 (OAT2) in fulfilment of post-authorisation measure MEA 001. In addition, the MAH took the opportunity to make minor editorial changes in the Package Leaflet (Patient Alert Card) to be aligned with Annex II. Furthermore, the updated RMP version 3.1 has been agreed as part of this application." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 14.09.2017.	
Opdivo - nivolumab - EMEA/H/C/003985/II/0038 MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 4.8 of the SmPC with longer follow-up for subjects proceeding to allogeneic transplant following nivolumab treatment, of section 5.1 of the SmPC with efficacy data from longer follow-up based on final results from study CA209205 listed as a PAES in the Annex II; this is a Phase 2, non-comparative, multi-cohort, single-arm, open-label study of nivolumab (BMS-936558) in cHL subjects after failure of ASCT Annex II is updated accordingly. Version 7.7 of the RMP has been submitted." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 14.09.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Otezla - apremilast - EMEA/H/C/003746/II/0017 MAH: Celgene Europe Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Eva A. Segovia, "Update of section 4.4 of the SmPC to include a warning on serious diarrhea, nausea, and vomiting following a safety cumulative review of all data source. The PL has been updated accordingly. RMP version 9.0 has been included to classify serious diarrhea, nausea, and vomiting as important potential risk. In addition the MAH took the opportunity to introduce editorial changes in Annex IIIA and to align the PI with QRD template 10.0." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 12.10.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Praxbind - idarucizumab - EMEA/H/C/003986/II/0007 MAH: Boehringer Ingelheim International GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to reflect the final results from a study 1321.3 titled "A Phase III, case series clinical study of the reversal of the anticoagulant effects of dabigatran by intravenous administration of 5.0 g idarucizumab (BI 655075) in patients treated with dabigatran etexilate who have uncontrolled bleeding or require emergency surgery or procedures. RE-VERSE-AD (A study of the RE-VERSal Effects of Idarucizumab on Active Dabigatran) trial" listed as a category 3 study in the RMP (MEA 001). In addition the MAH took the opportunity to make a minor edit to section 4.2. The RMP version 3.1 has been updated to reflect the completion of the study. In addition, the Marketing authorisation holder took the opportunity to update the immunogenicity section in 5.1 of SmPC." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 14.09.2017, 20.07.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Remicade - infliximab - EMEA/H/C/000240/II/0204 MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final registry report from the C0168T71 study (a review and analysis of birth outcomes from Swedish, Danish and Finish medical birth registers) and an evaluation of pregnancy data from multiple sources. Section 4.6 of the SmPC, relevant section of the PL and the RMP version 13.2 has been updated to reflect the study results. The MAH has also taken the opportunity to bring the product in line with the QRD template and update the local representative section of the PL." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 14.09.2017, 22.06.2017, 23.03.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Spedra - avanafil - EMEA/H/C/002581/II/0027/G	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP

MAH: Menarini International Operations Luxembourg S.A., Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Dolores Montero Corominas, "Update of section 4.4. to reflect the results of clinical study TA-402 "A Double-Blind, Randomized, Placebo-Controlled, Single-Dose, Parallel Study to Assess the Effects of Avanafil on Multiple Parameters of Vision, including, but Not Limited to Visual Acuity, Intraocular Pressure, Pupillometry, and Color Vision Discrimination, in Healthy Male Subjects). Update of section 4.6. of the SmPC in order to reflect the results of clinical study TA-401 "A Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Multicenter Clinical Trial of the Effect of Avanafil on Spermatogenesis in Healthy Adult Males and Adult Males with Mild Erectile Dysfunction". The Package Leaflet is updated accordingly. The RMP version 5.1has also been submitted. In addition, the MAH took the opportunity to make an editorial correction on the approved SmPc by adding the missing adverse reaction epistaxis from the tabulated list of adverse reactions reported in section 4.8. Additionally, the MAH took the opportunity of this variation to align the information included in Section 3 "How to take Spedra" in the Package Leaflet to section 4.2 "Posology" in the SmPC. Some additional minor amendments, due to translation mistakes are proposed for the French Product Information." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 14.09.2017.	Members were in agreement with the CHMP recommendation.
Tamiflu - oseltamivir - EMEA/H/C/000402/II/0128 MAH: Roche Registration Limited, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "Update of section 4.6 of the SmPC in order to reflect the final study results from non-interventional safety study BV29684, which assessed the safety of oseltamivir exposure in pregnant women, and was listed as a category 3 study in the RMP (MEA099). The RMP version 15.0 has also been updated to reflect the study results." Request for Supplementary Information adopted	Request for Supplementary Information adopted

on 09.11.2017, 20.07.2017.	
Vemlidy - tenofovir alafenamide - EMEA/H/C/004169/II/0004 MAH: Gilead Sciences International Limited, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Amelia Cupelli, "Update of sections 4.8 and 5.1 of the Vemlidy SmPC in order to provide 96 week data from Studies GS-US-320-0108 and GS-US-320-0110, listed as category 3 studies in the RMP; GS-US-320-0108 is an ongoing Phase 3, randomized, double-blind, non-inferiority study evaluating the safety and efficacy of Vemlidy 25 mg compared with tenofovir disoproxil fumarate 300 mg in HBeAg-negative subjects with Chronic hepatitis B. GS-US-320-0110 is a an ongoing Phase 3, randomized, double-blind, noninferiority study evaluating the safety and efficacy of Vemlidy versus tenofovir disoproxil fumarate for the treatment of HBeAg-positive subjects with chronic hepatitis B; the Package Leaflet is updated accordingly. The RMP version 2.0 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." Opinion adopted on 09.11.2017.	Positive Opinion adopted by consensus on 09.11.2017. 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 14.1) are updated accordingly. In addition the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Package Leaflet, to include some editorial changes and correct some typos throughout the product information, and to bring the product information in line with the latest QRD template version 10." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 01.09.2017, 05.05.2017.	
WS1026 **Rasilez-EMEA/H/C/000780/WS1026/0110** **Rasilez HCT-EMEA/H/C/000964/WS1026/0080** MAH: Noden Pharma DAC, Lead Rapporteur: Daniela Melchiorri, Lead PRAC Rapporteur: Carmela Macchiarulo, "Update of section 5.1 of the SmPC in order to reflect the results of study SPP100F2301 (ATMOSPHERE) a multicenter, randomized, doubleblind, parallel group, active-controlled study to evaluate the efficacy and safety of both aliskiren monotherapy and aliskiren/enalapril combination therapy compared to enalapril monotherapy, on morbidity and mortality in patients with chronic heart failure (NYHA Class II - IV). The RMP (v 13) has also been updated to reflect the study results." Request for Supplementary Information adopted on 09.11.2017, 14.09.2017, 22.06.2017, 21.04.2017, 15.12.2016.	Request for Supplementary Information adopted
WS1117/G **Stocrin-EMEA/H/C/000250/WS1117/0110/G** **Sustiva-EMEA/H/C/000249/WS1117/0139/G** MAH: Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, "C.I.4 (Type II) - Update of sections 4.3, 4.4, 4.5 and 5.1 of the SmPC in order to add a warning and update the safety information on QTc prolongation based on the final results from study AI266959; this is an interventional study to determine the concentration-electrocardiographic effects of efavirenz in healthy subjects enriched for cyp2b6 polymorphisms; the Package Leaflet is updated accordingly. The RMP version 8 has also been submitted. C.I.4 (Type II) – Update of sections 4.4 and 4.8	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

to add catatonia as a Psychiatric symptom following an assessment of catatonia cases reported in the literature and via the United States (US) Food and Drug Administration Adverse Event Reporting System (FAERS)." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 01.09.2017, 06.07.2017, 06.04.2017.	
WS1180 **Corlentor-** **EMEA/H/C/000598/WS1180/0047** **Ivabradine Anpharm-** **EMEA/H/C/004187/WS1180/0006** **Procoralan-** **EMEA/H/C/000597/WS1180/0046** MAH: Les Laboratoires Servier, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, "Update to the section 4.8 of the SmPC with new ADRs: Ventricular tachycardia, Ventricular fibrillation and Torsade de pointes. The PL is updated accordingly. The RMP version 6 has also been submitted. In addition the MAH took the opportunity to align the PI with the latest QRD template 10.0." Request for Supplementary Information adopted on 26.10.2017, 01.09.2017.	Request for Supplementary Information adopted
WS1211 **Januvia-** **EMEA/H/C/000722/WS1211/0059** **Ristaben-** **EMEA/H/C/001234/WS1211/0051** **TESAVEL-** **EMEA/H/C/000910/WS1211/0059** **Xelevia-EMEA/H/C/000762/WS1211/0063** MAH: Merck Sharp & Dohme Limited, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to modify the information on dosing, an existing warning and administration instructions, respectively for use of sitagliptin in patients with type 2 diabetes mellitus and renal impairment. Consequently, the RMP version 8 has also been updated accordingly. In addition, the WSA took the opportunity to update the list of local representatives in the Package Leaflet for Tesavel and to bring the Product Information (PI) in line with the latest QRD template version 10. Minor editorial changes are also introduced	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

in the Product Information." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 14.09.2017.	
WS1212/G **Efficib-** **EMEA/H/C/000896/WS1212/0085/G** **Janumet-** **EMEA/H/C/000861/WS1212/0085/G** **Ristfor-** **EMEA/H/C/001235/WS1212/0072/G** **Velmetia-** **EMEA/H/C/000862/WS1212/0088/G** MAH: Merck Sharp & Dohme Limited, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2 and 5.2 of the SmPC in order to modify the information on dosing, and administration instructions respectively for use of sitagliptin/metformin in patients with type 2 diabetes mellitus and moderate renal impairment. Consequently, the RMP version 8 has also been updated accordingly. Section 4.5 of the SmPC is also updated to extend the existing warning on the concomitant use of metformin with cimetidine to other medicines potentially interfering the renal excretion of metformin, such as ranolazine, vandetanib and dolutegravir. In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet for Efficib and to bring the Product Information (PI) in line with the latest QRD template version 10. Minor editorial changes are also introduced in the PI." Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 14.09.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.4. PRAC assessed procedures

PRAC Led **Eperzan - albiglutide -** **EMEA/H/C/002735/II/0029/G** MAH: GlaxoSmithKline Trading Services Limited, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "II: C.I.11.b - Update of the RMP to amend Study 201805 (category 3 study): "Observational Study of the Risk of Common Malignant Neoplasms and Malignant	Request for Supplementary Information adopted

Neoplasms of Special Interest (Thyroid and Pancreatic Cancer) in Subjects Prescribed Albiglutide Compared to Those Prescribed Other Antidiabetic Agents", in order to use a different database to study the risk of neoplasms in association with albiglutide exposure II: C.I.11.b – Update of the RMP to add a new category 3 study as an additional pharmacovigilance activity – Study 207351: "Observational Study to Assess Maternal and Fetal Outcomes following exposure to Albiglutide during Pregnancy"" Request for Supplementary Information adopted on 09.11.2017, 22.06.2017, 26.01.2017.	
PRAC Led **Multaq - dronedarone - EMEA/H/C/001043/II/0039/G** MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "C.I.13: Submission of the final report from study DRONE_C_05917 listed as a category 3 study in the RMP. This is a non-interventional epidemiological study aimed for the surveillance of serious liver injuries/diseases (SLD) with the use of dronedarone using multiple databases in the US, including the addendum on surveillance of interstitial lung disease (ILD). The RMP version 11.0 has also been submitted. C.I.13: Submission of the final report from study DRONE_C_05911 listed as a category 3 study in the RMP. This is a non-interventional epidemiological study aimed to study the concomitant use of dronedarone and digoxin (or statins) and the risk of digitalis intoxication (or rhabdomyolysis and myopathy). The RMP version 11.0 has also been submitted." Request for Supplementary Information adopted on 26.10.2017.	Request for Supplementary Information adopted
PRAC Led **Plenadren - hydrocortisone - EMEA/H/C/002185/II/0024, Orphan** MAH: Shire Services BVBA, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, 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,	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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." Opinion adopted on 26.10.2017. Request for Supplementary Information adopted on 01.09.2017, 05.05.2017.	
PRAC Led **WS1197** **Actraphane-** **EMEA/H/C/000427/WS1197/0072** **Actrapid-** **EMEA/H/C/000424/WS1197/0066** **Insulatard-** **EMEA/H/C/000441/WS1197/0069** **Mixtard-** **EMEA/H/C/000428/WS1197/0073** **Protaphane-** **EMEA/H/C/000442/WS1197/0068** MAH: Novo Nordisk A/S, Lead Rapporteur: Hanne Lomholt Larsen, Lead PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 2.2 according to GVP Module V, in order to remove three important potential risks (immunogenicity, allergic reactions and lack of efficacy) related to the new NN729 manufacturing process from the RMP, remove hypoglycaemia and anaphylactic reactions, remove peripheral neuropathy, refraction disorders, lipodystrophy, urticaria, rash, oedema and diabetic retinopathy and remove missing information concerning special populations. No changes are proposed to the product information." Opinion adopted on 26.10.2017. Request for Supplementary Information adopted on 01.09.2017.	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1221** **Brimica Genuair-** **EMEA/H/C/003969/WS1221/0017** **Duaklir Genuair-**	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

EMEA/H/C/003745/WS1221/0017 MAH: AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, Lead PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Robert James Hemmings, "To provide an updated RMP, version 3, to promote "Hypersensitivity (anaphylactic responses, angioedema, and urticaria)" from Important Potential Risk to Important Identified Risk, remove "Use in non-Caucasian patients" as Missing Information (with the completion of clinical studies in Asian patients), and include milestones and due dates for a cardiovascular PASS (D6560R00004) and a drug utilisation study (DUS2: D6560R00002)." Opinion adopted on 26.10.2017.	
PRAC Led **WS1261** **Enbrel-EMEA/H/C/000262/WS1261/0212** **LIFMIOR-EMEA/H/C/004167/WS1261/0010** MAH: Pfizer Limited, Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Robert James Hemmings, "Submission of the final report for the Anti-Rheumatic Treatment in Sweden Registry-Etanercept Cohort Study listed as a category 3 study in the RMP. This non-interventional PASS aimed at providing an assessment of a number of pre-specified safety outcomes for Enbrel as used in the treatment of RA in Sweden, using data from the ARTIS system, in total and from 2006." Opinion adopted on 26.10.2017.	Positive Opinion adopted by consensus on 26.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.5. CHMP-CAT assessed procedures

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

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

WS1214 **Aflunov-EMEA/H/C/002094/WS1214/0039** **Foclivia-EMEA/H/C/001208/WS1214/0033** MAH: Seqirus S.r.l, Lead Rapporteur: Daniela	Positive Opinion adopted by consensus on 19.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Melchiorri Opinion adopted on 19.10.2017. Request for Supplementary Information adopted on 14.09.2017.	
WS1215 **Infanrix hexa-EMEA/H/C/000296/WS1215/0224** MAH: GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 19.10.2017.	Positive Opinion adopted by consensus on 19.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1223 **Ambirix-EMEA/H/C/000426/WS1223/0086** **Fendrix-EMEA/H/C/000550/WS1223/0059** **Infanrix hexa-EMEA/H/C/000296/WS1223/0226** **Twinrix Adult-EMEA/H/C/000112/WS1223/0120** **Twinrix Paediatric-EMEA/H/C/000129/WS1223/0121** MAH: GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 09.11.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation
WS1227 **Infanrix hexa-EMEA/H/C/000296/WS1227/0225** MAH: GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 02.11.2017.	Positive Opinion adopted by consensus on 02.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation
WS1230 **Lixiana-EMEA/H/C/002629/WS1230/0014** **Roteas-EMEA/H/C/004339/WS1230/0002** MAH: Daiichi Sankyo Europe GmbH, Lead Rapporteur: Concepcion Prieto Yerro Opinion adopted on 19.10.2017.	Positive Opinion adopted by consensus on 19.10.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1238/G **Leganto-EMEA/H/C/002380/WS1238/0025/G** **Neupro-EMEA/H/C/000626/WS1238/0079/G** MAH: UCB Pharma S.A., Lead Rapporteur: Bruno Sepodes Opinion adopted on 09.11.2017. Request for Supplementary Information adopted on 05.10.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1239/G	Positive Opinion adopted by consensus on

Infanrix hexa- **EMEA/H/C/000296/WS1239/0227/G** MAH: GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 09.11.2017.	09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1240/G **Ambirix-** **EMEA/H/C/000426/WS1240/0087/G** **Twinrix Adult-** **EMEA/H/C/000112/WS1240/0121/G** **Twinrix Paediatric-** **EMEA/H/C/000129/WS1240/0122/G** MAH: GlaxoSmithkline Biologicals SA, Lead Rapporteur: Robert James Hemmings Opinion adopted on 09.11.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation
WS1253 **Iblias-EMEA/H/C/004147/WS1253/0009** **Kovaltry-** **EMEA/H/C/003825/WS1253/0012** MAH: Bayer AG, Lead Rapporteur: Kristina Dunder Opinion adopted on 02.11.2017.	Positive Opinion adopted by consensus on 02.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1288 **Kinzalmono-** **EMEA/H/C/000211/WS1288/0109** **Micardis-** **EMEA/H/C/000209/WS1288/0113** **Pritor-EMEA/H/C/000210/WS1288/0122** MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Daniela Melchiorri Opinion adopted on 09.11.2017.	Positive Opinion adopted by consensus on 09.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Hexacima- **EMEA/H/C/002702/WS1231/0069** **Hexaxim-** **EMEA/H/W/002495/WS1231/0074** **Hexyon-** **EMEA/H/C/002796/WS1231/0073** MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 02.11.2017.	Positive Opinion adopted by consensus on 02.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Kuvan - sapropterin - **EMEA/H/C/000943/II/0053, Orphan** MAH: BioMarin International Limited, Rapporteur: Peter Kiely Withdrawal request submitted on 20.10.2017.	The MAH withdrew the procedure on 20.10.2017.

Kyprolis - carfilzomib - EMEA/H/C/003790/II/0018, Orphan MAH: Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez" Request for Supplementary Information adopted on 12.10.2017. Withdrawal request submitted on 19.10.2017.	The MAH withdrew the procedure on 19.10.2017.
Ganfort - bimatoprost / timolol - EMEA/H/C/000668/II/0027/G MAH: Allergan Pharmaceuticals Ireland, Rapporteur: Hanne Lomholt Larsen Request for Supplementary Information adopted on 14.09.2017, 09.06.2017.	The MAH withdrew the procedure on 17.10.2017

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

Bexsero - meningococcal group B vaccine (rDNA, component, adsorbed) - EMEA/H/C/002333/II/0059 MAH: GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, , Update of section 4.2 of the SmPC to update the dosing schedule for infants (2 months to 5 months of age) to allow for 2 primary doses plus 1 booster dose in the second year of life based on the results from study V72_28 and its extension V72_28E1 and to update the intervals between primary doses for children (2 years to 10 years of age) to not less than 1 month based on the results from the extension study V72_28E1. Update of section 4.8 of the SmPC to include the number of subjects exposed to at least 1 dose based on the results from the studies V72_28 and V72_28E1. Update of section 5.1 of the SmPC to update the information about immunogenicity in infants and children based on the results from the studies V72_28 and V72_28E1. The Package leaflet is updated accordingly. In addition, the MAH took the opportunity to make some editorial changes in the SmPC and labelling." Request for Supplementary Information adopted on 12.10.2017	The Committee agreed to a request for extension to respond to Request for Supplementary Information adopted on 12.10.2017.

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

entolimod - EMEA/H/C/004656, Orphan,
treatment of acute radiation syndrome

mogamulizumab - EMEA/H/C/004232,
Orphan, treatment of cutaneous T-cell
lymphoma

pegfilgrastim - EMEA/H/C/004802,
treatment of neutropenia

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

ibrutinib - EMEA/H/C/003791/X/0037,
Orphan
MAH: Janssen-Cilag International NV,

sevelamer carbonate -
EMEA/H/C/000993/X/0039

sevelamer / sevelamer carbonate -
EMEA/H/C/003971/X/0011

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

roflumilast - EMEA/H/C/002398/X/0031

roflumilast - EMEA/H/C/001179/X/0035

efavirenz / emtricitabine / tenofovir
disoproxil - EMEA/H/C/004274
, treatment of HIV-1 infection,
List of Questions adopted on 14.09.2017.

eteplirsen - EMEA/H/C/004355, Orphan
Applicant: AVI Biopharma International Ltd,
treatment of Duchenne muscular dystrophy
List of Questions adopted on 21.04.2017.

roflumilast - EMEA/H/C/002399/X/0032

olaparib - EMEA/H/C/003726/X/0016/G,
Orphan
MAH: AstraZeneca AB,
List of Questions adopted on 14.09.2017.

metreleptin - EMEA/H/C/004218, Orphan
Applicant: Aegerion Pharmaceuticals Limited,
treatment of leptin deficiency (lipodystrophy)
List of Questions adopted on 18.05.2017.

gemtuzumab ozogamicin -
EMEA/H/C/004204, Orphan
Applicant: Pfizer Limited, combination therapy with daunorubicin (DNR) and cytarabine (AraC) for the treatment of adult patients with previously untreated, de novo acute myeloid leukaemia (AML).
List of Questions adopted on 21.04.2017.

simoctocog alfa -
EMEA/H/C/002813/X/0020
List of Questions adopted on 14.09.2017.

prasugrel - EMEA/H/C/004644, prevention of atherothrombotic events,
List of Questions adopted on 14.09.2017.

pegfilgrastim - EMEA/H/C/004413,
treatment of neutropenia
List of Questions adopted on 23.03.2017.

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

Raxone - idebenone -
EMEA/H/C/003834/S/0009, Orphan
MAH: Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Carmela Macchiarulo

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

Bosulif - bosutinib -
EMEA/H/C/002373/R/0027, Orphan
MAH: Pfizer Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber

Imatinib Accord - imatinib -
EMEA/H/C/002681/R/0020
MAH: Accord Healthcare Limited, Generic, Generic of Glivec, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia

Maci - matrix applied characterised autologous cultured chondrocytes -
EMEA/H/C/002522/R/0017, ATMP
MAH: Vericel Denmark ApS, Rapporteur: Christiane Niederlaender, Co-Rapporteur: Johannes Hendrikus Ovelgonne, CHMP Coordinator: Greg Markey and Johann Lodewijk Hillege, PRAC Rapporteur: Julie Williams

Natpar - parathyroid hormone -
EMEA/H/C/003861/R/0007, Orphan
MAH: Shire Pharmaceuticals Ireland Ltd,

Rapporteur: Bart Van der Schueren, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Almath Spooner
Pheburane - sodium phenylbutyrate - EMEA/H/C/002500/R/0017 MAH: Lucane Pharma, Rapporteur: Jayne Crowe, PRAC Rapporteur: Almath Spooner

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

Ivemend - fosaprepitant - EMEA/H/C/000743/II/0037 MAH: Merck Sharp & Dohme Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Extension of Indication to include adolescents, infants, toddlers and children aged 6 months and older for prevention of nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 5.0 has also been submitted."
Opdivo - nivolumab - EMEA/H/C/003985/II/0041 MAH: Bristol-Myers Squibb Pharma EEIG, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension of Indication to include adjuvant treatment of adults and adolescents 12 years of age and older with completely resected Stage III and IV melanoma for OPDIVO; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add efficacy and safety information from the pivotal Study CA209238. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to the PI. The RMP version 12.0 has also been submitted. The MAH also took the opportunity to revise the due dates for two Category 4 studies (CA209172 and CA209171) to a later date."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Axumin - fluciclovine (18f) - EMEA/H/C/004197/II/0001/G
MAH: Blue Earth Diagnostics Ltd, Rapporteur: Harald Enzmann

Axumin - fluciclovine (18f) - EMEA/H/C/004197/II/0002/G
MAH: Blue Earth Diagnostics Ltd, Rapporteur: Harald Enzmann

Blincyto - blinatumomab - EMEA/H/C/003731/II/0020/G, Orphan
MAH: Amgen Europe B.V., Rapporteur: Alexandre Moreau

Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0075/G
MAH: AstraZeneca AB, Rapporteur: Bart Van der Schueren

Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0091
MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Kyprolis - carfilzomib - EMEA/H/C/003790/II/0022/G, Orphan
MAH: Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez

Memantine ratiopharm - memantine - EMEA/H/C/002671/II/0012
MAH: ratiopharm GmbH, Generic, Generic of Ebixa, Rapporteur: Bart Van der Schueren

Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0025/G
MAH: GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus

NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0021/G
MAH: Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus

Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (H5N1) (live attenuated, nasal) - EMEA/H/C/003963/II/0009/G
MAH: AstraZeneca AB, Rapporteur: Jan Mueller-

Berghaus

Privigen - human normal immunoglobulin -
EMEA/H/C/000831/II/0127
MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Tecentriq - atezolizumab -
EMEA/H/C/004143/II/0001
MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac

WS1232
Infanrix hexa-
EMEA/H/C/000296/WS1232/0232
MAH: GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1262
Cerezyme-
EMEA/H/C/000157/WS1262/0106
Fabrazyme-
EMEA/H/C/000370/WS1262/0101
Myozyme-
EMEA/H/C/000636/WS1262/0067
Thyrogen-
EMEA/H/C/000220/WS1262/0093
MAH: Genzyme Europe BV, Lead Rapporteur: Johann Lodewijk Hillege

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

Afstyla - lonoctocog alfa -
EMEA/H/C/004075/II/0007
MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC in order to include information on inhibitor development in Previously Untreated Patients (PUPs), based on the ongoing Phase III study CSL627_3001 which aims to evaluate the long-term safety and efficacy of rVIII-Single Chain for routine prophylaxis and on-demand treatment of bleeding episodes in children, adolescents and adults with severe hemophilia A (ie, FVIII activity of ≤ 1%). The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make editorial changes related to the secondary packaging in section 6.5 and 6.6 of the SmPC, in section 4 of the Labelling and sections 3 and 6 of the Package leaflet.

Moreover, the MAH took the opportunity to update the list of local representatives (for Bulgaria) in the Package Leaflet."	
DuoTrav - travoprost / timolol - EMEA/H/C/000665/II/0052 MAH: Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, "Update of sections 4.8 of the SmPC in order to add "lid sulcus deepened" and "iris hyperpigmentation" as new adverse drug reactions and to upgrade the frequency of "skin hyperpigmentation (periocular)" from rare to uncommon based on the post-approval review of the safety data. In addition, section 4.8 of SmPC has been updated to align Adverse Drug Reactions table for the travoprost monotherapy. Based on the same safety review, section 4.6 of SmPC has been updated with dose margin estimates. In addition, the MAH took the opportunity to align the Product information with the currently approved travoprost EU SmPC and QRD version 10 and to update the list of local representatives."	
Jevtana - cabazitaxel - EMEA/H/C/002018/II/0038 MAH: sanofi-aventis groupe, Rapporteur: Alexandre Moreau, "Submission of the final PK analysis report with data from studies EFC11784, EFC11785, TCD11068, and TCD 11870 to provide information on relationship between allelic variants of genes coding for CY3A4 enzyme and cabazitaxel. No changes to the PI are proposed."	
Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0002 MAH: AbbVie Limited, Rapporteur: Joseph Emmerich, "Update of sections 4.8 and 5.1 of the SmPC in order to add information on clinical efficacy and safety in HCV/HIV-1 co-infected subjects, based on new clinical data from Study M14-730 (EXPEDITION-2), a post-registrational Phase 3 study which evaluated the efficacy and safety of the glecaprevir/pibrentasvir regimen in chronic HCV GT1-GT6/HIV-1 co-infected subjects who were HCV treatment-naïve or treatment-experienced. In addition, the SmPC was revised to make minor grammatical and formatting amendments and to correct errors in	

section 5.2."

Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0003
MAH: AbbVie Limited, Rapporteur: Joseph Emmerich, "Update of section 4.5 of the SmPC in order to remove the restriction relating to co-administration with omeprazole, based on new analyses of previously submitted data from the Phase 1 study M14-715 (Open-label study to assess the effect of acid reducing agent on the pharmacokinetics, safety and tolerability of ABT-493/ABT-530 in healthy adult subjects) and on pharmacokinetic as well as efficacy results from Phase 2 and 3 clinical studies for the subjects who were coadministered GLE/PIB and PPIs including omeprazole 40 mg daily. The Package Leaflet is updated accordingly."

Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0023
MAH: Orexigen Therapeutics Ireland Limited, Rapporteur: Hanne Lomholt Larsen, "Update of sections 4.2, 4.3, 4.4, 4.8 and 5.2 of the SmPC in order to update the dosage recommendation and safety information for patients with moderate renal impairment based on final results from study NaltrexBuprop-1006 - A Phase 1, Open-Label, Parallel Study to Evaluate the Pharmacokinetics of a Single Oral Dose of Extended-Release Combination of Naltrexone and Bupropion in Subjects With Normal Renal Function or Varying Degrees of Impaired Renal Function. The Package Leaflet is updated accordingly."

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

Nimenrix - meningococcal group A, C,

W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0071

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

Simponi - golimumab - EMEA/H/C/000992/II/0078/G

MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning on agranulocytosis and update neutropenia from uncommon to common based on new safety information in the Company Core Data Sheet (CCDS).
The Marketing Authorisation Holder has taken the opportunity to include the safety data from the intravenous (IV) psoriatic arthritis (PsA), and IV ankylosing spondylitis (AS) studies that were recently included in the CCDS.

The Package Leaflet is updated accordingly."

Tafinlar - dabrafenib - EMEA/H/C/002604/II/0027

MAH: Novartis Europharm Limited, Rapporteur: Filip Josephson, "Submission of the final report from study BRF113683 (BREAK-3) listed as a category 3 study in the RMP. This is a phase III,

randomised, two-arm, open label study comparing dabrafenib to dacarbazine (DTIC) in previously untreated patients with BRAF mutation positive advanced (stage III) or metastatic (stage IV) melanoma. This study is aimed to confirm the superior efficacy of dabrafenib compared to DTIC."

Torisel - temsirolimus - EMEA/H/C/000799/II/0069, Orphan

MAH: Pfizer Limited, Rapporteur: Harald Enzmann, "Update of section 4.3 of the SmPC in order to specify that the use of temsirolimus in patients with mantle cell lymphoma (MCL) with moderate or severe hepatic impairment is an absolute contraindication, as requested to be clarified during the renewal procedure (EMEA/H/C/000799/R/0065). In addition, the MAH took the opportunity to make minor editorial changes in the Package Leaflet."

Translarna - ataluren - EMEA/H/C/002720/II/0039, Orphan

MAH: PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4, and 5.2 of the SmPC to include new clinical information based on final results from study PTC124-GD-033-HV (Study 033) listed as a category 3 study in the RMP (MEA009); this is a Safety and PK study in patients with moderate to severe hepatic impairment; the Package Leaflet and Labelling are 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 implement some editorial changes."

Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0002/G

MAH: Pfizer Limited, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.4of the SmPC in order to add a warning on syncope based on review post-marketing data. Update of section 4.8 of the SmPC in order to update the safety information regarding booster vaccination based a review of adverse events data reported in the interim clinical study report (B1971033). The package leaflet is updated accordingly. In addition, the MAH took the opportunity to make a clarification on interchangeability of Trumenba

in section 4.2 of the SmPC and to update the list of local representatives in the package leaflet.”	
Venclyxto - venetoclax - EMEA/H/C/004106/II/0007/G, Orphan MAH: AbbVie Limited, Rapporteur: Filip Josephson, “Update of section 4.5 of the SmPC in order to update the drug-drug interaction between venetoclax and dogixin based on final results from study M16-042; this is study to assess the effect of venetoclax on the pharmacokinetics of digoxin in healthy female subjects. Update of section 4.5 of the SmPC in order to update the drug-drug interaction between venetoclax and ritonavir, based on final results from study M15-719; this is study to assess the effect of ritonavir on the pharmacokinetics of venetoclax in healthy female subjects of non-childbearing potential. Update of section 4.5 of the SmPC in order to update the drug-drug interaction between venetoclax and azithomycin, based on final results from study M16-068; this is study to assess effect of azithromycin on the pharmacokinetics of venetoclax in healthy female subjects. The MAH took the opportunity to update the Product Information with minor editorial and QRD updates.”	

B.6.10. CHMP-PRAC assessed procedures

Caprelsa - vandetanib - EMEA/H/C/002315/II/0028 MAH: Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, “Update of sections 4.1, 4.4 and 5.1 of the SmPC in order to delete the information regarding Rearranged during Transfection (RET) mutation. The application addresses SOB 001 and the MAH proposes to revert from conditional marketing authorisation to standard marketing authorisation. Annex II and Package Leaflet are updated accordingly. The RMP version 12.2 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template	

version 10."

Cerdelga - eliglustat - EMEA/H/C/003724/II/0015/G, Orphan

MAH: Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Dolores Montero Corominas, "Update of sections 4.2., 4.3. ,4.4, 4.5. and 5.2. of the SmPC based on the final data from studies POP13777 "Pharmacokinetics of Oral Single-Dose eliglustat in Subjects with Hepatic Impairment" (MEA003.3) and POP13778 "Pharmacokinetics of Oral Single-Dose eliglustat in Subjects with Renal Impairment" (MEA004.3). Annex II D - Conditions Or Restrictions With Regard To The Safe And Effective Use Of The Medicinal Product of the Product Information, additional risk minimisation measures has likewise been amended. The Package Leaflet is updated accordingly. The RMP version 5.0 has also been submitted."

Keytruda - pembrolizumab - EMEA/H/C/003820/II/0037/G

MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus, "Update of sections 4.4 and 4.8 of the SmPC to add information regarding the risks of encephalitis, sarcoidosis and graft versus host disease (GVHD) that have been reported in patients treated with pembrolizumab. The Package Leaflet and the 'additional risk minimization measures' section (educational material) in the Annex II have been updated accordingly. In addition, the MAH has implemented minor changes in the SmPC section 5.1 and editorial changes in the Package Leaflet.
An updated RMP version 13.0 was provided as part of the application."

Olumiant - baricitinib - EMEA/H/C/004085/II/0003

MAH: Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Patrick Batty, "Update of section 4.4 of the SmPC in order to include results of a vaccination sub-study of the long term extension study I4V-MC-JADY (I4V-MC-JADY: 'A Phase 3, Multicenter Study to Evaluate the Long-Term Safety and Efficacy of Baricitinib in Patients with Rheumatoid Arthritis'). In addition, the updated

RMP version 4.0 has been submitted as part of this application.”	
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0002/G MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Grouped variations consisting of: 1) update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add myocarditis as a new adverse reaction, based on the results of a cumulative review of cases of suspected myocarditis . As a consequence, the information regarding the posology and special warnings have been updated. Annex II, the Package Leaflet and the RMP (version 2.0) have been updated accordingly;2) update of the RMP to add haemolytic anaemia as a new important identified potential risk.”	
Zydelig - idelalisib - EMEA/H/C/003843/II/0038 MAH: Gilead Sciences International Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, “Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to reflect information from a recent cumulative safety review of cases of organising pneumonia. The safety review resulted from the Marketing authorisation holder (MAH) MAH ongoing pharmacovigilance and signal detection for Zydelig. The RMP version 2.6 has also been submitted to extend the deadlines for submission of final CSRs for three studies linked with Annex II conditions. The Package Leaflet and Labelling are updated accordingly.”	
WS1292 **Evotaz-EMEA/H/C/003904/WS1292/0019** **Reyataz-EMEA/H/C/000494/WS1292/0114** MAH: Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Joseph Emmerich, Lead PRAC Rapporteur: Caroline Laborde, “Update of section 4.3 and 4.5 of the SmPC in order to add a contraindication with lurasidone to reflect this interaction based on literature data. The Package Leaflet is updated accordingly. The RMP of Reyataz/Evotaz versions 14 and 6 respectively have been submitted.”	

B.6.11. PRAC assessed procedures

B.6.12. CHMP-CAT assessed procedures

Maci - matrix applied characterised autologous cultured chondrocytes - EMEA/H/C/002522/II/0014/G, ATMP
MAH: Vericel Denmark ApS, Rapporteur: Christiane Niederlaender, CHMP Coordinator: Greg Markey

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

WS1250/G
Infanrix hexa- EMEA/H/C/000296/WS1250/0230/G
MAH: GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1255
Infanrix hexa- EMEA/H/C/000296/WS1255/0231
MAH: GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1257
Infanrix hexa- EMEA/H/C/000296/WS1257/0229
MAH: GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1271/G
Ebymect- EMEA/H/C/004162/WS1271/0028/G
Qtern- EMEA/H/C/004057/WS1271/0010/G
Xigduo- EMEA/H/C/002672/WS1271/0039/G
MAH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder

WS1287
Abseamed- EMEA/H/C/000727/WS1287/0066
Binocrit- EMEA/H/C/000725/WS1287/0066
Epoetin alfa Hexal-

EMEA/H/C/000726/WS1287/0065
MAH: Sandoz GmbH, Lead Rapporteur:
Alexandre Moreau

WS1290
Abseamed-
EMEA/H/C/000727/WS1290/0067
Binocrit-
EMEA/H/C/000725/WS1290/0067
Epoetin alfa Hexal-
EMEA/H/C/000726/WS1290/0066
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

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

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

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

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

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

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

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

G. ANNEX G

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

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

Qualification of Biomarkers:

HTA:

G.2. Ongoing procedures

G.3. PRIME

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

G.3.1. List of procedures concluding at 06-09 November 2017 CHMP plenary:

Haematology-haemostaseology		
1.	(SME)Prevention of bleeding in patients with haemophilia B	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Oncology		
2.	**Autologous T lymphocyte-enriched population of cells transduced with a lentiviral vector encoding a chimeric antigen**	The CHMP granted eligibility to PRIME and adopted the critical summary report.

	receptor targeting human B cell maturation antigen with 4-1BB and CD3-zeta intracellular signalling domains (bb2121), ATMP, Treatment of relapsed and refractory multiple myeloma	
3.	(SME)Treatment of breast cancer in men	The CHMP denied eligibility to PRIME and adopted the critical summary report.
4.	Treatment of non-muscle invasive bladder cancer (NMIBC)	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Immunology-Rheumatology-Transplantation		
5.	Treatment of Steroid Resistant Acute Graft-Versus-Host Disease	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Musculo-skeletal		
6.	**Recombinant humanised monoclonal IgG2 lambda antibody against human sclerostin (BPS804)**,(SME), Treatment of osteogenesis imperfecta Types I, III and IV	The CHMP granted eligibility to PRIME and adopted the critical summary report.
Neurology		
7.	Treatment of X-linked Adrenoleukodystrophy	The CHMP denied eligibility to PRIME and adopted the critical summary report.
8.	Treatment of Huntington's disease	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Infectious Diseases		
9.	**LR12** Treatment of Septic Shock	The CHMP granted eligibility to *PRIME*and adopted the critical summary report.

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

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