8 March 2018
EMA/108712/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Minutes of the meeting on 22-25 January 2018

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).

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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) January 2018 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 22-25 January 2018 (to be published post February 2018 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 22-25 January 2018

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 11-14 December 2017

The CHMP adopted the CHMP minutes for 11-14 December 2017. The Minutes of the January 2018 CHMP ORGAM meeting held on 15 January 2018, together with all decisions taken at that meeting, were adopted.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. trastuzumab - EMEA/H/C/004361

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

Scope: Oral explanation

Action: Oral explanation to be held on 24 January 2018 at time 09:00

List of Outstanding Issues adopted on 09.11.2017. List of Questions adopted on 20.07.2017.

An oral explanation was held on 24 January 2018 at time 09:00. The presentation by the applicant focused on quality and clinical data to support biosimilarity.

2.1.2. 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: Oral explanation, SAG report

Action: Oral explanation to be held on 23 January 2018 at time 09:00

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

The CHMP noted the report from SAG Oncology meeting held on 11 January 2018.The experts were of the view that based on objective responses reported from small trials in the metastatic setting, neratinib appears to be associated with relevant antitumour activity. The SAG also agreed that the conduct of the main study for this application, due to various reasons has a number of limitations, including missing data that are not possible to correct and result in uncertainties about the magnitude of the effect. However, the views of the SAG diverged on a number of key conclusions such as the importance of uncertainties, the strength of the evidence for clinical efficacy, the clinical relevance of the primary endpoint iDFS (time between the date of randomization to the first occurrence of invasive recurrence, i.e. local/regional, ipsilateral, or contralateral breast cancer; distant recurrence, or death from any cause), the observed magnitude of effect in terms of iDFS, and the importance of the observed toxicity. Regarding the risk of gastrointestinal toxicity, the SAG agreed that the role of loperamide is not well understood in view of the conflicting results in the studies submitted. Trial 6201, which was specifically designed to answer the toxicity handling question, is still in progress and early data from the trial as presented at the meeting show a significant number of patients still having clinically relevant grades of diarrhoea. Further prospective research needs to be conducted to establish optimal antidiarrhoeal prophylaxis and treatment regimens. The SAG views also diverged in terms of acceptability of the observed toxicity.

The CHMP noted the study design of the single pivotal trial supporting this application as well as the Applicant's proposed indication. An oral explanation was held on 23 January 2018 at time 09:00. The Applicant's presentation focussed on the proposed indication as well as on the overview of efficacy and safety.

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

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

Santhera Pharmaceuticals (Deutschland) GmbH

Scope: Oral explanation/SAG report

Action: Oral explanation to be held on 23 January 2018 at time 11:00

Opinion adopted on 27.09.2017.

Participation of patient representatives

An Oral explanation was held on 23 January 2018 at time 11:00

See 5.3

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. EnCyzix - enclomifene - EMEA/H/C/004198

Renable Pharma Limited; treatment of hypogonadotrophic hypogonadism

Scope: Opinion

Action: For adoption

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

Oral explanation held on 14.12.2017. List of Outstanding Issues adopted on 12.10.2017. List of Questions adopted on 26.01.2017.

The Committee adopted a negative opinion by majority (25 negative out of 29 votes) recommending the refusal of the marketing authorisation application. The CHMP adopted the CHMP assessment report.

The Norwegian Member was in agreement with the CHMP recommendation and the Icelandic Member was against.

The divergent position (Kristina Dunder, Koenraad Norga, Bart van der Schueren, Agnes Gyurasics, Hrefna Gudmundsdottir) was appended to the opinion.

The refusal question and answers document was circulated for information.

3.1.2. Hemlibra - emicizumab - EMEA/H/C/004406

Accelerated assessment

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

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 12.12.2017. List of Questions adopted on 10.10.2017.

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 emicizumab is a new active substance, as claimed by the applicant.

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

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

The CHMP noted the letter of recommendation dated 25 January 2018.

The summary of opinion was circulated for information.

3.1.3. Lamzede - 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: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 14.12.2017, 14.09.2017. List of Questions adopted on 26.01.2017.

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

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

Furthermore, the CHMP considered that velmanase alfa 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.

3.1.4. Segluromet - ertugliflozin / metformin hydrochloride - EMEA/H/C/004314

Merck Sharp & Dohme Limited; treatment of type 2 diabetes mellitus

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 09.11.2017. List of Questions adopted on 22.06.2017.

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 ertugliflozin is a new active substance, as claimed by the marketing authorisation holder.

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.

3.1.5. Semglee - insulin glargine - EMEA/H/C/004280

Mylan S.A.S; treatment of diabetes mellitus

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 12.10.2017. List of Questions adopted on 23.02.2017.

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

The Committee adopted a positive opinion 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 19 January 2018.

3.1.6. Shingrix - herpes zoster vaccine - EMEA/H/C/004336

GlaxoSmithkline Biologicals SA; prevention of herpes zoster (HZ) and post-herpetic neuralgia (PHN), in adults 50 years of age or older

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 14.12.2017, 14.09.2017. List of Questions adopted on 21.04.2017.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (25 positive out of 28 votes) together with the CHMP assessment report and translation timetable.

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

The divergent position (Greg Markey, Robert James Hemmings, Johann Lodewijk Hillege) was appended to the opinion.

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 23 January 2018.

3.1.7. Steglatro - ertugliflozin - EMEA/H/C/004315

Merck Sharp & Dohme Limited; type 2 diabetes mellitus

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 09.11.2017. List of Questions adopted on 22.06.2017.

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 ertugliflozin is a new active substance, as claimed by the applicant.

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

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

The summary of opinion was circulated for information.

3.1.8. Steglujan - ertugliflozin / sitagliptin - EMEA/H/C/004313

Merck Sharp & Dohme Limited; type 2 diabetes mellitus

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 09.11.2017. List of Questions adopted on 22.06.2017.

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 ertugliflozin is a new active substance, as claimed by the applicant.

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

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

The summary of opinion was circulated for information.

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

3.2.1. peramivir - EMEA/H/C/004299

treatment of influenza

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 12.10.2017. 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 2nd list of outstanding issues with a specific timetable.

3.2.2. brigatinib - EMEA/H/C/004248

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

Scope: 2nd day 180 list of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 12.10.2017. 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 2nd list of outstanding issues with a specific timetable.

3.2.3. betrixaban - EMEA/H/C/004309

treatment of prophylaxis of venous thromboembolism (VTE)

Scope: Revised 2nd day 180 list of outstanding issue, adopted by written procedure on 22 December 2017.

Action: For information

List of Outstanding Issues adopted on 14.12.2017, 12.10.2017. List of Questions adopted on 21.04.2017.

The Committee noted the revised 2nd list of outstanding issues which was adopted by written procedure on 22 December 2017.

3.2.4. caplacizumab - Orphan - EMEA/H/C/004426

Ablynx NV; indicated for the treatment of acquired thrombotic thrombocytopenic purpura (aTTP)

Scope: Day 180 list of outstanding issue,
Request for extension of clock stop to respond to list of outstanding issues to be adopted at the January 2018 meeting.

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.

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

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

treatment of HIV

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 12.10.2017.

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. pemetrexed - EMEA/H/C/003958

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

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 12.10.2017.

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. buprenorphine - EMEA/H/C/004651

treatment of opioid dependence within a framework of medical, social and psychological treatment

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. durvalumab - EMEA/H/C/004771

treatment of locally advanced, unresectable non-small cell lung cancer (NSCLC)

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. damoctocog alfa pegol - Orphan - EMEA/H/C/004054

Bayer AG; Treatment and prophylaxis of haemophilia A

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. pegfilgrastim - EMEA/H/C/004700

treatment of neutropenia

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

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

Scope: Appointment of re-examination rapporteurs, draft timetable

Letter from the applicant dated 3 January 2018 requesting a re-examination of the Opinion adopted on 14 December 2017.

Action: For adoption

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

Opinion 14.12.2017

The CHMP appointed a re-examination Rapporteur and a re-examination Co-Rapporteur.

The CHMP noted the draft re-examination timetable.

3.4.2. 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: Request for an extension of clock stop to respond to the List of Questions adopted in November 2017
Action: For adoption

List of Questions adopted on 09.11.2017.

The CHMP agreed to the request by the applicant for an additional extension of clock stop to respond to the List of Questions adopted in November 2017

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

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

Scope: Request for an extension of clock stop to respond to the List of Questions adopted in November 2017

Action: For adoption

The CHMP agreed to the request by the applicant for an additional extension of clock stop to respond to the List of Questions adopted in November 2017

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

Clovis Oncology UK Ltd; treatment of ovarian cancer

Scope: Draft list of experts for the SAG Oncology meeting on 13 February 2018.

Action: For adoption

Oral explanation held on 08.11.2017. List of Outstanding Issues adopted on 14.12.2017, 09.11.2017, 14.09.2017. List of Questions adopted on 23.03.2017.

The CHMP adopted the list of experts for the SAG Oncology meeting and a list of questions to this group.

3.4.5. abaloparatide - EMEA/H/C/004157

treatment of osteoporosis

Scope: Request for extension of clock stop to respond to List of outstanding issue adopted in December 2017
List of questions and draft list of experts for the ad-hoc expert group meeting on 1 March 2018.

Action: For adoption

Oral explanation held on 13.12.2017. List of Outstanding Issues adopted on 14.12.2017, 20.07.2017, 15.12.2016. List of Questions adopted on 01.04.2016.

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

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of outstanding issue adopted in December 2017.

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

treatment of infections

Scope: Request for extension of clock stop to respond to List of Questions adopted in November 2017.

Action: For adoption

List of Questions adopted on 09.11.2017

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Questions adopted in November 2017.

3.4.7. volanesorsen - Orphan - EMEA/H/C/004538

Akcea Therapeutics UK Ltd.; indicated as an adjunct to diet for the treatment of patients with familial chylomicronemia syndrome (FCS).

Scope: Request for extension of clock stop to respond to List of Questions adopted in December 2017.

Action: For adoption

List of Questions adopted on 14.12.2017

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Questions adopted in December 2017.

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

No items

3.6. Initial applications in the decision-making phase

3.6.1. Lokelma - sodium zirconium cyclosilicate - EMEA/H/C/004029

AstraZeneca AB; for the treatment of hyperkalaemia

Scope: Re-adoption of opinion

Action: For adoption

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

Opinion adopted 23.02.2017.

Following an inspection of the manufacturing site for Lokelma's active substance confirming that the site is compliant with good manufacturing practice, the Committee confirmed its previous positive opinion and recommended by consensus the granting of a marketing authorisation together with the CHMP assessment report and translation timetable.

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

The summary of opinion was circulated for information.

3.7. Withdrawals of initial marketing authorisation application

3.7.1. Balimek - binimetinib - EMEA/H/C/004052

Pierre Fabre Médicament; treatment of unresectable or metastatic melanoma
Treatment of unresectable melanoma, with NRAS Q61 mutation

Scope: Withdrawal of initial marketing authorisation application

Action: For information

The CHMP noted the withdrawal of initial marketing authorisation application.

3.7.2. Rotigotine Mylan - rotigotine - EMEA/H/C/004286

Mylan S.A.S; treatment of idiopathic Restless Legs Syndrome and Parkinson's disease

Scope: Withdrawal of initial marketing authorisation application

Action: For information

The CHMP noted the withdrawal of initial 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. Nuwiq - simoctocog alfa - EMEA/H/C/002813/X/0020

Octapharma AB

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add new strengths of 2500 IU, 3000 IU, 4000 IU for Nuwiq, powder and solvent for solution for injection.
The RMP (version 5.4) is updated accordingly."

Action: For adoption

List of Outstanding Issues adopted on 14.12.2017. List of Questions 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 by consensus together with the CHMP Assessment Report and translation timetable.

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

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

4.2.1. Bortezomib Accord - bortezomib - EMEA/H/C/003984/X/0008

Accord Healthcare Ltd

Rapporteur: Milena Stain, PRAC Rapporteur: Carmela Macchiarulo

Scope: "Extension application to add a new strength of powder for solution for injection (1 mg) to the currently approved strength (3.5 mg) of Bortezomib Accord."

Action: For adoption

List of Questions adopted on 20.07.2017.

The Committee discussed the issues identified in this application. The outstanding issues related to the quality and clinical issues. It was noted that the applicant should provide an updated similarity report.

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

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

4.3.1. Bydureon - exenatide - EMEA/H/C/002020/X/0048/G

AstraZeneca AB

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

Scope: "Extension application to introduce new pharmaceutical form (prolonged-release suspension for injection) grouped with type II variation to align the PI for the approved Bydureon products (powder and solvent for prolonged-release suspension for injection, and powder and solvent for prolonged-release suspension for injection in pre-filled pen) with the PI proposed for the Bydureon new pharmaceutical form (prolonged-release suspension for injection in autoinjector). In addition, the MAH took the opportunity to make minor editorial changes through SmPC. Moreover, RMP version 28 has been submitted as part of this application."

Action: For adoption

The Committee discussed the issues identified in this application. It was noted that only minor issues were remaining, which should be clarified by the applicant.

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

4.4.1. Xeljanz - tofacitinib - EMEA/H/C/004214/X/0005/G

Pfizer Limited

Rapporteur: Robert James Hemmings, PRAC Rapporteur: Sabine Straus

Scope: "Extension application to introduce a new strength (10 mg film coated tablets). In addition, the MAH proposed a type II variation (C.I.6.a) to extend the indication to include 'the induction and maintenance of treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent"

Clockstop extension requested to respond to LoQ

Action: For adoption

List of Questions adopted on 14.12.2017.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to List of questions adopted in December 2017.

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

CSL Behring GmbH

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

Scope: "Extension of Indication to include immunomodulatory therapy in adults, children and adolescents (0-18 years), for the treatment of patients with chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy after stabilization with IVIg.

As a consequence, sections 4.1, 4.2, 4.7, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP is updated (v. 4.2)"

Action: For adoption

Request for Supplementary Information adopted on 14.12.2017, 12.10.2017.

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. Ivemend - fosaprepitant - EMEA/H/C/000743/II/0037

Merck Sharp & Dohme Limited

Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "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."

Action: For adoption

The Committee discussed the issues identified in this application. The CHMP noted a few questions to be addressed by the applicant, on quality and on the MoS exercise and particularly anticipated exposure in the smallest children.

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

5.1.3. Opdivo - nivolumab - EMEA/H/C/003985/II/0041

Bristol-Myers Squibb Pharma EEIG

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

Scope: "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."

Action: For adoption

The Committee discussed the issues identified in this application. The CHMP discussed the RFS and OS data and noted that benefit in terms of long-term survival is unclear. Therefore the applicant should justify the relevance of the currently available efficacy data and to explore to what extent there could be a loss of chance by using nivolumab in the adjuvant treatment of melanoma for the use of, in particular check-point inhibitors, in the advanced melanoma setting. The Committee discussed the need for SAG. The Committee proposed to consult SAG Oncology.

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

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

Pfizer Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

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

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 wording of the indication. The Committee discussed in particular the appropriate target population in line with the patient population from the clinical study.

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

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

Glaxo Group Ltd

Lead Rapporteur: Concepcion Prieto Yerro

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

Action: For adoption

Request for Supplementary Information adopted on 09.11.2017.

The Committee discussed the wording of the indication and confirmed that all issues previously identified in this application had been addressed.

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

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

The summary of opinion was circulated for information.

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

No items

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

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

Santhera Pharmaceuticals (Deutschland) GmbH

Scope: Opinion

Action: For adoption

Opinion adopted on 27.09.2017.

See 2.3

Participation of patient representatives

The CHMP noted the report from the SAG. The experts expressed some uncertainties on the interpretation of the observed effect. On the actual use of the primary endpoint the views of the experts were split. The group considered that the observed effect could be clinically relevant provided that the effect would be maintained over several years, which could not be concluded beyond the period of 1 year. The experts agreed that the proposed patient population exists but pointed out some difficulties in the definition of the patient on an individual basis.

An oral explanation was held on 23 January 2018 at time 11:00.

After the oral explanation the members reflected on the available data. Some members expressed doubts on the reliability of the results, outlining methodological issues in the study conduct. The members also debated whether the 1 year clinical data could be considered to sufficiently support the efficacy. Different views were expressed.

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

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

The divergent position was appended to the opinion.

The refusal question and answers document was circulated for information.

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. Vitrolife IVF media - recombinant human albumin solution - EMEA/H/D/004693

DNV Nemko Presafe AS; human assisted reproductive techniques including in-vitro fertilisation procedures

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 09.11.2017. List of Questions adopted on 18.05.2017.

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

The Committee adopted a positive opinion recommending by consensus the granting of a favourable opinion on the quality and safety including the clinical benefit/risk profile of recombinant human albumin solution used as ancillary medicinal substances in the above mentioned medical device. The CHMP adopted the CHMP assessment report.

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

The summary of opinion was circulated for information.

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. apalutamide - H0004452

Apalutamide is intended for the treatment of adult men with NM-CRPC who are at high risk of developing metastatic disease.

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

Action: For adoption

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

8.2. 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: all 9 were denied.

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

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Buccolam - midazolam - EMEA/H/C/002267/QD2017-173

Shire Services BVBA

Scope: defect with oral syringes, DHPC and communication plan

Action: For information

Adopted by written procedure on 16 November 2017 and 12 January 2018.

The CHMP noted the update on the quality issue with the oral syringe tip-cap leading to a phased recall of product. The members were also informed about the measures taken by the MAH. The CHMP agreed to the updated DHPC and communication plan.

9.1.2. Insulin Human Winthrop - insulin human winthrop - EMEA/H/C/000761

Sanofi-Aventis Deutschland GmbH

Rapporteurs: Bart Van der Schueren, Co-Rapporteur: Johann Lodewijk Hillege

Scope: Withdrawal of marketing authorisation

Action: For information

The CHMP noted the withdrawal of the marketing authorisation.

9.1.3. Epivir - lamivudine - EMEA/H/C/000107/II/0104

ViiV Healthcare UK Limited

Rapporteur: Joseph Emmerich

Scope: "Update of section 4.5 of the SmPC of both Epivir tablets and oral solution, and section 4.4 of the SmPC for Epivir Oral solution only, to add information regarding the potential for interaction between lamivudine and sorbitol based on the results of Study 204857. Further, a minor amendment has been implemented throughout the SmPC to update the clinical terminology for 'Pneumocystis carinii pneumonia' to 'Pneumocystis jiroveci pneumonia'. In addition, the MAH has taken the opportunity to align the product information with the QRD template version 10, to make minor editorial changes in the annexes and to update the contact details of the local representative in Norway in the Package Leaflet."

Action: For discussion

Request for Supplementary Information adopted on 14.12.2017, 21.09.2017, 05.05.2017

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.

9.1.4. Zeffix - lamivudine - EMEA/H/C/000242/II/0069

Glaxo Group Ltd,

Rapporteur: Joseph Emmerich

Scope: "Update of section 4.5 of the SmPC to add information regarding a potential interaction with sorbitol-containing medicines. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement a minor change in the labelling in line with the QRD template version 10."

Action: For discussion

Request for Supplementary Information adopted on 14.12.2017, 21.09.2017, 05.05.2017

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. WS1156
Combivir-EMEA/H/C/000190/WS1156/0090
Kivexa-EMEA/H/C/000581/WS1156/0072
Triumeq-EMEA/H/C/002754/WS1156/0042
Trizivir-EMEA/H/C/000338/WS1156/0104

ViiV Healthcare UK Limited

Rapporteur: Joseph Emmerich

Scope: "Update of section 4.5 of the SmPC to add information regarding the potential interaction between lamivudine and sorbitol based on the results of Study 204857. The Package Leaflet has been updated accordingly. Further, a minor amendment has been implemented throughout the SmPC in order to update the clinical terminology of Pneumocystis carinii pneumonia to Pneumocystis jiroveci pneumonia. In addition, the MAH takes the opportunity to make minor editorial changes, to align the annexes with the QRD template version 10 and to update the contact details of the local representative in Norway in the Package Leaflet."

Action: For discussion

Request for Supplementary Information adopted on 14.12.2017, 21.09.2017, 05.05.2017

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.

9.1.6. Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0027/G

Biofrontera Bioscience GmbH

Rapporteur: Harald Enzmann

Scope: "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.

Change in the legal status of Ameluz from "medicinal product subject to restricted medical prescription" to "medicinal product subject to medical prescription."

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the labelling in line with the QRD template and the list of local representatives in the Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 09.11.2017, 12.10.2017.

The members discussed the request for the switch from "restricted medical prescription" to "medical prescription". It was highlighted that similar nationally authorised products are marketed in the EU. The Committee discussed the SmPC wording of sections 4.2 and 4.4, also in comparison with the labelling of the nationally authorised product Metvix.

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.

10. Referral procedures

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

10.9. Disagreement between Member States on Type II variation– Arbitration procedure initiated by MAH under Article 6(13) 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

January 2018 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

The CHMP noted the January 2018 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. First experiences working with HTA bodies at the time of Market Entry

Action: For discussion

The CHMP noted the first experiences working with HTA bodies at the time of Market Entry.

14.1.2. Reflection paper on the wording of therapeutic indication in the centralised procedure

CHMP Coordinator: Kristina Dunder

Action: For discussion

The CHMP noted the reflection paper.

Comments should be sent by 9 February 2018. Further discussion is expected during the February Plenary.

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 8-11 January 2018

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 January 2018

Action: For adoption

The CHMP noted the information.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 17-19 January 2018

Action: For information

The CHMP noted the draft minutes.

Draft guideline on safety and efficacy follow-up and risk management of Advanced Therapy Medicinal Products (EMEA/149995/2008 rev.1)

Action: For adoption for 3 months public consultation

The CHMP adopted the guideline for 3 months public consultation.

14.2.3. Paediatric Committee (PDCO)

PIPs reaching D30 at January 2018 PDCO

Action: For information

The CHMP noted the PIPs reaching D30 at January 2018 PDCO.

Report from the PDCO meeting held on 23-26 January 2018

Action: For information

The CHMP noted the report.

14.2.4. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 16-18 January 2018
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 22-24 January 2018

Action: For information

The CHMP noted the report.

CMDh questions to SWP on anaesthetics and sedatives in young children and pregnant

women (following January 2018 PRAC advice)

Action: For adoption

The CHMP endorsed the CMDh list of questions to the SWP.

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 8-11 January 2018. 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. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse,

Reports from BWP January 2018 meeting to CHMP for adoption:

- 13 reports on products in scientific advice and protocol assistance
- 07 reports on products in pre-authorisation procedures
- 00 reports on products in post-authorisation procedures
- 04 reports on products in plasma master file

Action: For adoption

The CHMP adopted the BWP reports.

Scope: Review of seed sequencing data - annual influenza vaccines 2017-2018

BWP report

Action: For adoption

The CHMP adopted the BWP report and noted the review.

14.3.3. Biostatistics Working Party (BSWP)

Chair: Anja Schiel/Thomas Lang

Scope: Election of a new Vice-Chair of the Biostatistics Working Party (BSWP)

Action: For adoption

The CHMP elected Jörg Zinserling (DE) as Vice-Chair to BSWP.

Nomination of additional assessors (observer) to BSWP

Action: For adoption

The CHMP nominated Florian Klinglmüller (AT) and Khadija Rantell (UK) as additional assessors (observers) to BSWP.

14.3.4. Blood Products Working Party (BPWP)

Chair: Jacqueline Kerr

Nomination of new alternate member to the BPWP.
Action: For adoption

The CHMP appointed Sara Franco (FR) as alternate member to the BPWP.

Nomination of additional expert to the BPWP

Action: For adoption

The CHMP nominated Claudia Reichmann (DE) as additional expert to BPWP.

14.3.5. Cardiovascular Working Party (CVSWP)

Chair: Kristina Dunder

Guideline on clinical investigation of medicinal products in the treatment or prevention of diabetes mellitus (CPMP/EWP/1080/00 Rev. 2)

Action: For adoption for 6 months public consultation

The CHMP discussed the guideline.

Post-meeting note: The guideline was adopted for 6 months public consultation via written procedure on 29 January 2018.

14.3.6. Central Nervous System Working Party (CNSWP)

Chair: Karl Broich/André Elferink,

Guideline on the clinical investigation of medicines for the treatment of Alzheimer's disease and other dementias (CPMP/EWP/553/95 Rev.2)

Action: For adoption

The CHMP postponed the adoption of the guideline. Further discussions should be held in February.

14.3.7. Geriatric Expert Group (GEG)

Chair: Katarina Vučić

Reflection paper on physical frailty: instruments for baseline characterisation of older populations in clinical trials (EMA/CHMP/778709/2015)

Action: For adoption

The CHMP adopted the Reflection paper on physical frailty.

14.3.8. Safety Working Party (SWP)

Chair: Jan Willem Van der Laan

EC consultation on Pharmaceuticals in the environment

The SWP is responding on behalf of the CHMP to the targeted stakeholder consultation

Action: For adoption

The CHMP mainly discussed questions 7 and 11 and adopted the proposal.

14.3.9. Vaccines Working Party (VWP)

Chair: Mair Powell/Svein Rune Andersen

Nomination of additional assessor (observer) to VWP

Action: For adoption

Postponed

14.3.10. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink/Henrike Potthast

CHMP request on biosimilarity to Pharmacokinetics Working Party (PKWP) (EMA/CHMP/230419/2017)

Action: For information

The CHMP noted the questions-and-answers document on request on biosimilarity to Pharmacokinetics Working Party (PKWP). The document will be published.

14.3.11. Biosimilar Medicinal Product Working Party (BMWP)

Chair: Elena Wolff-Holz/Niklas Ekman,

Nomination of additional assessor (observer) to BMWP

Action: For adoption

The CHMP nominated Simona Badoi (RO) as additional assessor (observer) to BMWP.

14.3.12. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus

RIWP membership: call for experts to participate in guideline development

Action: For information

Please send nominations for experts/members to support the development of the following guidelines.

For the development of a "Concept paper on development strategies for allergen products intended for allergies with low prevalence" experts with regulatory and/or clinical expertise for this topic are sought. Three new members are envisaged.

For the development of a "Concept paper on the need for guidance on the development of medicinal products for acute kidney injury" experts with regulatory and/or clinical expertise for this topic are sought. Two new members are envisaged.

The CHMP noted the call.

14.3.13. Name Review Group (NRG)

NRG outcome, adopted by NRG via written procedure January 2018

Action: For adoption

The CHMP noted the NRG outcome.

14.3.14. Discussion on additional assessors (observers) to working parties

CHMP: Tomas Salmonson

Action: For discussion

The CHMP was asked whether the number of additional assessors nominated to temporary working parties should be limited. Various opinions were expressed that did not lead to an agreement. It was agreed to continue the discussion in February based on a proposal to be prepared by EMA.

14.4. Cooperation within the EU regulatory network

14.4.1. Evaluation of orphan and paediatrics legislations

Action: For information

The CHMP noted the presentation.

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

14.7.1. CHMP 2018 Work Plan

Action: For adoption

The adoption was postponed. Further changes will be done based on comments received.

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

The CHMP noted the information.

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 22 – 25 January 2018 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Tomas Salmonson	Chair	Sweden	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Milena Stain	Alternate	Austria	No interests declared	
Bart Van der Schueren	Member	Belgium	No interests declared	
Christophe Focke	Alternate	Belgium	No restrictions applicable to this meeting	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Katarina Vučić	Member	Croatia	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Sinan B. Sarac	Member	Denmark	No interests declared	
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Tuomo Lapveteläinen	Alternate	Finland	No interests declared	
Alexandre Moreau	Member	France	No interests declared	
Joseph Emmerich	Alternate	France	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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:	4.4.1. Xeljanz - tofacitinib - EMEA/H/C/004214/X/0005/G
Natalja Karpova	Alternate	Latvia	No interests declared	
Rugile Pilviniene	Alternate	Lithuania	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	
Svein Rune Andersen	Member	Norway	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Bjorg Bolstad	Alternate	Norway	No restrictions applicable to this meeting	
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Bruno Sepodes	Member	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meeting	
Simona Badoi	Member	Romania	No interests declared	
Dana Gabriela Marin	Alternate	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:	3.1.2. Hemlibra - emicizumab - EMEA/H/C/004406
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	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
			this meeting	
Koenraad Norga	Co-opted member	Belgium	No participation in final deliberations and voting on:	3.1.6. Shingrix - human herpesvirus 3 - EMEA/H/C/004336 5.1.5. Relvar Ellipta/Revinty Ellipta - fluticasone furoate / vilanterol - EMEA/H/C/WS1208 9.1.6. Zeffix - lamivudine - EMEA/H/C/000242/II/0069 - duplicate of Epivir
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Liliana Civjane (Tzivian)	Expert - in person*	Latvia	No interests declared	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Milena Peraita Ezcurra	Expert - in person*	Spain	No interests declared	
Marie Louise Schougaard Christiansen	Expert - in person*	Denmark	No interests declared	
Mette Tranholm	Expert - in person*	Denmark	No interests declared	
Kristofer Olofsson	Expert - in person*	Sweden	No restrictions applicable to this meeting	
Mette Linnert Jensen	Expert - in person*	Denmark	No interests declared	
Babs Fabriek	Expert - in person*	Netherlands	No interests declared	
Shirley Hopper	Expert - in person*	United Kingdom	No interests declared	
Anita Andersson	Expert - via telephone*	Sweden	No interests declared	
Hanne Lomholt Larsen	Expert - via telephone*	Denmark	No interests declared	
Jonas Bergh	Expert - via telephone*	Sweden	No restrictions	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
			applicable to this meeting	
Mats Welin	Expert - via telephone*	Sweden	No interests declared	
Peter Mol	Expert - via telephone*	Netherlands	No interests declared	
Charlotta Bergquist	Expert - via telephone*	Sweden	No interests declared	
Benjamin Hofner	Expert - via phone*	Germany	No restrictions applicable to this meeting	
Ingrid Schellens	Expert - via telephone*	Netherlands	No interests declared	
Annemarie Voute	Expert - via telephone*	Netherlands	No interests declared	
Jacqueline van Kuijk	Expert - via telephone*	Netherlands	No restrictions applicable to this meeting	
Marion Haberkamp	Expert - via telephone*	Germany	No interests declared	
Valentina Mantua	Expert - via telephone*	Italy	No restrictions applicable to this meeting	
Greeves Kondowe	Expert - via telephone*	United Kingdom	No interests declared	
Parvinder Singh Phul	Expert - via telephone*	United Kingdom	No interests declared	
Laila Sortvik Nilssen	Expert - via phone*	Norway	No restrictions applicable to this meeting	
Lopes de Oliveira	Expert - via telephone*	Portugal	No interests declared	
Joao Freire	Expert - via telephone*	Portugal	No restrictions applicable to this meeting	
Serge Bakchine	Expert - via	France	No interests	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
	telephone*		declared	
René Anour	Expert - via telephone*	Austria	No interests declared	
Stephan Lehr	Expert - via telephone*	Austria	No interests declared	
Benjamin Hofner	Expert - via Adobe*	Germany	No restrictions applicable to this meeting	
Eva Malikova	Expert - via Adobe*	Slovakia	No interests declared	
Patients' representative	Patient observer - via telephone*		No interests declared	
Patients' representative	Patient observer		No interests declared	
Representative from the European Commission attended the meeting				
Meeting run with support from relevant EMA staff				

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

17. Explanatory notes

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

Oral explanations *(section 2)*

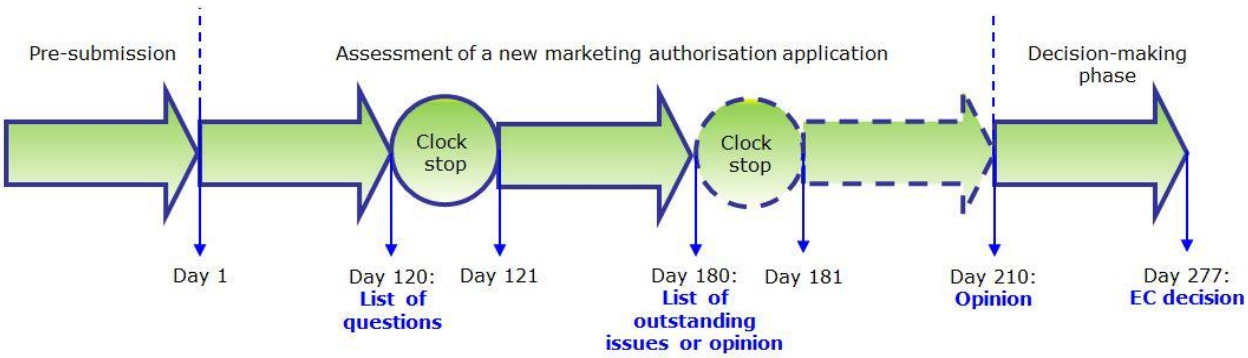
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

Initial applications *(section 3)*

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

Re-examination procedures *(section5.3)*

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

Withdrawal of application *(section 3.7)*

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

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

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

Pre-submission issues *(section 8)*

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

Post-authorisation issues *(section 9)*

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

Referral procedures *(section 10)*

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

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

Pharmacovigilance issues *(section 11)*

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

Inspections Issues *(section 12)*

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

Innovation task force *(section 13)*

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

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

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

Satellite groups / other committees *(section 14.2)*

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

Invented name issues *(section 14.3)*

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

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

8 March 2018
EMA/CHMP/142590/2018

Annex to 22-25 January 2018 CHMP Minutes

Pre submission and post authorisation issues

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Send a question via our website www.ema.europa.eu/contact

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for January 2018: **For adoption**	Adopted.

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

Final Outcome of Rapporteurship allocation for January 2018: **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

Lojuxta - lomitapide - EMEA/H/C/002578/S/0026 MAH: Aegerion Pharmaceuticals Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 09.11.2017.	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.
Raxone - idebenone - EMEA/H/C/003834/S/0009, Orphan MAH: Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Carmela Macchiarulo Request for Supplementary Information adopted on 25.01.2018.	Request for Supplementary Information adopted

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Imatinib Accord - imatinib - EMEA/H/C/002681/R/0020	Request for Supplementary Information adopted

MAH: Accord Healthcare Limited, Generic, Generic of Glivec, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia Request for Supplementary Information adopted on 25.01.2018.	
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, PRAC Rapporteur: Julie Williams Request for Supplementary Information adopted on 19.01.2018.	Request for Supplementary Information adopted
Pheburane - sodium phenylbutyrate - EMEA/H/C/002500/R/0017 MAH: Lucane Pharma, Rapporteur: Jayne Crowe, PRAC Rapporteur: Almath Spooner	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.

B.2.3. Renewals of Conditional Marketing Authorisations

Blincyto - blinatumomab - EMEA/H/C/003731/R/0013, Orphan MAH: Amgen Europe B.V., Rapporteur: Alexandre Moreau, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Eva Jirsová Request for Supplementary Information adopted on 20.07.2017.	Positive Opinion adopted by consensus together with the CHMP assessment report. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Deltyba - delamanid - EMEA/H/C/002552/R/0027, Orphan MAH: Otsuka Novel Products GmbH, Rapporteur: Greg Markey, Co-Rapporteur: Koenraad Norga, PRAC Rapporteur: Julie Williams Request for Supplementary Information adopted on 25.01.2018.	Request for Supplementary Information adopted
Natpar - parathyroid hormone - EMEA/H/C/003861/R/0007, Orphan MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Bart Van der Schueren, Co-	Request for Supplementary Information adopted

Rapporteur: Greg Markey, PRAC Rapporteur: Almath Spooner Request for Supplementary Information adopted on 25.01.2018.	
Pixuvri - pixantrone - EMEA/H/C/002055/R/0042 MAH: CTI Life Sciences Limited, Rapporteur: Greg Markey, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty	Positive Opinion adopted by consensus together with the CHMP assessment report. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
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.	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.

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection PRAC recommendations on signals adopted at the PRAC meeting held on 8-11 January 2018 PRAC:	
Signal of gastrointestinal stenosis and obstruction: **Trulicity - Dulaglutide - EMEA/H/C/002825** MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey, Co-Rapporteur: Martina Weise, PRAC recommendation on a variation: **For adoption**	Adopted.
Signal of pulmonary alveolar haemorrhage: **Jylamvo - Methotrexate - EMEA/H/C/003756** MAH: Therakind Limited, Rapporteur: Bruno Sepodes, PRAC recommendation on a variation: **For adoption**	Adopted.
Signal of nephrogenic diabetes insipidus:	Adopted.

Alimta - Pemetrexed - EMEA/H/C/000564, MAH: Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, Co-Rapporteur: Harald Enzmann, PRAC recommendation on a variation: **For adoption**	
PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its January 2018 meeting:	
EMEA/H/C/PSUSA/00010550/201705 (mycophenolate mofetil, mycophenolic acid) CAPS: **CellCept** (EMEA/H/C/000082) (mycophenolate mofetil), MAH: Roche Registration Limited, Rapporteur: Greg Markey **Myclausen** (EMEA/H/C/001218) (mycophenolate mofetil), MAH: Passauer Pharma GmbH, Rapporteur: Andrea Laslop **Mycophenolate mofetil Teva** (EMEA/H/C/000882) (mycophenolate mofetil), MAH: Teva B.V., Rapporteur: Greg Markey **Myfenax** (EMEA/H/C/000884) (mycophenolate mofetil), MAH: Teva B.V., Rapporteur: Greg Markey NAPS: please see PRAC AR PRAC Rapporteur: Patrick Batty, "3 May 2016 - 2 May 2017"	Re-adoption due to a request from the EC to clarify implementation instructions within Annex II of the CHMP Opinion (NAPs) and the PRAC AR. No content related changes were made.
EMEA/H/C/PSUSA/00002772/201703 (somatropin) CAPS: **NutropinAq** (EMEA/H/C/000315) (somatropin), MAH: Ipsen Pharma, Rapporteur: Hanne Lomholt Larsen **Omnitrope** (EMEA/H/C/000607) (somatropin), MAH: Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege **Somatropin Biopartners** (EMEA/H/C/002196) (somatropin), MAH: BioPartners GmbH, Rapporteur: Martina Weise NAPS: **NAPS** - EU , PRAC Rapporteur: Doris Stenver, "01/10/2015 - 31/03/2017"	Re-adoption due to a call from the EC to add an introductory statement within Annex II of the CHMP Opinion. No content related changes were made.
EMEA/H/C/PSUSA/00010379/201707 (nivolumab) CAPS: **Opdivo** (EMEA/H/C/003985) (nivolumab), MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur:	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

Brigitte Keller-Stanislawski, "04 January 2017 - 03 July 2017"	above mentioned medicinal product, concerning the following change: Update of section 4.8 of the SmPC to add the adverse reaction Tumour lysis syndrome with frequency not known. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010391/201706 (lutetium (177Lu) chloride) CAPS: **EndolucinBeta** (EMEA/H/C/003999) (lutetium (177Lu) chloride), MAH: ITG Isotope Technologies Garching GmbH, Rapporteur: Peter Kiely **LuMark** (EMEA/H/C/002749) (lutetium, isotope of mass 177), MAH: I.D.B. Holland B.V., Rapporteur: Nithyanandan Nagercoil NAPS: **NAP** - EU PRAC Rapporteur: Almath Spooner, "December 20, 2016 to June 19, 2017"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisations for the medicinal products containing the above referred active substances, concerning the following changes: • Update of section 4.8 of the SmPC to add Alopecia. 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/00010460/201706 (blinatumomab) CAPS: **Blincyto** (EMEA/H/C/003731) (blinatumomab), MAH: Amgen Europe B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Eva Jirsová, "3 May 2016 to 2 June 2017 Update of section 4.8 of the SmPC to add "Ataxia" with frequency common. The Package leaflet is updated accordingly."	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).
EMEA/H/C/PSUSA/00010518/201705 (daclizumab) CAPS: **Zinbryta** (EMEA/H/C/003862) (daclizumab beta), MAH: Biogen Idec Ltd, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Eva A. Segovia, "27 November 2016 - 26 May 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 sarcoidosis with a frequency uncommon and the adverse reaction colitis with a frequency common.

	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/00010555/201706 (obeticholic acid) CAPS: **Ocaliva** (EMEA/H/C/004093) (obeticholic acid), MAH: Intercept Pharma Ltd, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst, "Update of section 4.2, 4.4 and 5.2 of the SmPC to add clarify advice on recommended dosing in PBC patients with hepatic moderate and severe hepatic impairment, add a warning regarding dosing errors and to clarify advice on recommended dosing in patients with hepatic impairment. The Package leaflet is updated accordingly. The RMP has also updated (version 1.1)."	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). Update of section 4.2, 4.4 and 5.2 of the SmPC to add clear advice on recommended dosing in PBC patients with hepatic moderate and severe hepatic impairment, add a warning regarding dosing errors and to clarify advice on recommended dosing in patients with hepatic impairment. The Package leaflet is updated accordingly. The RMP has also updated (version 1.1). The CHMP also agreed to the DHPC and communication plan.

B.4. EPARs / WPARs

Adynovi - rurioctocog alfa pegol - EMEA/H/C/004195 Applicant: Baxalta Innovations GmbH, treatment of haemophilia A, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Alkindi - hydrocortisone - EMEA/H/C/004416, PUMA Applicant: Diurnal Limited, treatment of adrenal insufficiency, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	adopted.
Alofisel - darvadstrocel - EMEA/H/C/004258, Orphan, ATMP Applicant: TIGENIX, S.A.U., treatment of complex perianal fistula(s), New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Anagrelide Mylan - anagrelide - EMEA/H/C/004585 Applicant: Mylan S.A.S, reduction of elevated platelet counts in at risk essential thrombocythaemia patients, Generic, Generic of Xagrid, Generic application (Article 10(1) of Directive No 2001/83/EC)	adopted.

Aplidin - plitidepsin - EMEA/H/C/004354, Orphan Applicant: Pharma Mar, S.A., treatment of multiple myeloma, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Balimek - binimetinib - EMEA/H/C/004052 Applicant: Pierre Fabre Medicament, treatment of unresectable or metastatic melanoma Treatment of unresectable melanoma, with NRA Q61 mutation., New active substance (Article 8(3) of Directive No 2001/83/EC) **WPAR**	adopted.
Crysvita - burosumab - EMEA/H/C/004275, Orphan Applicant: Kyowa Kirin Limited, treatment of X-linked hypophosphataemia (XLH), New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Efavirenz/Emtricitabine/Tenofovir disoproxil Krka - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/004274 Applicant: KRKA, d.d., Novo mesto, treatment of HIV-1 infection, Generic, Generic of Atripla, Generic application (Article 10(1) of Directive No 2001/83/EC)	adopted.
Herzuma - trastuzumab - EMEA/H/C/002575 Applicant: Celltrion Healthcare Hungary Kft., treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC), Similar biological application (Article 10(4) of Directive No 2001/83/EC)	adopted.
Infinia - alpha-1-antitrypsin - Orphan - EMEA/H/C/003934 Applicant: Kamada BioPharma Limited at Fieldfisher LLP, Known active substance (Article 8(3) of Directive No 2001/83/EC) **WPAR**	adopted.
Intrarosa - prasterone - EMEA/H/C/004138 Applicant: Endoceutics Limited, treatment of vulvar and vaginal atrophy in postmenopausal women having moderate to severe symptoms, New active substance (Article 8(3) of Directive No 2001/83/EC)	adopted.
Ozempic - semaglutide -	adopted.

EMEA/H/C/004174 Applicant: Novo Nordisk A/S, to improve glycaemic control in adults with type 2 diabetes and to prevent cardiovascular events, New active substance (Article 8(3) of Directive No 2001/83/EC)	
Rotigotine Mylan - rotigotine - EMEA/H/C/004286 Applicant: Mylan S.A.S, treatment of idiopathic Restless Legs Syndrome and Parkinson's disease, Generic, Generic of Neupro, Generic application (Article 10(1) of Directive No 2001/83/EC) **WPAR**	adopted.
Qizenday - d-biotin - EMEA/H/C/004153 Applicant: Medday Pharmaceuticals, treatment of progressive multiple sclerosis (primary or secondary), Known 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

Bortezomib Accord - bortezomib - EMEA/H/C/003984/II/0012 MAH: Accord Healthcare Ltd, Generic, Generic of VELCADE, Rapporteur: Milena Stain Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cinryze - c1-esterase inhibitor (human) - EMEA/H/C/001207/II/0058/G MAH: Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 18.01.2018.	Request for Supplementary Information adopted
Cosentyx - secukinumab - EMEA/H/C/003729/II/0031/G MAH: Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen Request for Supplementary Information adopted on 25.01.2018.	Request for Supplementary Information adopted
Ilaris - canakinumab - EMEA/H/C/001109/II/0053/G MAH: Novartis Europharm Limited, Rapporteur:	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Jan Mueller-Berghaus Opinion adopted on 18.01.2018.	recommendation.
Lojuxta - lomitapide - EMEA/H/C/002578/II/0028 MAH: Aegerion Pharmaceuticals Limited, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 18.01.2018.	Request for Supplementary Information adopted
Memantine ratiopharm - memantine - EMEA/H/C/002671/II/0012 MAH: ratiopharm GmbH, Generic, Generic of Ebixa, Rapporteur: Bart Van der Schueren Request for Supplementary Information adopted on 18.01.2018.	Request for Supplementary Information adopted
Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0069 MAH: Pfizer Limited, Rapporteur: Greg Markey Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 16.11.2017.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Nplate - romiplostim - EMEA/H/C/000942/II/0066, Orphan MAH: Amgen Europe B.V., Rapporteur: Concepcion Prieto Yerro Opinion adopted on 25.01.2018.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Nucala - mepolizumab - EMEA/H/C/003860/II/0011 MAH: GlaxoSmithKline Trading Services Limited, Rapporteur: Nithyanandan Nagercoil Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 23.11.2017.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Opsumit - macitentan - EMEA/H/C/002697/II/0025/G, Orphan MAH: Actelion Registration Limited, Rapporteur: Concepcion Prieto Yerro Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Oxervate - cenegermin - EMEA/H/C/004209/II/0002, Orphan MAH: Dompe farmaceutici S.p.A., Rapporteur: Concepcion Prieto Yerro Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (H5N1) (live attenuated, nasal) -	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

EMEA/H/C/003963/II/0009/G MAH: AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 14.12.2017.	recommendation.
Plegridy - peginterferon beta-1a - EMEA/H/C/002827/II/0040 MAH: Biogen Idec Ltd, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 18.01.2018.	Request for Supplementary Information adopted
Praluent - alirocumab - EMEA/H/C/003882/II/0032/G MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Scenesse - afamelanotide - EMEA/H/C/002548/II/0017, Orphan MAH: Clinuvel (UK) Limited, Rapporteur: Harald Enzmann Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 30.11.2017.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Torisel - temsirolimus - EMEA/H/C/000799/II/0070/G, Orphan MAH: Pfizer Limited, Rapporteur: Harald Enzmann Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. 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 Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 23.11.2017, 19.10.2017.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Trulicity - dulaglutide - EMEA/H/C/002825/II/0023 MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vpriv - velaglucerase alfa - EMEA/H/C/001249/II/0035, Orphan MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Harald Enzmann Request for Supplementary Information adopted	Request for Supplementary Information adopted

on 18.01.2018.	
Vyndaqel - tafamidis - EMEA/H/C/002294/II/0041/G, Orphan MAH: Pfizer Limited, Rapporteur: Joseph Emmerich Opinion adopted on 18.01.2018. Request for Supplementary Information adopted on 19.10.2017.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xadago - safinamide - EMEA/H/C/002396/II/0020 MAH: Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 25.01.2018, 19.10.2017.	Request for Supplementary Information adopted
WS1177/G **Neulasta- EMEA/H/C/000420/WS1177/0097/G** **Ristempa (SRD)- EMEA/H/C/003910/WS1177/0012/G** MAH: Amgen Europe B.V., Lead Rapporteur: Robert James Hemmings Request for Supplementary Information adopted on 25.01.2018, 14.09.2017.	Request for Supplementary Information adopted
WS1237/G **Ambirix- EMEA/H/C/000426/WS1237/0089/G** **Fendrix- EMEA/H/C/000550/WS1237/0061/G** **Infanrix hexa- EMEA/H/C/000296/WS1237/0233/G** **Twinrix Adult- EMEA/H/C/000112/WS1237/0123/G** **Twinrix Paediatric- EMEA/H/C/000129/WS1237/0124/G** MAH: GlaxoSmithKline Biologicals, Lead Rapporteur: Bart Van der Schueren Request for Supplementary Information adopted on 18.01.2018.	Request for Supplementary Information adopted
WS1276/G **Incruse- EMEA/H/C/002809/WS1276/0017/G** **Rolufta- EMEA/H/C/004654/WS1276/0003/G** MAH: Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro Request for Supplementary Information adopted on 18.01.2018.	Request for Supplementary Information adopted

WS1281/G **Hexacima-** **EMEA/H/C/002702/WS1281/0072/G** **Hexaxim-** **EMEA/H/W/002495/WS1281/0077/G** **Hexyon-** **EMEA/H/C/002796/WS1281/0076/G** MAH: Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 25.01.2018.	Request for Supplementary Information adopted
WS1317/G **Helixate NexGen-** **EMEA/H/C/000276/WS1317/0194/G** **KOGENATE Bayer-** **EMEA/H/C/000275/WS1317/0202/G** MAH: Bayer AG, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Adempas - riociguat - **EMEA/H/C/002737/II/0023, Orphan** MAH: Bayer AG, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.2 of the SmPC in order to add new information regarding posology for transitioning to and from riociguat based on results from study 16719: An open-label, international, multicentre, single-arm, uncontrolled, phase IIIb study of riociguat in patients with pulmonary arterial hypertension (PAH) who demonstrate an insufficient response to treatment with phosphodiesterase-5 inhibitors (PDE-5i). Section 4.5 of the SmPC was updated in parallel to reflect on the main study results concerning pharmacodynamic interactions. Minor editorial changes were also implemented throughout the SmPC. The Package Leaflet was updated accordingly." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 12.10.2017.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Advate - octocog alfa - **EMEA/H/C/000520/II/0088** MAH: Baxter AG, Rapporteur: Jan Mueller-Berghaus, "Submission of the final report from study 061301 (China PTP). This is an interventional, open-label study aimed to	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

evaluate the efficacy and safety of Advate in the treatment of previously treated patients with haemophilia A." Opinion adopted on 18.01.2018.	
Advate - octocog alfa - EMEA/H/C/000520/II/0090 MAH: Baxter AG, Rapporteur: Jan Mueller-Berghaus, "Submission of the final clinical study report from study 060402. This was an interventional, randomised, controlled study aimed to compare the efficacy and safety of continuous infusion versus intermittent bolus infusion in patients with haemophilia A undergoing major orthopaedic surgery." Request for Supplementary Information adopted on 18.01.2018.	Request for Supplementary Information adopted
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 evaluating 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 haemophilia A and the outcome of the Referral EMEA/H/A-31/1448.). 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." Request for Supplementary Information adopted on 25.01.2018, 14.12.2017.	Request for Supplementary Information adopted
Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0027/G MAH: Biofrontera Bioscience GmbH, Rapporteur: Harald Enzmann, "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	See 9.1

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. Change in the legal status of Ameluz from "medicinal product subject to restricted medical prescription" to "medicinal product subject to medical prescription". In addition, the Marketing authorisation holder (MAH) took the opportunity to update the labelling in line with the QRD template and the list of local representatives in the Package Leaflet." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 09.11.2017, 12.10.2017.	
Blincyto - blinatumomab - EMEA/H/C/003731/II/0009, Orphan MAH: Amgen Europe B.V., Rapporteur: Alexandre Moreau, "Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC, Annex II and Package Leaflet based on the clinical study 103311 (TOWER): a Study of BITE antibody blinatumomab versus standard of care chemotherapy in adult subjects with relapsed/refractory b-precursor acute lymphoblastic leukaemia (ALL). The RMP (version 7.0) has been updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took this opportunity to make editorials changes in section 6.6 of the SmPC." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 14.12.2017, 20.07.2017, 26.01.2017.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
CellCept - mycophenolate mofetil - EMEA/H/C/000082/II/0137 MAH: Roche Registration Limited, Rapporteur: Greg Markey, "Update of section 4.4 of the SmPC in order to update the information on concomitant use of tacrolimus with CellCept and to provide recommendations on therapeutic drug monitoring for management of transplant patients, based on reviews of the medical	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

literature and clinical treatment guidelines. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct inconsistencies in the Package Leaflet." Opinion adopted on 18.01.2018.	
PRAC Led **Cetrotide - cetrorelix - EMEA/H/C/000233/II/0064** MAH: Merck Serono Europe Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Valerie Strassmann, PRAC-CHMP liaison: Martina Weise, "Submission of an updated RMP version 5.0 in order to update the list of important identified risks by adding Ovarian Hyperstimulation Syndrome (OHSS) and removing injection site reactions (ISRs). In addition, further minor RMP updates were introduced." Request for Supplementary Information adopted on 11.01.2018.	Request for Supplementary Information adopted
Cubicin - daptomycin - EMEA/H/C/000637/II/0066 MAH: Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, "Update of section 4.8 of the SmPC in order to add the adverse events Leukocytosis, Muscle cramps and Eye irritation with the frequency Uncommon, based on data from two previously submitted adult multicentre, randomized clinical studies investigating the safety and efficacy of IV daptomycin compared with that of vancomycin or a semi-synthetic penicillin, in the treatment of complicated skin and skin structure infections due to Gram-positive bacteria (DAP-SST-98-01) or in the treatment of adult hospitalized subjects with complicated bacterial skin and soft tissue infections due, at least in part, to Gram-positive bacteria (DAP-SST9901)." Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Deltyba - delamanid - EMEA/H/C/002552/II/0021, Orphan MAH: Otsuka Novel Products GmbH, Rapporteur: Greg Markey, "Update of sections 4.2, 4.4, 4.8, 4.9, 5.1 and 5.2 of the SmPC to reflect the results of the final study report of 242-09-213 (A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel Group Trial to Evaluate the Safety and Efficacy of Delamanid (OPC-67683)	Request for Supplementary Information adopted

Administered Orally as 200 mg Total Daily Dose for Six Months in Patients With Pulmonary Sputum Culture-positive, Multidrug-resistant Tuberculosis), submitted to fulfill SOB-01. The Package leaflet is updated accordingly." Request for Supplementary Information adopted on 25.01.2018, 14.09.2017.	
Descovy - emtricitabine / tenofovir alafenamide - EMEA/H/C/004094/II/0025 MAH: Gilead Sciences International Limited, Rapporteur: Robert James Hemmings, "Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to provide week 48 results from study GS-US-311-1717(include study identifier) listed as a category 3 study in the RMP; this is a Phase 3b, Randomized, Double-Blind, Switch Study to Evaluate F/TAF in HIV-1 Infected Subjects who are Virologically Suppressed on Regimens containing ABC/3TC. In addition, the Marketing authorisation holder (MAH) took the opportunity to make administrative updateds and Minor Linguistic Amendments to the Product Information." Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Epivir - lamivudine - EMEA/H/C/000107/II/0104 MAH: ViiV Healthcare UK Limited, Rapporteur: Joseph Emmerich, "Update of section 4.5 of the SmPC of both Epivir tablets and oral solution, and section 4.4 of the SmPC for Epivir Oral solution only, to add information regarding the potential for interaction between lamivudine and sorbitol based on the results of Study 204857. Further, a minor amendment has been implemented throughout the SmPC to update the clinical terminology for 'Pneumocystis carinii pneumonia' to 'Pneumocystis jiroveci pneumonia'. In addition, the MAH has taken the opportunity to align the product information with the QRD template version 10, to make minor editorial changes in the annexes and to update the contact details of the local representative in Norway in the Package Leaflet." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 14.12.2017, 21.09.2017, 05.05.2017.	See 9.1

Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0076 MAH: AstraZeneca AB, Rapporteur: Bart Van der Schueren, "Update of section 4.6 of the SmPC with regards to pregnancy and breast-feeding information based on the review and summary of pregnancy and lactation data from published literature and MAH pharmacovigilance database. The package leaflet has been updated accordingly." Request for Supplementary Information adopted on 25.01.2018.	Request for Supplementary Information adopted
Glivec - imatinib - EMEA/H/C/000406/II/0109 MAH: Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, "Update of section 4.8 of the SmPC to add the new adverse drug reaction (ADR) 'pseudoporphyria' following a revision of the company's core data sheet (CDS). The package leaflet has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of the local representatives in Bulgaria, Hungary and Latvija in the Package Leaflet." Request for Supplementary Information adopted on 18.01.2018.	Request for Supplementary Information adopted
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0039, Orphan MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, "Submission of the final report from the in vitro rabbit ventricular and atrial wedge study (study 16-088-B-X-IV-CT), listed as a category 3 study in the RMP. This in vitro exploratory safety pharmacology study was designed to further elucidate a mechanism or potential association of ibrutinib's effects on ECG signaling." Opinion adopted on 25.01.2018.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Invokana - canagliflozin - EMEA/H/C/002649/II/0033/G MAH: Janssen-Cilag International NV, Rapporteur: Martina Weise, "Update of section 5.1 of the SmPC in order to update the safety information on 'Canagliflozin as initial combination therapy with metformin' based on final results from the DIA3011 study, which is	Request for Supplementary Information adopted

Randomized, Double-Blind, 5-Arm, Parallel-Group, 26-Week, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin in Combination With Metformin as Initial Combination Therapy in the Treatment of Subjects With Type 2 Diabetes Mellitus With Inadequate Glycemic Control With Diet and Exercise. Update of section 5.1 of the SmPC in order to update the safety information on 'Add-on combination therapy with Metformin and Dipeptidyl-peptidase-4 Inhibitor' based on final results from the DIA4004 study, which is a Randomized, Double-blind, Placebo Controlled, 2-arm, Parallel-group, 26-week, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin in the Treatment of Subjects with Type 2 Diabetes Mellitus with Inadequate Glycemic Control on Metformin and Sitagliptin Therapy." Request for Supplementary Information adopted on 18.01.2018	
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 Natpar, a recombinant human parathyroid hormone (rhPTH[1-84]), for the treatment of adults with hypoparathyroidism – a clinical extension study (RACE)." Opinion adopted on 25.01.2018.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
NexoBrid - concentrate of proteolytic enzymes enriched in bromelain - EMEA/H/C/002246/II/0032, Orphan MAH: MediWound Germany GmbH, Rapporteur: Harald Enzmann, "Submission of the clinical study report MW2008-09-03 "Enzymatic Debridement in Patients with Partial Thickness Burns." an open label, single-arm study evaluating the safety (primary), PK (NexoBrid transcutaneous absorption) and efficacy (exploratory) of NexoBrid in hospitalized adult with partial thickness (mid and deep dermal) thermal burns	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

of 4-30% total body surface area." Opinion adopted on 18.01.2018.	
Strensiq - asfotase alfa - EMEA/H/C/003794/II/0019/G, Orphan 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 (and its extension ENB-008-10) and ENB-009-10 listed as an obligation in the Annex II (ANX002)." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 09.11.2017, 14.09.2017.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Sutent - sunitinib - EMEA/H/C/000687/II/0068 MAH: Pfizer Limited, Rapporteur: Daniela Melchiorri, "Update of section 4.8 of the SmPC in order to include available long-term safety data pooled from 9 Pfizer-sponsored sunitinib clinical studies in patients with metastatic renal cell carcinoma (MRCC) from a recently published journal article by Porta et al (2016)." Request for Supplementary Information adopted on 18.01.2018.	Request for Supplementary Information adopted
Tafinlar - dabrafenib - EMEA/H/C/002604/II/0029 MAH: Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 5.2 of the SmPC in order to update the information on the in vitro evaluation of drug-drug interaction potential (to include that dabrafenib is a human BCRP substrate and a OCT2 inhibitor but that the risk of a drug drug interaction is minimal with substrates of OAT1, OAT3 and OTC2 based on clinical exposure of dabrafenib and its metabolites), based on the results of non-clinical studies 2014N220059 and 2015N235499." Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Telzir - fosamprenavir - EMEA/H/C/000534/II/0089 MAH: ViiV Healthcare UK Limited, Rapporteur: Joseph Emmerich, "Update of sections 4.6, 5.2 and 5.3 of the SmPC in order to include new information on pregnancy based on data regarding placental transfer of amprenavir and a summary of the available data on fosamprenavir Antiviral Pregnancy Registry (APR) and PK data derived from the use of FPV/rtv in pregnant	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

women. In addition, the MAH took this opportunity to make some QRD V10 updates in the labelling and some typographical corrections to the SmPC. The local representatives in the PL were updated." Opinion adopted on 18.01.2018. Request for Supplementary Information adopted on 12.10.2017.	
Vectibix - panitumumab - EMEA/H/C/000741/II/0086 MAH: Amgen Europe B.V., Rapporteur: Robert James Hemmings, "Update of section 4.4 and section 4.8 of the SmPC and relevant sections of the PL to reflect a re-analysis of the safety information which pooled data from all the indications requiring a change in the overall incidence, severity, and seriousness of some of the currently labelled ADRs." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 07.12.2017.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/II/0039 MAH: AbbVie Limited, Rapporteur: Filip Josephson, "Update of sections 4.3 and 4.5 of the SmPC to add disopyramide in the list of contraindicated medicines and in the list of medicines which interact with Viekirax. The Package Leaflet is updated accordingly." Opinion adopted on 25.01.2018.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vokanamet - canagliflozin / metformin - EMEA/H/C/002656/II/0033/G MAH: Janssen-Cilag International NV, Rapporteur: Martina Weise, "Update of section 5.1 of the SmPC in order to update the safety information on 'Canagliflozin as initial combination therapy with metformin' based on final results from the DIA3011 study, which is Randomized, Double-Blind, 5-Arm, Parallel-Group, 26-Week, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin in Combination With Metformin as Initial Combination Therapy in the Treatment of Subjects With Type 2 Diabetes Mellitus With Inadequate Glycemic Control With Diet and Exercise. Update of section 5.1 of the SmPC in order to update the safety information on 'Add-on	Request for Supplementary Information adopted

combination therapy with Metformin and Dipeptidyl-peptidase-4 Inhibitor' based on final results from the DIA4004 study, which is a Randomized, Double-blind, Placebo Controlled, 2-arm, Parallel-group, 26-week, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of Canagliflozin in the Treatment of Subjects with Type 2 Diabetes Mellitus with Inadequate Glycemic Control on Metformin and Sitagliptin Therapy." Request for Supplementary Information adopted on 18.01.2018.	
Votrient - pazopanib - EMEA/H/C/001141/II/0043 MAH: Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to update the frequency of the adverse drug reaction 'infection' from uncommon to common. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct some discrepancies, in sections 4.4, 4.5 and 4.8 of the SmPC. The PL is updated accordingly." Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
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." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 09.11.2017.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
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	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

patients from paliperidone ER tablets to paliperidone palmitate long acting injection (PP1M). An editorial update to clarify the contents of the treatment initiation pack has also been introduced in the Information for Users in the package leaflet to improve readability." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 09.11.2017, 14.09.2017, 20.07.2017.	
Zeffix - lamivudine - EMEA/H/C/000242/II/0069 MAH: Glaxo Group Ltd, Duplicate, Duplicate of Epivir, Rapporteur: Joseph Emmerich, "Update of section 4.5 of the SmPC to add information regarding a potential interaction with sorbitol-containing medicines. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement a minor change in the labelling in line with the QRD template version 10." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 14.12.2017, 21.09.2017, 05.05.2017.	See 9.1
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 make minor changes to the SmPC and Package Leaflet in order to improve clarity and consistency of the information." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 09.11.2017.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1156 Combivir-EMEA/H/C/000190/WS1156/0090 Kivexa-EMEA/H/C/000581/WS1156/0072 Triumeq-EMEA/H/C/002754/WS1156/0042 Trizivir-EMEA/H/C/000338/WS1156/0104 MAH: ViiV Healthcare UK Limited, Lead	See 9.1

Rapporteur: Joseph Emmerich, "Update of section 4.5 of the SmPC to add information regarding the potential interaction between lamivudine and sorbitol based on the results of Study 204857. The Package Leaflet has been updated accordingly. Further, a minor amendment has been implemented throughout the SmPC in order to update the clinical terminology of Pneumocystis carinii pneumonia to Pneumocystis jiroveci pneumonia. In addition, the MAH takes the opportunity to make minor editorial changes , to align the annexes with the QRD template version 10 and to update the contact details of the local representative in Norway in the Package Leaflet." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 14.12.2017, 21.09.2017, 05.05.2017.	
WS1210/G **Mekinist-** **EMEA/H/C/002643/WS1210/0021/G** **Tafinlar-** **EMEA/H/C/002604/WS1210/0026/G** MAH: Novartis Europharm Limited, Lead Rapporteur: Paula Boudewina van Hennik, "Update of section 5.1 of the Mekinist (trametinib) and Tafinlar (dabrafenib) SmPC to include the 3-years overall survival (OS) results from study MEK115306 (COMBI-d), a phase III, randomised, double-blinded study comparing the combination of dabrafenib and trametinib to dabrafenib and placebo in first-line therapy for subjects with unresectable or metastatic BRAF V600/K mutation-positive cutaneous melanoma. Update of section 5.1 of the Mekinist (trametinib) and Tafinlar (dabrafenib) SmPC to include the 3-years overall survival (OS) results from study MEK116513 (COMBI-v), a phase III, open-label, 2 arm, randomised study comparing dabrafenib and trametinib combination therapy with vemurafenib monotherapy in BRAF V600 mutation-positive metastatic melanoma." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 30.11.2017, 05.10.2017.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1234/G **Genvoya-** **EMEA/H/C/004042/WS1234/0036/G** **Stribild-**	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

EMEA/H/C/002574/WS1234/0084/G Tybost-EMEA/H/C/002572/WS1234/0038/G MAH: Gilead Sciences International Limited, Lead Rapporteur: Robert James Hemmings, "Update of sections 4.4 and 4.5 of the SmPC based on data from the following Pharamacology Studies (GS-US-216-1008 and GS-US-216-4032). Study GS-US-216-1008 is a Phase 1, randomized, fixed-sequence, open -label, single_and multiple -dose, multiple-cohort, single-center study that evaluated the drug interaction potential between darunavir (DRV)+COBI, atazanavir (ATV)+COBI, or Genvoya and the 3 hydroxy-3-methylglutaryl-coenzyme A (HMG CoA) reductase inhibitors rosuvastatin and/or atorvastatin. Study GS-US-216-4032 is an open-label, single -center, multiple-cohort, fixed_sequence, Phase 1 study that evaluated the effect of DRV+COBI or ATV+COBI on the pharmacokinetic (PK) of a representative hormonal contraceptive medication, drospirenone/ethinyl estradiol. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to make administrative changes to the PI of all three products and update the list of local representatives for Estonia, Latvia and Lithuania for Tybost and Stribild. Minor linguistic amendments were made to the Product Information." Opinion adopted on 18.01.2018. Request for Supplementary Information adopted on 14.09.2017.	recommendation.
WS1258 **Clopidogrel Zentiva-EMEA/H/C/000975/WS1258/0059** **Clopidogrel/Acetylsalicylic acid Zentiva-EMEA/H/C/001144/WS1258/0050** **DuoPlavin-EMEA/H/C/001143/WS1258/0049** **Iscover-EMEA/H/C/000175/WS1258/0132** **Plavix-EMEA/H/C/000174/WS1258/0129** MAH: Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, "Update of section 4.8 of the SmPC in	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

order to add the undesirable effect 'ageusia'. The PL is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to introduce a clarification in section 4.2 of the Duoplavin and Clopidogrel/Acetylsalicylic acid Zentiva SmPC; update the German local representative in the Package Leaflet; and bring the PI in line with the latest QRD template version 10." Opinion adopted on 18.01.2018.	
WS1302 **Exviera-EMEA/H/C/003837/WS1302/0032** **Viekirax-EMEA/H/C/003839/WS1302/0037** MAH: AbbVie Limited, Lead Rapporteur: Filip Josephson, "Submission of the final report from study (M13-102) listed as a category 3 study in the RMP. This is a phase 3, long-term follow-up study to assess resistance and durability of response to direct-acting antiviral agent (DAA) therapy in subjects who participated in phase 2 or 3 clinical studies for the treatment of chronic hepatitis C virus (HCV) infection." Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1307 **Ofev-EMEA/H/C/003821/WS1307/0019** **Vargatef-EMEA/H/C/002569/WS1307/0019** MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Sinan B. Sarac, "Update of section 4.4 of the SmPC for Ofev and Vargatef to amend the current warning on drug induced liver injury based one case of sever liver injury with fatal outcome reported for Ofev during the post-marketing phase. In addition section 4.4 of the Ofev SmPC is updated to include when the majority of the hepatic events occurred and on the need for hepatic transaminases and bilirubin levels to be measured at regular intervals during the first 3 months of treatment. Section 4.8 of the Vargatef SmPC is also updated to include in the summary of the safety profile that the safety data is also based on post-marketing data. The Package Leaflet is updated accordingly. The MAH is proposing to distribute a DHPC for Ofev. In addition, the Worksharing applicant (WSA) took the opportunity to make some corrections to the Bulagrian, Estonian, Icelandic, Latvian and Maltese translations for Ofev and Bulgarian,	Request for Supplementary Information adopted

Estonian, Latvian and Maltese translations for Vargatef." Request for Supplementary Information adopted on 25.01.2018.	
WS1308/G **Exviera-** **EMEA/H/C/003837/WS1308/0033/G** **Viekirax-** **EMEA/H/C/003839/WS1308/0038/G** MAH: AbbVie Limited, Lead Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC to add the adverse reactions anaphylactic reactions and erythema multiforme with unknown frequency following a safety review. The package leaflet is updated accordingly." Request for Supplementary Information adopted on 25.01.2018.	Request for Supplementary Information adopted

B.5.3. CHMP-PRAC assessed procedures

Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0049, Orphan MAH: Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC with data from study C25002; a phase 1/2 study of brentuximab vedotin (SGN-35) in paediatric patients with relapsed or refractory systemic anaplastic large cell lymphoma or Hodgkin's lymphoma (listed in the agreed PIP covering the conditions of Hodgkin lymphoma and anaplastic large cell lymphoma for ADCETRIS (EMEA-000980-PIP01-10-M04)). An updated RMP version 12.3 was provided as part of the application." Opinion adopted on 11.01.2018. Request for Supplementary Information adopted on 01.09.2017.	Positive Opinion adopted by consensus on 11.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Adenuric - febuxostat - EMEA/H/C/000777/II/0047 MAH: Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop, PRAC Rapporteur: Jan Neuhauser, "Update of sections 4.4 and 4.5 of the SmPC in order to reflect the results of preclinical study MRPO-2015-PKM-005 "Pharmacokinetic of azathioprine in the rat after one-week daily oral treatment at three different dosages and with the	Request for Supplementary Information adopted

concomitant oral administration of febuxostat or allopurinol" and clinical study REP-POPPK-MRP-2015-PKM-005 "Population Pharmacokinetic analysis from study titled Pharmacokinetic of azathioprine in the rat after one-week daily oral treatment at three different dosages and with the concomitant oral administration of febuxostat or allopurinol", investigating the drug-drug interaction with azathioprine when co-administered with febuxostat. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to correct the typing errors and to bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 25.01.2018, 14.09.2017.	
Benlysta - belimumab - EMEA/H/C/002015/II/0052 MAH: Glaxo Group Ltd, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from study HGS1006-C1074 (BEL112234) "A Multi-Center, Continuation Trial of Belimumab (HGS1006, LymphoStat-B™), a Fully Human Monoclonal Anti-BLyS Antibody, in Subjects with Systemic Lupus Erythematosus (SLE) who Completed the Phase 3 Protocol HGS1006-C1056 or HGS1006-C1057". The study is listed as a category 3 study in the RMP (MEA012). The RMP version 26.0 is updated accordingly. In addition the MAH has taken the occasion to update the RMP for the due date for final study report and introduction of protocol changes (reduced study sample size) already discussed and agreed in recent procedure EMEA/H/C/002015/MEA/006.4 and EMEA/H/C/002015/MEA/006.5 for study BEL116027." Request for Supplementary Information adopted on 11.01.2018.	Request for Supplementary Information adopted
Eliquis - apixaban - EMEA/H/C/002148/II/0050 MAH: Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2 and 5.1 of the SmPC in order to update the posology, method of administration and efficacy and safety information based on final results from study (EMANATE – b0661025/CV185267) listed as a PAES in the	Request for Supplementary Information adopted

RMP; this is a phase 4 study to assess the effectiveness of apixaban compared with usual care anticoagulant in subjects with non-valvular atrial fibrillation (NVAF) undergoing cardioversion; the Package Leaflet is updated accordingly. The RMP version 19 has also been submitted. In addition, the Marketing authorisation holder took the opportunity to update the address of the MAH in the product information." Request for Supplementary Information adopted on 25.01.2018.	
Giotrif - afatinib - EMEA/H/C/002280/II/0025 MAH: Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from study 1200.217 listed as a category 3 study in the RMP. This is a phase IV study to assess the efficacy and safety of afatinib as second-line therapy for patients with locally advanced or metastatic non-small cell lung cancer harbouring an EGFR mutation who have failed first-line treatment with platinum-based chemotherapy. Risk Management Plan (version 6.0) has been updated accordingly." Opinion adopted on 11.01.2018.	Positive Opinion adopted by consensus on 11.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Imnovid - pomalidomide - EMEA/H/C/002682/II/0027, Orphan MAH: Celgene Europe Limited, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Patrick Batty, "Update of sections 4.2, 4.4, and 4.8 of the SmPC in order to add new ADRs SJS, TEN and DRESS following a review of reports on severe skin reactions. The Package Leaflet is updated accordingly. The RMP version 12.0 has also been submitted." Request for Supplementary Information adopted on 11.01.2018.	Request for Supplementary Information adopted
Invokana - canagliflozin - EMEA/H/C/002649/II/0034 MAH: Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Valerie Strassmann, "Update of sections 4.1, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information on cardiovascular events following final results from CANVAS Program (DIA3008 and	Request for supplementary information adopted

DIA4003); the Package Leaflet is updated accordingly. Study DIA3008 is phase 3 Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of JNJ-28431754 on Cardiovascular Outcomes in Adult Subjects With Type 2 Diabetes Mellitus Study DIA4004 is phase 4 Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of Canagliflozin on Renal Endpoints in Adult Subjects With Type 2 Diabetes Mellitus The RMP version 7.2 has also been submitted." Request for Supplementary Information adopted on 25.01.2018.	
Keppra - levetiracetam - EMEA/H/C/000277/II/0169/G MAH: UCB Pharma S.A., Rapporteur: Koenraad Norga, PRAC Rapporteur: Laurence de Fays, "1) C.I.4 (type II): Update of section 4.8 of the SmPC to add the ADR Gait Disturbance, to address the CHMP recommendations from P46/085; 2) C.I.4 (type II): Update of section 4.2 of the SmPC to add Dysgeusia as a potential experience post administration and to section 4.5 of the SmPC to remove drug interaction with Methotrexate, in accordance with the latest Levetiracetam Company Core Data Sheet); 3) C.I.4 (type II): Update of Section 4.6 to add information on 'Women of childbearing potential' and to update the Pregnancy section, to address PRAC recommendations from LEG-084.1; The Package Leaflet is updated accordingly. An updated to the Risk Management Plan (version 8) is included to address PRAC recommendations from LEG 84.1." Request for Supplementary Information adopted on 25.01.2018.	Request for Supplementary Information adopted
Kyprolis - carfilzomib - EMEA/H/C/003790/II/0017/G, Orphan MAH: Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Nikica Mirošević Skvrce, "C.I.4 Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information based on the second interim analysis of the overall survival data from study ENDEAVOR (study 20130398); this is a	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

randomised, multicentre, open-label, phase 3 study of carfilzomib and dexamethasone compared to bortezomib with dexamethasone in patients with relapse multiple myeloma. The Package Leaflet is updated accordingly. The RMP version 9.0 has also been submitted. C.I.4 Update of section 4.8 of the SmPC in order to revise the frequencies of certain adverse drug reactions based on the pooled data set including ENDEAVOR and 7 recently completed studies. In addition, the Marketing authorisation holder (MAH) took the opportunity to add editorial changes in sections 4.2, 4.4, 6.3 and 6.6 of the SmPC. Editorial changes have also been included in the package leaflet and labelling." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 14.12.2017, 12.10.2017.	
Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0004 MAH: AbbVie Limited, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC in order to update information on the use of Maviret in liver or kidney transplant patients, based on new clinical data from study M13-596 (MAGELLAN-2), a post-registrational Phase 3 study listed as a category 3 study in the RMP, which evaluated the efficacy and safety of the glecaprevir/pibrentasvir regimen in adult subjects with chronic hepatitis C virus genotypes 1-6 infection, who have received a liver or renal transplant. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted." Request for Supplementary Information adopted on 25.01.2018.	Request for Supplementary Information adopted
Odomzo - sonidegib - EMEA/H/C/002839/II/0016 MAH: Sun Pharmaceutical Industries Europe B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Patrick Batty, "Update of Annex II to delete the condition "Post-authorisation efficacy study (PAES): The MAH should submit the final CSR for Study CLDE225A2201, including an updated analysis of outcomes by aggressive vs non-aggressive	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

histological subtypes." The RMP (version 7.0) is updated to reflect the fulfilment of the Annex II condition." Opinion adopted on 25.01.2018.	
Ofev - nintedanib - EMEA/H/C/003821/II/0018/G, Orphan MAH: Boehringer Ingelheim International GmbH, Rapporteur: Jayne Crowe, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of section 4.4 in order to remove the current warning on co-administration with pirfenidone and update of section 5.1 to include the results of study 1199.222, a phase IV, 12 week, open label, randomised, parallel group study to evaluate the safety, tolerability and PK of oral nintedanib in combination with oral pirfenidone in comparison with nintedanib alone in patients with IPF. Update of section 5.2 of the SmPC in order to include the results of study 1199.229, a phase IV, open label, multi-dose, 2 groups study to investigate the DDI between nintedanib anfd pirfenidone in patients with IPF, a category 3 study in the RMP. The RMP version 5.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement some corrections to the French and Swedish translations." Request for Supplementary Information adopted on 11.01.2018.	Request for Supplementary Information adopted
Olumiant - baricitinib - EMEA/H/C/004085/II/0003 MAH: Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Patrick Batty, "Update of sections 4.4 and 5.1 of the SmPC in order to include results of a vaccination sub-study which was part of the long term extension study 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, consolidated RMP version 5.0 has been agreed as part of this application." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 14.12.2017.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Raxone - idebenone - EMEA/H/C/003834/II/0008, Orphan	Request for Supplementary Information adopted

MAH: Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Carmela Macchiarulo, "Update of SmPC section 4.5 to include that CYP3A4 substrates known to have a narrow therapeutic index should be administered with caution in patients receiving idebenone, based on the final study report for study SNT-I-017: "An open-label study to assess the potential for pre-systemic inhibition of cytochrome P450 3A4 (CYP3A) by idebenone in healthy male subjects using midazolam as a substrate". The Package Leafelt was updated accordingly. An updated RMP version 1.5 was submitted as part of the application. The provision of the study report addresses the post-authorisation measure MEA 005.1." Request for Supplementary Information adopted on 11.01.2018.	
ReFacto AF - moroctocog alfa - EMEA/H/C/000232/II/0143 MAH: Pfizer Limited, Rapporteur: Hanne Lomholt Larsen, PRAC Rapporteur: Doris Stenver, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update the existing safety, efficacy and pharmacokinetic information based on the final results from studies B1831005 and B1831006 listed as category 3 in the RMP (MEA 111 and 113) and assessed in procedures P46-143 and P46-145 respectively. Study B1831005 is a non-randomized, open label study to evaluate the safety, efficacy, and pharmacokinetics (PK) of ReFacto AF in previously treated children less than 12 years of age with severe haemophilia A (FVIII:C<1%)(already submitted in P46-143). Study B1831006 is an open-label study on the safety and efficacy of ReFacto AF in previously untreated patients (PUPs) in usual care settings (already submitted in P46-145). In addition, the MAH took the opportunity to updated Sections 4.4 and 4.8 of the SmPC and as well as Sections 2 and 4 of the PIL in line with the agreed wording of the PRAC referral (EMEA/H/A-31/1448). In addition, the PI is brought in line with the latest QRD template (version 10) and the unique identifier 2D barcode added to the labelling. An editorial change has been made to the Package Leaflets (CZ local representative	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

address). The updated RMP version 12.0 (new template, revision 2) has been submitted in order to add information regarding the above mentioned studies and from study B1831083 an open-label, single-arm, post-authorization pragmatic clinical trial on the safety and efficacy of Xyntha in subjects with Hemophilia A in usual care settings in China, listed as category 3 in the RMP and already submitted as P46-144." Opinion adopted on 25.01.2018.	
Remicade - infliximab - EMEA/H/C/000240/II/0209 MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the current warning on colon cancer and dysplasia of Section 4.4 of the SmPC based on final report of the OPUS Registry (Prospective, Observational, Non-Interventional, Post-marketing Safety Surveillance Program in Subjects with UC; P04808) as per MEA 121. In addition, the MAH is taking the opportunity to add a warning on screening tests for tuberculosis to align it with current medical practice, add a reminder on the patient alert card in package leaflet and include some editorial changes in line with the QRD template." Request for Supplementary Information adopted on 11.01.2018.	Request for Supplementary Information adopted
RoActemra - tocilizumab - EMEA/H/C/000955/II/0074/G MAH: Roche Registration Limited, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski Request for Supplementary Information adopted on 11.01.2018.	Request for Supplementary Information adopted
Stribild - elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil - EMEA/H/C/002574/II/0087 MAH: Gilead Sciences International Limited, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Julie Williams, "Submission of the final study report for Study GS-EU-236-0141, listed as a category 3 study in the Risk Management Plan, in order to fulfil a post-authorisation measure (PAM) MEA 006 for Stribild; This study is an Observational Drug	Request for Supplementary Information adopted

Utilization Study of Stribild in Adults with HIV-1 Infection. With this application and as agreed with the EMA, Gilead is also taking this opportunity to address the outstanding questions from MEA 002.3." Request for Supplementary Information adopted on 11.01.2018.	
Symtuza - darunavir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004391/II/0002/G MAH: Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Julie Williams, "C.I.13-II to submit the results of the study GS-US-311-1089 "A Phase 3, Randomized, Double-Blind, Switch Study to Evaluate F/TAF in HIV 1 Positive Subjects who are Virologically Suppressed on Regimens containing FTC/TDF". The RMP has been updated to reflect the completion of the study. C.I.11.z- II to update the RMP to remove pancreatitis, convulsion, and cardiac conduction abnormalities as risks in the RMP in alignment with the RMP for Prezista and Rezolsta." Request for Supplementary Information adopted on 11.01.2018	Request for Supplementary Information adopted
Trulicity - dulaglutide - EMEA/H/C/002825/II/0022 MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey, PRAC Rapporteur: Carmela Macchiarulo, "Update of sections 4.2, 5.1 and 5.2 of the SmPC for Trulicity following completion of a Phase 3 study (H9X-MCGBDX (GBDX)) comparing the effect of once-weekly Trulicity with insulin glargine on glycaemic control over 52 weeks in patients with type 2 Diabetes Mellitus and moderate or severe chronic kidney disease. In addition, an update to the ATC code and a correction to the "Instructions for use" in Section 6.6 of the SmPC to make it consistent with instructions on "How to store Trulicity" in the Package Insert Leaflet (PL) are proposed. The RMP version 1.11 has also been submitted." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 30.11.2017.	
Tyverb - lapatinib - EMEA/H/C/000795/II/0050/G MAH: Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "1. Type II- C.I.13: Submission of the final non-clinical study report 09DMR047 listed as a category 3 study in the RMP. This is a non-clinical mechanistic study related to lapatinib metabolite identification in dog plasma, bile and liver. An updated RMP (version 33) is included to reflect the completion of a dog study and integration of the results. 2. Type IB- C.I.11.Z: Change to the final due date of study EGF117165 to evaluate biomarkers of drug resistance in patients with HER2+ metastatic breast cancer whilst on treatment with trastuzumab in combination with either lapatinib or chemotherapy (category 1, ANX034.2) from Jun-2018 to Jun-2019 in the RMP and Annex II. In addition, the MAH took the opportunity to implement the recent PRAC PSUR recommendation into the RMP version 33, including the removal of two identified risks (rash, diarrhoea) and update of missing information wording (hepatic impairment and renal impairment)." Opinion adopted on 25.01.2018.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and Haemophilus type B conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0021 MAH: MCM Vaccine B.V., Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 5.1 of the SmPC in order to update the efficacy section on immune persistence based on the final results from study PRI03C - Long-term Persistence of Hepatitis B and Pertussis Antibody Responses in Healthy 4- to 5-year-old Children Previously Vaccinated with a 2 dose or 3 dose Infants Series and Toddler dose of Vaxelis or INFANRIX hexa listed as P46 study in the PIP. Tthe RMP version 2.2 has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes in Annex IIIa"	Positive Opinion adopted by consensus on 11.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 11.01.2018.	
Vokanamet - canagliflozin / metformin - EMEA/H/C/002656/II/0034 MAH: Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.1, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information on cardiovascular events following final results from CANVAS Program (DIA3008 and DIA4003); the Package Leaflet is updated accordingly. Study DIA3008 is phase 3 Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of JNJ-28431754 on Cardiovascular Outcomes in Adult Subjects With Type 2 Diabetes Mellitus Study DIA4004 is phase 4 Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of Canagliflozin on Renal Endpoints in Adult Subjects With Type 2 Diabetes Mellitus The RMP version 7.2 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 andto bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 25.01.2018.	Request for Supplementary Information adopted
Zelboraf - vemurafenib - EMEA/H/C/002409/II/0042/G MAH: Roche Registration Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from studies MO25515 (MEA006) [An Open-Label, Multicenter Study to Assess the Safety of RO5185426 (Vemurafenib) in Patients with Metastatic Melanoma] and GP28492 (MEA010) [ZeSS: A Prospective Observational Safety Study of Patients with BRAFV600 Mutationpositive Unresectable or Metastatic Melanoma Treated with Vemurafenib (Zelboraf®)]" Request for Supplementary Information adopted on 18.01.2018, 28.09.2017.	Request for Supplementary Information adopted
Zydelig - idelalisib - EMEA/H/C/003843/II/0038	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP

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 MAH took this opportunity to make a minor amendment in the Labelling and to update the local representatives in the package leaflet." Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 14.12.2017.	Members were in agreement with the CHMP recommendation.
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 of the RMP with current information on epidemiology, post-authorisation exposure and post authorisation studies status including the due date of the final study report for Ivabradine Drug Utilisation Study. The Annex II has been updated accordingly. In addition the MAH took the opportunity to align the PI with the latest QRD template 10.0 and introduce minor updates to the ADR terms." Opinion adopted on 11.01.2018. Request for Supplementary Information adopted on 26.10.2017, 01.09.2017.	Positive Opinion adopted by consensus on 11.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1190/G **Enbrel-** **EMEA/H/C/000262/WS1190/0210/G** **Lifmior-** **EMEA/H/C/004167/WS1190/0009/G** MAH: Pfizer Limited, Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Patrick Batty	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 25.01.2018. Request for Supplementary Information adopted on 20.12.2017, 28.09.2017.	

B.5.4. PRAC assessed procedures

PRAC Led **Aclasta - zoledronic acid - EMEA/H/C/000595/II/0069** MAH: Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final 5-year report from study (ZOL446H2422) listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study using health registries to compare safety of Aclasta against oral bisphosphonates and untreated population controls." Request for Supplementary Information adopted on 11.01.2018, 06.07.2017.	Request for Supplementary Information adopted
PRAC Led **Advate - octocog alfa - EMEA/H/C/000520/II/0089** MAH: Baxter AG, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from study 061501. This was a retrospective chart review aimed to evaluate safety and tolerability of Advate among previously untreated patients with moderate to severe Haemophilia A." Opinion adopted on 11.01.2018.	Positive Opinion adopted by consensus on 11.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Baraclude - entecavir - EMEA/H/C/000623/II/0053** MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Qun-Ying Yue, PRAC-CHMP liaison: Filip Josephson, "Submission of the final study report for study AI463080, a long-term outcomes study (10 years), to assess the rates of malignant neoplasm (all, non- hepatocellular carcinoma, and hepatocellular carcinoma), liver-related events of HBV disease progression, and mortality. Risk Management Plan Version 14 has been updated accordingly." Opinion adopted on 11.01.2018.	Positive Opinion adopted by consensus on 11.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led	Positive Opinion adopted by consensus on

Betaferon - interferon beta-1b - EMEA/H/C/000081/II/0118 MAH: Bayer AG, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "Submission of the final report from study BETAPAEDIC, listed as a category 3 study in the RMP. This was a non-interventional study evaluating safety and tolerability of Betaferon in paediatric patients with multiple sclerosis. The RMP version 3.2 has also been submitted." Opinion adopted on 11.01.2018. Request for Supplementary Information adopted on 30.11.2017.	11.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Fiasp - insulin aspart - EMEA/H/C/004046/II/0003/G** MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "Update of the RMP to upgrade the risk of mix-up between basal and bolus insulin from a potential to an important identified risk (RMP version 2.0). In addition, to update the secondary packaging material (carton, Label, IFU) design and change colour of selected plastic components from yellow to red. Also the MAH submitted as part of this variation a proposal for communication to Health Care Professionals and Patients (indirectly) regarding similarity of Fiasp and Tresiba products that are currently on the market." Request for Supplementary Information adopted on 11.01.2018.	Request for Supplementary Information adopted
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.	Request for Supplementary Information adopted

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 11.01.2018, 26.10.2017.	
PRAC Led **Mycamine - micafungin - EMEA/H/C/000734/II/0035** MAH: Astellas Pharma Europe B.V., Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "Submission of the final survey report regarding Educational tools in the RMP and Educational tools as a LEG (39) and updated RMP version 18.0." Request for Supplementary Information adopted on 11.01.2018.	Request for Supplementary Information adopted
PRAC Led **Orencia - abatacept - EMEA/H/C/000701/II/0116/G** MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, PRAC-CHMP liaison: Outi Mäki-Ikola, "Grouping of two Type II variations, as follows: C.I.13: Submission of the final report from study IM101537 listed as a category 3 study in the RMP. This is a non-interventional HCP/patient cross-sectional survey and retrospective chart review Post Authorisation Safety Study to evaluate the effectiveness of the Patient Alert Card for both IV and SC abatacept in a sample of EU countries. C.I.11: Submission of an updated RMP (version 24) in order to reflect the early closure of another RMP category 3 study: Study IM101212, which closed in September 2017 and for which no further data will be available. A number of other administrative updates to the RMP are being carried out in the context of this procedure." Opinion adopted on 11.01.2018.	Positive Opinion adopted by consensus on 11.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led	Positive Opinion adopted by consensus on

ReFacto AF - moroctocog alfa - EMEA/H/C/000232/II/0142 MAH: Pfizer Limited, PRAC Rapporteur: Doris Stenver, "Submission of the final study report from study B1831016, listed as a category 3 in the RMP (MEA 108.3). This is a non-interventional open-label study conducted at haemophilia treatment centres in Germany and Austria to generate information regarding the safety and effectiveness of treatment with ReFacto AF under routine clinical conditions." Opinion adopted on 11.01.2018.	11.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Scenesse - afamelanotide - EMEA/H/C/002548/II/0018, Orphan** MAH: Clinuvel (UK) Limited, PRAC Rapporteur: Valerie Strassmann, PRAC-CHMP liaison: Harald Enzmann, "Submission of an updated RMP version 8.0 which aims to address the comments made in procedure IB/14 and including: - Updates from pre-approval information to post-marketing information - Update of number of patients treated in clinical trials, special access schemes and commercial distribution - Change in development of the custom-made device - Postponement of pharmacokinetic study CUV052 (no timeframe yet) - Update on timelines for safety extension study CUV037 from Q12013 to Q12018 - Update on timelines for on-going and planned PV studies - key elements of educational and training programme (annex 10) - Correction: replacement of pigmentary lesions by pigmentary expressions - General update of safety information" Request for Supplementary Information adopted on 11.01.2018	Request for Supplementary Information adopted
PRAC Led **Sebivo - telbivudine - EMEA/H/C/000713/II/0048** MAH: Novartis Europharm Limited, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Caroline Laborde, PRAC-CHMP liaison: Joseph Emmerich, "Submission of an updated RMP version 11.0 in order to upgrade the risk of lactic acidosis from	Request for Supplementary Information adopted

an important potential to an important identified risk and to include a targeted questionnaire for fatal cases as additional risk minimisation measure as requested by the PRAC as part of the assessment of PSUSA/00002880/201608." Request for Supplementary Information adopted on , 30.11.2017.	
PRAC Led **Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0124/G** MAH: GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final study reports from two 5-year Invasive Pneumococcal Disease (IPD) post-marketing surveillance (PMS) studies "Monitoring the Population Effectiveness of Pneumococcal Conjugate Vaccination in the Finnish National Vaccination Programme" (MEA 019) and "Epidemiology of invasive pneumococcal disease in the Netherlands" (MEA 020), addressing the potential risks of "possible serotype replacement of disease isolates" and "possible breakthrough infections/vaccine failure". The MAH also submitted data from IPD surveillance in 5 other European countries (Austria, Bulgaria, Cyprus, Iceland and Sweden) and 6-year update results from a 5-year PMS in Kenya (Pneumococcal Conjugate Vaccine Impact Study (PCVIS), MEA 021). Submission of an updated RMP version 17 to reflect data from the PMS studies, close MEA 019 and MEA 020, extend MEA 021 and implement the latest RMP template (revision 2). No changes to the Product Information are proposed with this submission." Request for Supplementary Information adopted on 11.01.2018	Request for Supplementary Information adopted
PRAC Led **WS1283** **Relvar Ellipta-** **EMEA/H/C/002673/WS1283/0035** **Revinty Ellipta-** **EMEA/H/C/002745/WS1283/0031** MAH: Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, PRAC-CHMP liaison: Concepcion Prieto Yerro, "Submission of the final report from study 205052 (PRJ2214).	Request for Supplementary Information adopted

This is a drug utilization study to identify the extent of any off-label prescribing fluticasone furoate/vilanterol FF/VI in any dose in children less than 12 years of age; and prescribing of FF/VI 200/25 mcg in patients with a diagnosis of chronic obstructive pulmonary disease COPD, considering the presence of a concurrent diagnosis of asthma. The RMP version 9.1 has been updated accordingly." Request for Supplementary Information adopted on 11.01.2018.	
PRAC Led **WS1293** **Exelon-EMEA/H/C/000169/WS1293/0115** **Prometax-EMEA/H/C/000255/WS1293/0115** MAH: Novartis Europharm Limited, Lead Rapporteur: Alexandre Moreau, Lead PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "To update the Rivastigmine RMP with: - Milestone changes for Drug Utilization Study (DUS) (ENA713D2409) - Based on PRAC Assessment Report (AR) (EMEA/H/C/000169/MEA 034.2 & EMEA/H/C/000255/MEA 035.1) Protocol Amendment version 2, as finalized. - Removal of important identified risk "pancreatitis" - Based on PRAC PSUR 23 (01-Feb-2014 to 31-Jan-2015) AR (EMEA/H/C/PSUSA/00002654/201501) - Discontinue the use of the targeted checklist to document cases of medication error/misuse - Based on PRAC PSUR 24 (01-Feb-2015 to 31-Jan-2016) AR (EMEA/H/C/PSUSA/00002654/201601) - Change of 6 monthly report on "the effectiveness of risk minimization measures for multiple patch use" to annual report - Based on the AR of the fourth 6 monthly report on "the effectiveness of risk minimization measures for multiple patch use." The following activities which occurred after the DLP of 31-Jan-16 are also included in the Rivastigmine RMP update: information about the submission of an interim analysis report for DUS ENA713D2409 dated 10-Mar-2016 to PRAC, information about distribution of a health care	Positive Opinion adopted by consensus on 11.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

professional (HCP) letter in Japan, information about the request from the Brazilian health authority to include a statement in local Exelon patch leaflet to minimize the potential risk of skin irritation, information that the Exelon/Prometax CDS was amended on 04 -Mar -2016 to include "nightmares" as an ADR. Furthermore e.g. updates of RMP Parts and RMP Annexes to align with the status provided in PSUR 24 (DLP 31-Jan-16) are included." Opinion adopted on 11.01.2018.	
PRAC Led **WS1342** **Exviera-EMEA/H/C/003837/WS1342/0034** **Viekirax-EMEA/H/C/003839/WS1342/0041** MAH: AbbVie Limited, Lead PRAC Rapporteur: Dolores Montero Corominas, PRAC-CHMP liaison: Concepcion Prieto Yerro, "To update the RMP to incorporate changes requested by PRAC during assessment of the 24 month PSUR applications (EMEA/H/C/PSUSA/00010363/201701 and EMEA/H/C/PSUSA/00010367/201701). These changes are as follows: 1. Addition of a new potential risk of depression and suicide in Module SVII.1 - Newly identified safety concerns. 2. Removal of off-label use and medication error as potential risks from Module SVII. 3. Renaming of the potential risk of development of resistance to Lack of Efficacy/Risk of Development of Resistance in Module SVII.3. In addition, the commitment dates for 4 ongoing studies listed in Part III.5.1 (Table of On-going and planned additional pharmacovigilance studies/activities in the pharmacovigilance plan) have been revised." Request for Supplementary Information adopted on 11.01.2018 Clockstop extension of, responses expected 15.03.2018. Adopted.	Request for Supplementary Information adopted

B.5.5. CHMP-CAT assessed procedures

Zalmoxis - allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - EMEA/H/C/002801/II/0005/G, Orphan, ATMP MAH: MolMed SpA, Rapporteur: Johannes Hendrikus Ovelgonne, Request for Supplementary Information adopted on 06.10.2017.	recommendation.

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

WS1269 **Rotarix-EMEA/H/C/000639/WS1269/0103** MAH: GlaxoSmithKline Biologicals S.A., Lead Rapporteur: Bart Van der Schueren Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1272 **Epclusa-EMEA/H/C/004210/WS1272/0020** **Vosevi-EMEA/H/C/004350/WS1272/0007** MAH: Gilead Sciences International Limited, Lead Rapporteur: Filip Josephson Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1305 **Descovy-EMEA/H/C/004094/WS1305/0024** **Genvoya-EMEA/H/C/004042/WS1305/0039** **Odefsey-EMEA/H/C/004156/WS1305/0023** **Vemlidy-EMEA/H/C/004169/WS1305/0007** MAH: Gilead Sciences International Limited, Lead Rapporteur: Robert James Hemmings, Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1319/G **Helixate NexGen-EMEA/H/C/000276/WS1319/0195/G** **Kogenate Bayer-EMEA/H/C/000275/WS1319/0203/G** MAH: Bayer AG, Lead Rapporteur: Jan Mueller-Berghaus	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 18.01.2018.	
WS1321 **Exelon-EMEA/H/C/000169/WS1321/0116** **Prometax-EMEA/H/C/000255/WS1321/0116** MAH: Novartis Europharm Limited, Lead Rapporteur: Alexandre Moreau, "To update the Product Information in line with the latest QRD template. In addition the MAH took this opportunity to update the contact details of the local representatives in Bulgaria, Hungary, Latvia, Estonia and Lithuania." Opinion adopted on 25.01.2018.	Positive Opinion adopted by consensus on 25.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1325 **M-M-RVAXPRO-EMEA/H/C/000604/WS1325/0086** **ProQuad-EMEA/H/C/000622/WS1325/0122** MAH: MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 18.01.2018.	Positive Opinion adopted by consensus on 18.01.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Hexacima-EMEA/H/C/002702/WS1306/0074 **Hexaxim-EMEA/H/W/002495/WS1306/0079** **Hexyon-EMEA/H/C/002796/WS1306/0078** MAH: Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 25.01.2018.	Request for Supplementary Information adopted

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

Buccolam - midazolam - EMEA/H/C/002267/II/0035 MAH: Shire Services BVBA, Rapporteur: Johann Lodewijk Hillege. Withdrawal request submitted on 21.12.2017.	The MAH withdrew the procedure on 21.12.2017.
Reagila - cariprazine - EMEA/H/C/002770/II/0002 MAH: Gedeon Richter Plc., Rapporteur: Kristina Dunder. Withdrawal request submitted on 15.01.2018.	The MAH withdrew the procedure on 15.01.2018.
WS1296 **Osseor-EMEA/H/C/000561/WS1296/0043** **Protelos-**	The MAH withdrew the procedure on 15.01.2018.

EMEA/H/C/000560/WS1296/0048
MAH: Les Laboratoires Servier, Lead
Rapporteur: Kristina Dunder
Withdrawal request submitted on 15.01.2018.

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

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

avacopan - EMEA/H/C/004487, Orphan, induction of response in adult patients with granulomatosis with polyangiitis (Wegener's) (GPA) or microscopic polyangiitis (MPA)	
beclometasone dipropionate anhydrous / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004836, symptomatic treatment and reduction of exacerbations in adult patients with chronic obstructive pulmonary disease (COPD) with airflow limitation and who are at risk of exacerbations, Informed Consent of Trimbow	
zanamivir - EMEA/H/C/004102, treatment of influenza A or B virus infection	
romosozumab - EMEA/H/C/004465, Treatment of osteoporosis	
fexinidazole - EMEA/H/W/002320, Article 58, treatment of human African trypanosomiasis (HAT)	**Accelerated review**
adalimumab - EMEA/H/C/004866, treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, uveitis, paediatric uveitis	
adalimumab - EMEA/H/C/004865, Juvenile idiopathic arthritis, Axial spondyloarthritis, Psoriatic arthritis, Psoriasis, Paediatric plaque psoriasis, Hidradenitis suppurativa (HS), Uveitis Paediatric uveitis	
patisiran - EMEA/H/C/004699, Orphan, treatment of hereditary transthyretin-mediated amyloidosis.	**Accelerated review**
beclometasone dipropionate	

anhydrous/formoterol fumarate dihydrate/glycopyrronium - EMEA/H/C/004702, symptomatic treatment and reduction of exacerbations in adult patients with chronic obstructive pulmonary disease (COPD) with airflow limitation and who are at risk of exacerbations, Informed Consent of Trimbow

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

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

erenumab - EMEA/H/C/004447, indicated for prophylaxis of migraine in adults
List of Questions adopted on 12.10.2017.

bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449, treatment of adults infected with human immunodeficiency virus-1 (HIV-1)
List of Questions adopted on 09.11.2017.

Bosulif - bosutinib - EMEA/H/C/002373/X/0026, Orphan
MAH: Pfizer Limited, Rapporteur: Harald Enzmann, "Extension application to add a new strength of 400mg film-coated tablets."
List of Questions adopted on 14.12.2017.

sufentanil - EMEA/H/C/004335, management of acute moderate to severe pain
List of Questions adopted on 20.07.2017.

adalimumab - EMEA/H/C/004320, treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa (HS), Crohn's disease, paediatric Crohn's disease, ulcerative colitis, uveitis, paediatric uveitis
List of Questions adopted on 14.09.2017.

vestronidase alfa - EMEA/H/C/004438, Orphan
Applicant: Ultragenyx Germany GmbH, indicated for the treatment of Mucopolysaccharidosis VII (MPS VII; Sly syndrome) for patients of all ages
List of Questions adopted on 14.09.2017.

nitisinone - EMEA/H/C/004582

, treatment of hereditary tyrosinemia type 1, Generic, Generic of Orfadin
List of Questions adopted on 22.06.2017.

sodium benzoate - EMEA/H/C/004150, Orphan
Applicant: Lucane Pharma, treatment of non ketotic hyperglycinemia, urea cycle disorders including carbamoyl-phosphate synthase-1 deficiency, ornithine transcarbamylase deficiency, citrullinaemia type 1, argininosuccinic aciduria, hyperargininaemia, n-acetylglutamate synthase deficiency, ornithine translocase deficiency and lysinuric protein intolerance
List of Questions adopted on 22.06.2017.

naldemedine - EMEA/H/C/004256, treatment of opioid-induced constipation (OIC) in adult patients.
List of Questions adopted on 20.07.2017.

brexpiprazole - EMEA/H/C/003841, treatment of schizophrenia
List of Questions adopted on 20.07.2017.

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

2. C.I.6.a(type II) to include the treatment of children and adolescents aged 1 year to 18 years with Ph+ chronic phase CML for Sprycel. Sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, to add a warning on effects on growth and development in the paediatric population and to update the safety information. The Package Leaflet is updated in accordance."
List of Questions adopted on 14.09.2017.

sufentanil - EMEA/H/C/004335, management of acute moderate to severe pain
List of Questions adopted on 20.07.2017.

tezacaftor / ivacaftor - EMEA/H/C/004682, Orphan

, treatment of cystic fibrosis
List of Questions adopted on 14.12.2017.

vonicog alfa - EMEA/H/C/004454, Orphan
, Treatment of von Willebrand Disease (VWD)
List of Questions adopted on 12.10.2017.

Votubia - everolimus - EMEA/H/C/002311/X/0045, Orphan
MAH: Novartis Europharm Limited, Rapporteur: Harald Enzmann, Co-Rapporteur: Greg Markey, "Extension application to add a new strength of 1 mg everolimus dispersible tablet."
List of Questions adopted on 09.11.2017.

infliximab - EMEA/H/C/004647
, treatment of rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, psoriasis and ulcerative colitis
List of Questions adopted on 14.09.2017.

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

Defitelio - defibrotide - EMEA/H/C/002393/S/0029, Orphan
MAH: Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams

Kolbam - cholic acid - EMEA/H/C/002081/S/0025, Orphan
MAH: Retrophin Europe Ltd, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Patrick Batty

Vyndaqel - tafamidis - EMEA/H/C/002294/S/0044, Orphan
MAH: Pfizer Limited, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Ghania Chamouni

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

Aubagio - teriflunomide - EMEA/H/C/002514/R/0016
MAH: sanofi-aventis groupe, Rapporteur: Martina Weise, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber

Cholib - fenofibrate / simvastatin - EMEA/H/C/002559/R/0017
MAH: Mylan Products Limited, Rapporteur: Robert James Hemmings, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Julie Williams

Giotrif - afatinib -
EMEA/H/C/002280/R/0026
MAH: Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Ulla Wändel Liminga

Incresync - alogliptin / pioglitazone -
EMEA/H/C/002178/R/0023
MAH: Takeda Pharma A/S, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst

Lemtrada - alemtuzumab -
EMEA/H/C/003718/R/0020
MAH: Genzyme Therapeutics Ltd, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Hanne Lomholt Larsen, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver

Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (H5N1) (live attenuated, nasal) -
EMEA/H/C/003963/R/0011
MAH: AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Daniela Philadelphy

Procysbi - mercaptamine -
EMEA/H/C/002465/R/0019, Orphan
MAH: Chiesi Orphan B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Qun-Ying Yue

Tybost - cobicistat -
EMEA/H/C/002572/R/0041
MAH: Gilead Sciences International Limited, Rapporteur: Robert James Hemmings, Co-Rapporteur: Joseph Emmerich, PRAC Rapporteur: Julie Williams

Ultibro Breezhaler - indacaterol / glycopyrronium -
EMEA/H/C/002679/R/0024
MAH: Novartis Europharm Limited, Rapporteur: Hanne Lomholt Larsen, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Doris Stenver

Vipdomet - alogliptin / metformin -
EMEA/H/C/002654/R/0024
MAH: Takeda Pharma A/S, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst

Vipidia - alogliptin -
EMEA/H/C/002182/R/0019
MAH: Takeda Pharma A/S, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst

Xarelto - rivaroxaban -
EMEA/H/C/000944/R/0060
MAH: Bayer AG, Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Qun-Ying Yue

Xoterna Breezhaler - indacaterol / glycopyrronium -
EMEA/H/C/003755/R/0027
MAH: Novartis Europharm Limited, Duplicate, Duplicate of Ultibro Breezhaler, Rapporteur: Hanne Lomholt Larsen, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Doris Stenver

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

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

Darzalex - daratumumab -
EMEA/H/C/004077/II/0011, Orphan
MAH: Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Extension of Indication to include the combination with bortezomib, melphalan and prednisone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant for Darzalex; 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 3.1 (in version 2 of the RMP template) has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of the Lithuanian and Slovenian local representatives in the Package Leaflet."

Nucala - mepolizumab - EMEA/H/C/003860/II/0013/G

MAH: GlaxoSmithKline Trading Services Limited, Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Type II-C.I.6-Extension of Indication to include children and adolescents aged 6 to 17 years for Nucala; as a consequence, Sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC and Sections 1, 2, 3, 4 and Information for Healthcare Professionals in the Package Leaflet are updated accordingly.
n addition to the proposed SmPC/PL updates specific to the paediatric indication, as Nucala is a biological medicine, GSK is including wording in the NUCALA SmPC (Section 4.4) and PL (Information for Health Care Professionals) that the name and batch number of the administered product should be clearly recorded in the patient file.

Type IB-B.II.d.2.z- Change to the finished product justification of specifications for the dose dependent calculation as confirmation of acceptance criteria for Endotoxin (no changes to specification). To change the dose dependent controls for raw material clearance and exposure.

Type IB B.I.b.2.z –Change to the active substance justification of specifications for the dose dependent calculation as confirmation of acceptance criteria for Endotoxin (no changes to specification). To change the dose dependent controls for raw material clearance and exposure.

In addition, editorial changes are introduced in section P.5.5."

Tyverb - lapatinib - EMEA/H/C/000795/II/0051

MAH: Novartis Europharm Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.1 and 5.1 of the SmPC based on results from study EGF114299/LAP016A2307 listed as a condition (ANX027.4) in the Annex II; a Phase III trial to compare the safety and efficacy of
lapatinib plus trastuzumab plus an aromatase inhibitor (AI) versus trastuzumab plus an AI versus lapatinib plus an AI as first- or second-

line therapy in postmenopausal subjects with hormone receptor positive, HER2-positive metastatic breast cancer (MBC) who have received prior trastuzumab and endocrine therapies. Annex II has been updated accordingly. A revised RMP version 34.0 has also been submitted as part of the application."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Aloxi - palonosetron - EMEA/H/C/000563/II/0045/G
MAH: Helsinn Birex Pharmaceuticals Ltd, Rapporteur: Peter Kiely

ATryn - antithrombin alfa - EMEA/H/C/000587/II/0033/G
MAH: Laboratoire Francais du Fractionnement et des Biotechnologies, Rapporteur: Alexandre Moreau

Benepali - etanercept - EMEA/H/C/004007/II/0031/G
MAH: Samsung Bioepis UK Limited, Rapporteur: Andrea Laslop

Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0068/G
MAH: UCB Pharma S.A., Rapporteur: Kristina Dunder

Daptomycin Hospira - daptomycin - EMEA/H/C/004310/II/0006/G
MAH: Hospira UK Limited, Generic, Generic of Cubicin, Rapporteur: Kolbeinn Gudmundsson

Dupixent - dupilumab - EMEA/H/C/004390/II/0002
MAH: sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus

Eylea - aflibercept - EMEA/H/C/002392/II/0040/G
MAH: Bayer AG, Rapporteur: Alexandre Moreau

Eylea - aflibercept - EMEA/H/C/002392/II/0041/G
MAH: Bayer AG, Rapporteur: Alexandre Moreau

Gardasil - human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) - EMEA/H/C/000703/II/0075
MAH: MSD Vaccins, Rapporteur: Kristina Dunder

Imraldi - adalimumab -

EMEA/H/C/004279/II/0005/G
MAH: Samsung Bioepis UK Limited (SBUK), Rapporteur: Outi Mäki-Ikola

Infanrix hexa - 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/000296/II/0237/G
MAH: GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren

Inflectra - infliximab - EMEA/H/C/002778/II/0057
MAH: Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey

NovoSeven - eptacog alfa / eptacog alfa (activated) - EMEA/H/C/000074/II/0101/G
MAH: Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik

Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0030/G
MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Nithyanandan Nagercoil

Pegasys - peginterferon alfa-2a - EMEA/H/C/000395/II/0098/G
MAH: Roche Registration Limited, Rapporteur: Filip Josephson

Pegasys - peginterferon alfa-2a - EMEA/H/C/000395/II/0099/G
MAH: Roche Registration Limited, Rapporteur: Filip Josephson

Pergoveris - follitropin alfa / lutropin alfa - EMEA/H/C/000714/II/0054/G
MAH: Merck Serono Europe Limited, Rapporteur: Nithyanandan Nagercoil

Pioglitazone Accord - pioglitazone - EMEA/H/C/002277/II/0015/G
MAH: Accord Healthcare Limited, Generic, Generic of Actos, Rapporteur: Peter Kiely

Procysbi - mercaptamine - EMEA/H/C/002465/II/0018, Orphan
MAH: Chiesi Orphan B.V., Rapporteur: Kristina Dunder

Protopic - tacrolimus - EMEA/H/C/000374/II/0072/G
MAH: LEO Pharma A/S, Rapporteur: Peter Kiely

Raplixa - human fibrinogen / human thrombin - EMEA/H/C/002807/II/0027/G
MAH: Mallinckrodt Pharmaceuticals Ireland Limited, Rapporteur: Nithyanandan Nagercoil

Remsima - infliximab - EMEA/H/C/002576/II/0048
MAH: Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey

Stelara - ustekinumab - EMEA/H/C/000958/II/0062/G
MAH: Janssen-Cilag International NV, Rapporteur: Greg Markey

Strensiq - asfotase alfa - EMEA/H/C/003794/II/0027/G, Orphan
MAH: Alexion Europe SAS, Rapporteur: Greg Markey

Taltz - ixekizumab - EMEA/H/C/003943/II/0014
MAH: Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder

Trulicity - dulaglutide - EMEA/H/C/002825/II/0026
MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey

Trulicity - dulaglutide - EMEA/H/C/002825/II/0027
MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey

Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and Haemophilus type B conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0026
MAH: MCM Vaccine B.V., Rapporteur: Bart Van der Schueren

Vimizim - elosulfase alfa - EMEA/H/C/002779/II/0022/G, Orphan
MAH: BioMarin Europe Ltd, Rapporteur: Johann Lodewijk Hillege

Xalkori - crizotinib - EMEA/H/C/002489/II/0053/G
MAH: Pfizer Limited, Rapporteur: Alexandre

Moreau

Ziagen - abacavir -
EMEA/H/C/000252/II/0101/G
MAH: ViiV Healthcare UK Limited, Rapporteur: Joseph Emmerich

WS1275/G
Filgrastim Hexal-
EMEA/H/C/000918/WS1275/0038/G
Zarzio-
EMEA/H/C/000917/WS1275/0039/G
MAH: Hexal AG, Duplicate, Duplicate of Zarzio, Lead Rapporteur: Greg Markey

WS1303/G
Hexacima-
EMEA/H/C/002702/WS1303/0077/G
Hexaxim-
EMEA/H/W/002495/WS1303/0082/G
Hexyon-
EMEA/H/C/002796/WS1303/0081/G
MAH: Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

WS1339/G
Fertavid-
EMEA/H/C/001042/WS1339/0038/G
Puregon-
EMEA/H/C/000086/WS1339/0096/G
MAH: Merck Sharp & Dohme Limited, Lead Rapporteur: Nithyanandan Nagercoil

WS1347
Blitzima-
EMEA/H/C/004723/WS1347/0008
Ritemvia-
EMEA/H/C/004725/WS1347/0008
Rituzena-
EMEA/H/C/004724/WS1347/0009
Truxima-
EMEA/H/C/004112/WS1347/0009
MAH: Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz

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

Bosulif - bosutinib -
EMEA/H/C/002373/II/0028, Orphan
MAH: Pfizer Limited, Rapporteur: Harald Enzmann, "Update of section 5.2 of the SmPC following further analyses of the pharmacokinetic (PK) data from Study

B1871044 that has been already submitted to the EMA previously."	
Caprelsa - vandetanib - EMEA/H/C/002315/II/0029 MAH: Genzyme Europe BV, Rapporteur: Alexandre Moreau, "Update of section 5.3 of the SmPC to reflect the results from pre-clinical study titled "ZD6474: A 104 Week Carcinogenicity Study by Oral Gavage in Rats", study number 521826. In addition, the Marketing authorisation holder took the opportunity to update the list of local representatives in the Package Leaflet."	
Caprelsa - vandetanib - EMEA/H/C/002315/II/0030 MAH: Genzyme Europe BV, Rapporteur: Alexandre Moreau, "Update of section 5.1 of the SmPC to add information on overall survival based on the Addendum to clinical study report from the study D4200C00058 (cut-off date 2015): An International, Phase III, Randomized, Double-Blinded, Placebo-Controlled, Multi-Center Study to Assess the Efficacy of ZD6474 versus Placebo in Subjects with Unresectable Locally Advanced or Metastatic Medullary Thyroid Cancer."	
Ceplene - histamine dihydrochloride - EMEA/H/C/000796/II/0034, Orphan MAH: Noventia Pharma Srl, Rapporteur: Jayne Crowe, "Submission of study report X-03064-3306- to fulfil SOB 002 - A cohort study to follow-up Minimal Residual Disease (MRD) in patients with Acute Myeloid Leukemia (AML) in First Complete Remission (CR1) - Comparison of patients who receive Ceplene/Interleukin-2 as remission maintenance therapy with matched controls."	
Darzalex - daratumumab - EMEA/H/C/004077/II/0013, Orphan MAH: Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, "Update of sections 4.4 and 4.8 of the SmPC in order to add the adverse reaction serious infusion-related reactions, including anaphylactic reactions with frequency unknown based on the cumulative review of clinical trial and post-marketing data. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to add a traceability	

statement to bring the product information in line with the guideline on good pharmacovigilance practices and to add specific text relating to the excipient sodium to align the product information with the updated published EMA EU excipient guideline."

Darzalex - daratumumab - EMEA/H/C/004077/II/0014, Orphan

MAH: Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, "Update of section 4.5 of the SmPC in order to add information relating to the daratumumab interference with Serum Protein Electrophoresis (SPE) and Immunofixation (IFE) assays and the daratumumab-specific immunofixation reflex assay (DIRA)."

Eliquis - apixaban - EMEA/H/C/002148/II/0051

MAH: Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.8 of the SmPC in order to reflect a frequency of all adverse drug reactions for each indication based on clinical trials data. The package leaflet is updated accordingly."

Humira - adalimumab - EMEA/H/C/000481/II/0175

MAH: AbbVie Limited, Rapporteur: Kristina Dunder, "Update of sections 4.2 and 5.2 of the SmPC in order to include 80mg every other week (eow) as an alternative dosing option to the current approved 40 mg weekly dose in the following relevant indications; Rheumatoid arthritis (RA), Crohn's disease (CD), pediatric CD (patients ≥ 40 kg), psoriasis (Ps), ulcerative colitis (UC), hidradenitis suppurativa (HS), and adolescent HS. As a consequence section 4.1 and 5.1 of the SmPC for the 80 Mg strength has been modified introducing relevant information on Rheumatoid Arthritis. The Package Leaflet is updated accordingly."

Kyprolis - carfilzomib - EMEA/H/C/003790/II/0025, Orphan

MAH: Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.4, 4.8 and 5.1 of the SmPC to update information based on the final analysis of overall survival data from study PX-171-009 (ASPIRE): A Randomized, Multicenter, Phase 3 Study Comparing Carfilzomib, Lenalidomide, and

Dexamethasone (CRd) vs Lenalidomide and Dexamethasone (Rd) in Subjects with Relapsed Multiple Myeloma. This variation aims to fulfil the recommendation resulting from the initial MAA. 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."	
Lucentis - ranibizumab - EMEA/H/C/000715/II/0069 MAH: Novartis Europharm Limited, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to include information on the diabetic retinopathy score (DRSS) in diabetic macular edema patients (DME) based on pooled data from studies RFB002D2301 (RESTORE), RFB002D2303 (REVEAL) and RFB002D2305 (REFINE)."	
MabThera - rituximab - EMEA/H/C/000165/II/0143 MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, "Submission of the final CSR of the PRIMA study (MO18264), a stydy in Patients with Advanced Follicular Lymphoma Evaluating the Benefit of Maintenance Therapy with Rituximab after Induction of Response with Chemotherapy plus Rituximab in Comparison with No Maintenance Therapy."	
Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0073 MAH: Pfizer Limited, Rapporteur: Greg Markey, "Update of sections 4.4 and 5.1 of the SmPC to include information obtained from Study MenACWY-TT-084 regarding the immunogenicity, safety, and tolerability of MenACWY-TT in subjects with anatomic or functional asplenia, in line with the outcome of the Article 46/049 procedure."	
Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0074 MAH: Pfizer Limited, Rapporteur: Greg Markey, "Update of sections 4.5 and 4.8 of the SmPC to include new information regarding co-administration of Nimenrix with Boostrix and Cervarix in individuals from the age of 9 to 25 years, based on data from Studies MenACWY-	

TT-098 (116705- Phase 3 study to demonstrate the non-inferiority of Nimenrix co-administered with Boostrix compared to Nimenrix administered alone) and MenACWY-TT-054 (113823- phase 3 study to demonstrate the non-inferiority of Nimenrix co-administered with Cervarix compared to Nimenrix alone). The Package Leaflet is updated accordingly."

NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0023

MAH: Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to reflect data on untreated patients resulting from final results of the Guardian 2 (NN7008-3568) study and the Guardian 4 (NN7008-3809) study for Novoeight. The Package Leaflet was updated accordingly."

Perjeta - pertuzumab - EMEA/H/C/002547/II/0035

MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, "Update of section 4.2 of the SmPC to administer Perjeta with Herceptin SC as an alternative to the currently approved co-administration of Perjeta with Herceptin IV."

Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0108

MAH: Boehringer Ingelheim International GmbH, Rapporteur: Hanne Lomholt Larsen, "Update of sections 4.2, 4.4. and 5.1 (Pradaxa 110 and 150 mg) for the SPAF - DVT/PE indication are proposed based on the results from study 1160.186 recomending that patients with non-valvular atrial fibrillation who undergo a PCI with stenting can be treated with PRADAXA® in combination with antiplatelets after haemostasis is achieved. The prescriber guide is also being updated.

Study 1160.186 is `A prospective Randomised, open label, blinded endpoint (PROBE) study to Evaluate DUAL antithrombotic therapy with dabigatran etexilate (110 mg and 150 mg b.i.d.) plus clopidogrel or ticagrelor vs. triple therapy strategy with warfarin (INR 2.0-3.0) plus clopidogrel or ticagrelor and aspirin in patients with non-valvular atrial fibrillation that have undergone a percutaneous coronary intervention (PCI) with stenting (RE-DUAL PCI)'.

In addition, the MAH took the opportunity to

correct in section 4.3 a contraindication that refers to concomitant treatment with heparin, based on the data assessed in the context of variation II/103 to reflect the fact that heparin is administered during ablation procedure at the same time as dabigatran."

Revlimid - lenalidomide - EMEA/H/C/000717/II/0097, Orphan

MAH: Celgene Europe Limited, Rapporteur: Alexandre Moreau, "Update of the SmPC section 4.8. to include solid organ transplant rejection as an adverse reaction (ADR) consistent with the Revlimid Company Core Data Sheet (CCDS). This update is based on a Safety Topic Review (STR) to evaluate reports of solid organ transplant rejection after identifying a case report in a literature article as part of routine safety surveillance. The Package leaflet has been updated accordingly.
The MAH also took the opportunity to further align the section 4.8 with the CCDS by updating:
- table 2 of section 4.8 of the SmPC to identify the ADR terms reported as serious in the Revlimid Relapse/Refractory and/or Transplant Not Eligible MM (TNE MM) clinical trials (MM-009, MM-010, MM-015 and MM-020).
- tables in section 4.8 of the SmPC to annotate for ADR terms for which fatal events have been reported."

Simponi - golimumab - EMEA/H/C/000992/II/0079

MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder, "Update of sections 4.2 and 5.1 of the SmPC in order to update the information on maintenance regimen for patients weighing <80 kg based on analyses of PK, efficacy and safety from the pivotal C0524T18 study. The Package Leaflet is updated accordingly."

SonoVue - sulphur hexafluoride - EMEA/H/C/000303/II/0037/G

MAH: Bracco International B.V., Rapporteur: Alexandre Moreau, "Grouped variation application in order to align with Company Core Data Sheet (CCDS):

- Update of section 4.4 of the SmPC in order to reword warning on hypersensitivity reactions.
- Update of section 4.4 of the SmPC in order to

reword warning for patients with unstable cardiopulmonary status

- Update of section 4.4 of the SmPC in order to delete warning for patients on mechanical ventilation or with unstable neurological diseases
- Update of section 4.4 of the SmPC in order to delete warning for patients with clinically significant pulmonary disease, including severe chronic obstructive pulmonary disease
- Update of section 4.8 of the SmPC in order to revise table with Adverse Drug Reactions

The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes/corrections in sections 4.8 and 4.9 of the SmPC."

Sovaldi - sofosbuvir - EMEA/H/C/002798/II/0048

MAH: Gilead Sciences International Limited, Rapporteur: Filip Josephson, "Submission of the final report from study GS-US-334-1111, listed as a category 3 study in the RMP. This is a phase 1 relative bioavailability and food effect study of sofosbuvir (SOF) oral granules in healthy adult subjects."

Stelara - ustekinumab - EMEA/H/C/000958/II/0063

MAH: Janssen-Cilag International NV, Rapporteur: Greg Markey, "Update of section 4.8 of the SmPC in order to revise the immunogenicity rate in patients with psoriasis from "less than 8%" to "up to 12.4 %" following based on new data generated from a Phase 3b study in psoriasis patients, CNTO1275PSO3009 (PSTELLAR) - A Study of Ustekinumab to Evaluate a "Subject-tailored" Maintenance Dosing Approach in Subjects With Moderate-to-Severe Plaque Psoriasis (PSTELLAR).

In addition, the MAH took the opportunity to update section 4.4 of the SmPC and package leaflet with additional warning of the excipient sodium to align with the recent updates to the Annex of the EC guideline on excipients in labelling."

Tecfidera - dimethyl fumarate -

EMEA/H/C/002601/II/0050
MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, "Submission of the final report from an exploratory pharmacogenomics study. This is an exploratory, retrospective pharmacogenomics analysis to investigate the genomic risk factors for the development of severe and prolonged lymphopenia in patients with multiple sclerosis on treatment with Tecfidera."

Tivicay - dolutegravir - EMEA/H/C/002753/II/0031
MAH: ViiV Healthcare UK Limited, Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC to add the new ADR 'anxiety' based on post-marketing and clinical trial data. The Package Leaflet has been updated accordingly and minor editorial changes implemented."

Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/II/0049
MAH: ViiV Healthcare UK Limited, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC to add the new ADR 'anxiety' based on post-marketing and clinical trial data. The Package Leaflet has been updated accordingly."

Trulicity - dulaglutide - EMEA/H/C/002825/II/0025
MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey, "Update of sections 4.2 and 5.1 of the SmPC to reflect the use of dulaglutide in Type 2 Diabetes Mellitus patients as add-on to sodium-glucose co-transporter 2 inhibitors (SGLT2i) therapy following completion of a study that investigated the effect of once weekly dulaglutide 1.5 mg or 0.75 mg added to SGLT2is, with or without concomitant use of metformin, on glycemic control and safety over a 24-weeks in patients with inadequately controlled T2DM (Study H9X-MC-GBGE (GBGE)).
The Package Leaflet is updated accordingly."

Velcade - bortezomib - EMEA/H/C/000539/II/0088
MAH: Janssen-Cilag International NV, Rapporteur: Daniela Melchiorri, "Update of sections 4.2 and 5.1 of the SmPC in order to add a new dosing schedule for VELCADE (bortezomib) in combination with melphalan and prednisone (VMP) for the treatment of patients with newly diagnosed multiple myeloma who

are not eligible for high-dose chemotherapy with hematopoetic stem cell transplant. The proposed new dosing schedule is supported by analyses comparing the current approved VcMP schedule (from 26866138MMY3002 [VISTA] study) with pooled modified less intensive ("once-weekly") VcMP schedules (from 54767414MMY3007 [ALCYONE], GIMENA MM-03-05 [GIMENA]). Additional supportive efficacy and safety data come from GEM2005MAS65 [PETHEMA]. The PL (section 3) is amended accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the PL.”	
Vibativ - telavancin - EMEA/H/C/001240/II/0033 MAH: Theravance Biopharma Ireland Ltd, Rapporteur: Greg Markey, “C.I.13. Submission of the final report ‘Telavancin Global Surveillance Report for 2016’ to monitor the activity of telavancin and the microbiological resistance as compared to other agents, through the longitudinal resistance surveillance program, in fulfilment of the condition ANX-002.3.”	
Vimpat - lacosamide - EMEA/H/C/000863/II/0070/G MAH: UCB Pharma S.A., Rapporteur: Filip Josephson, “C.I.4 - Update of sections 4.8, 5.1, and 5.2 of the SmPC in order to update clinical efficacy and safety data in the paediatric population with the results from study SP0969: a phase 3, multicentre, double-blind, randomized, placebo-controlled, parallel-group study to evaluate the efficacy and safety of lacosamide as adjunctive therapy in subjects with epilepsy ≥4 years to <17 years of age with uncontrolled partial-onset seizures; 3 new ADRs (nasopharyngitis, pharyngitis, and pyrexia) have been added based on the results of the above mentioned study; C.I.4 - Update of section 5.2 of the SmPC in order to update the pharmacokinetic data in the paediatric population based on results from the CL0430 population pharmacokinetic (PK) analyses; C.I.4 - Update of section 4.8 of the SmPC in	

order to update the incidence of decreased appetite, lethargy, and abnormal behaviour in the paediatric population based on results from the updated safety data for Pool SPX-1 with clinical cut-off date of 01 November 2016. The Package Leaflet and Labelling are updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some editorial changes in the PI. The MAH also took the opportunity to revise Annex A as requested."

Wakix - pitolisant - EMEA/H/C/002616/II/0011, Orphan
MAH: BIOPROJET PHARMA, Rapporteur: Joseph Emmerich, "Update of section 5.2 of the SmPC in order to include investigations outcomes regarding the new identified metabolites, as requested in variation EMEA/H/C/002616/II/0004/G."

Xofigo - radium-223 - EMEA/H/C/002653/II/0029
MAH: Bayer AG, Rapporteur: Harald Enzmann, "Submission of Clinical Study Report for study 16506. This is an interventional re-treatment safety study of radium-223 dichloride in subjects with castration-resistant prostate cancer with bone metastases who received an initial course of six doses of radium-223 dichloride 50 kBq/kg every four weeks."

Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/II/0064
MAH: Bial - Portela & Cª, S.A., Rapporteur: Martina Weise, "Update of section 4.8 of the SmPC to add urticaria, angioedema and Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TEN) as adverse drug reactions with unknown frequency, based on recent safety signal evaluation information. The Package Leaflet is updated accordingly. In addition, revision of section 4.4 of the SmPC to align the information on the adverse event angioedema with the information already present in the Package Leaflet."

WS1289
Komboglyze- EMEA/H/C/002059/WS1289/0039
Onglyza- EMEA/H/C/001039/WS1289/0045

MAH: AstraZeneca AB, Lead Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to reflect the new saxagliptin renal cut-off value based on post hoc analysis of pooled data from 9 saxagliptin clinical trials.
In addition, the Worksharing applicant proposed to combine SmPCs of different strengths, for both Onglyza and Komboglyze.
Furthermore, the Worksharing applicant took the opportunity to include required information on two excipients, sodium and lactose, in sections 2 and 4.4 of the SmPC for Onglyza. The Package Leaflet is updated accordingly."

WS1295
Advagraf-
EMEA/H/C/000712/WS1295/0048
Modigraf-
EMEA/H/C/000954/WS1295/0026
MAH: Astellas Pharma Europe B.V., Lead Rapporteur: Jayne Crowe, "Update of section 4.8 of the SmPC in order to add pain in extremity reported as part of calcineurin-inhibitor induced pain syndrome (CIPS). In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor updates in sections 4.4 and 5.1 of the SmPC."

WS1298
Enurev Breezhaler-
EMEA/H/C/002691/WS1298/0024
Seebri Breezhaler-
EMEA/H/C/002430/WS1298/0024
Tovanor Breezhaler-
EMEA/H/C/002690/WS1298/0027
MAH: Novartis Europharm Limited, Lead Rapporteur: Hanne Lomholt Larsen, "Submission of the final study report of the Post-Authorisation Efficacy Study (PAES) to compare the efficacy, safety and tolerability of glycopyrronium given at a dose of 44 µg QD and 22 µg BID in patients with stable COPD and moderate to severe airflow obstruction."

WS1300/G
Prezista-
EMEA/H/C/000707/WS1300/0091/G
Rezolsta-
EMEA/H/C/002819/WS1300/0022/G
Symtuza-
EMEA/H/C/004391/WS1300/0004/G

MAH: Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege, "Update of section 4.5 of the Prezista, Rezolsta and Symtuza SmPC to reflect the drug-drug interaction results of the pharmacology studies GS-US-216-1008 (DDI between DRV+COBI and HMG CoA reductase inhibitors rosuvastatin and/or atorvastatin) and GS-US-216-4032 (DDI between DRV+COBI and the hormonal contraceptive medication drospirenone/ethinyl estradiol).
Update of section 4.9 of the Prezista, Rezolsta and Symtuza SmPC to remove the recommendations regarding emesis and administration of activated charcoal in case of overdose.

In addition, the Worksharing applicant (WSA) took the opportunity to harmonize between Prezista, Rezolsta and Symtuza the DDI information with emtricibine/tenofovir alafenamide, clonazepam, isavuconazole, lomitapide, fentanyl, oxycodone, tramadol and lorazepam.

The MAH also took the opportunity to align the in-use shelf-life in label and PL with the SmPC.

The PL is updated accordingly and the local representatives details are updated."

WS1307
Ofev-EMEA/H/C/003821/WS1307/0019
Vargatef-EMEA/H/C/002569/WS1307/0019

MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Sinan B. Sarac, "Update of section 4.4 of the SmPC for Ofev and Vargatef to amend the current warning on drug induced liver injury based one case of sever liver injury with fatal outcome reported for Ofev during the post-marketing phase. In addition section 4.4 of the Ofev SmPC is updated to include when the majority of the hepatic events occurred and on the need for hepatic transaminases and bilirubin levels to be measured at regular intervals during the first 3 months of treatment. Section 4.8 of the Vargatef SmPC is also updated to include in the summary of the safety profile that the safety data is also based on post-marketing data. The Package Leaflet is updated accordingly. The MAH is proposing to distribute a DHPC for Ofev.

In addition, the Worksharing applicant (WSA) took the opportunity to make some corrections to the Bulagrian, Estonian, Icelandic, Latvian and Maltese translations for Ofev and Bulgarian, Estonian, Latvian and Maltese translations for Vargatef." Request for Supplementary Information adopted on 25.01.2018.	
WS1316 **Glyxambi-** **EMEA/H/C/003833/WS1316/0011** **Jardiance-** **EMEA/H/C/002677/WS1316/0037** **Synjardy-** **EMEA/H/C/003770/WS1316/0032** MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC for Jardiance, Synjardy and Glyxambi in order to add clinically relevant information on hear failure and microvascular endpoints based on the results from trial 1245.25 (EMPA-REG OUTCOME study). The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to update section 4.4 of the SmPC to align the statement regarding diabetic ketoacidosis for all SGLT-2 Inhibitors."	
WS1322 **Genvoya-** **EMEA/H/C/004042/WS1322/0042** **Stribild-EMEA/H/C/002574/WS1322/0090** **Tybost-EMEA/H/C/002572/WS1322/0042** MAH: Gilead Sciences International Limited, Lead Rapporteur: Robert James Hemmings, "Update of Section 4.5 of the SmPC for Genvoya, Tybost and Stribild based on data on Drug-drug Interaction between cobicistat containing products and Direct Oral Anticoagulants (DOACs). The Patient Leaflet (PIL) has been updated for all three products as a consequence. The Worksharing MAH has taken this opportunity to introduce some minor administrative amendments throughout the product information for all three products respectively, as needed (i.e., correction of abbreviations, correction of formatting errors	

and correction of spelling mistakes). Minor administrative update is also made to Annex III for all three products.

The MAH has also taken this opportunity to implement some minor linguistic amendments (MLAs) to the translations of the respective product information annexes:

- Genvoya: CS, DA, DE, FI, HR, HU, IS, NO, PT and RO languages
- Tybost: DA, ES and HU languages
- Stribild: DA, DE, ES, FI, FR, IS, LV, MT, NO and RO languages"

WS1330
Bretaris Genuair-
EMEA/H/C/002706/WS1330/0036
Brimica Genuair-
EMEA/H/C/003969/WS1330/0019
Duaklir Genuair-
EMEA/H/C/003745/WS1330/0019
Eklira Genuair-
EMEA/H/C/002211/WS1330/0036
MAH: AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, "Update of sections 4.2 and 6.6 of the SmPC in order to optimize the Instructions for Use (IFU) for the products evaluated in a human factors study. The Package Leaflet is updated accordingly. In addition, the applicant has taken the opportunity to make some minor editorial corrections in the labelling section (Annex III A) of the Product Information for Duaklir Genuair and Brimica Genuair."

WS1332
Renvela-
EMEA/H/C/000993/WS1332/0041
Sevelamer carbonate Zentiva-
EMEA/H/C/003971/WS1332/0013
MAH: Genzyme Europe BV, Lead Rapporteur: Bart Van der Schueren, "Update of sections 4.2 and 6.6 of the SmPC in order to include the use of food and beverage as an alternative to water for administration of sevelamer carbonate powder for oral suspension.
The Package Leaflet is updated accordingly.
In addition, the Worksharing applicant (WSA) took the opportunity to revise the Annex A."

B.6.10. CHMP-PRAC assessed procedures

Alecensa - alectinib - EMEA/H/C/004164/II/0010

MAH: Roche Registration Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, "Update of sections 4.2 and 5.2 of the SmPC in order to update information on effect of hepatic impairment on PK of alectinib based on final results from study NP29783. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest EC guidance regarding warning statements on sodium."

Gilenya - fingolimod - EMEA/H/C/002202/II/0047

MAH: Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Submission of the CSR for Study D2399, a long-term safety and tolerability study of fingolimod 0.5 mg/day in approximately 5000 patients with relapsing multiple sclerosis."

Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/II/0064

MAH: Gilead Sciences International Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of section 4.2, 4.4,4.8, 5.1 and 5.2 of the SmPC in order to update the safety and efficacy information based on interim results from study GS-US-334-0154 listed as a category 3 study in the RMP; this is a study to evaluate the safety, efficacy and pharmacokinetics of treatment with Ledipasvir/Sofosbuvir Fixed-Dose Combination for 12 weeks in Genotype 1 or 4 HCV-Infected Subjects with Renal Insufficiency; the Package Leaflet is updated accordingly. The RMP version 3.2 has also been submitted."

Herceptin - trastuzumab - EMEA/H/C/000278/II/0140

MAH: Roche Registration Limited, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.4 and 4.8 of the SmPC for Herceptin 150mg powder for concentrate for solution for infusion and sections 4.4, 4.8 and 5.1 of the SmPC for Herceptin 600mg solution for injection in vial, in

order to update the safety information based on the final results from study BO22227 (Hannah) listed as a category 3 study in the RMP; this is a phase III, randomised, open-label study to compare pharmacokinetics, efficacy and safety of subcutaneous (SC) Herceptin with intravenous (IV) Herceptin administered in women with HER2 positive early breast cancer (EBC). The RMP version 19.0 has also been submitted."	
Opdivo - nivolumab - EMEA/H/C/003985/II/0047 MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning on the nivolumab use in patients who have previously undergone allogeneic HSCT and the increased risk of rapid onset and severe Graft versus Host Disease (GVHD) based on evidence from spontaneous case reports, literature case reports, and from 2 multicenter case series. Annex II.D and the Package Leaflet are updated accordingly. The RMP version 7.8 has also been submitted to include the "risk of GVHD with nivolumab after allogeneic HSCT" as an "Important Potential Risk" based on the RMP template (Revision 2). In addition, the Marketing authorisation holder (MAH) took the opportunity to make some minor editorial corrections to the PI."	
Rydapt - midostaurin - EMEA/H/C/004095/II/0002, Orphan MAH: Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of sections 4.5 and 5.2 of the SmPC in order to reflect the results from study R1600721 "Assessment of PKC412 and its metabolites (CGP052421 and CGP062221) as inhibitors of human bile salt export pump (BSEP) " and study R1701192 'In vitro assessment of cytochrome P450 3A4 and 3A5 enzyme inhibition by PKC412, CGP52421 and CGP62221', in fulfilment of the post-authorisation measures MEA 011 and REC 014. In addition, the MAH took the opportunity to update section 5.2 to correct figures as per Study A2107-Amendment 02 already assessed and to make editorial changes in the SmPC.	

The RMP (v 2.0) has also been updated to reflect the study results. In addition, the search criteria for the important identified risk pulmonary toxicity (including pleural effusion and interstitial lung disease) was updated to include the PT-pleural effusion."	
Truberzi - eluxadoline - EMEA/H/C/004098/II/0005/G MAH: Allergan Pharmaceuticals International Ltd, Rapporteur: Harald Enzmann, PRAC Rapporteur: Adam Przybylkowski, "C.I.13: Submission of the final report from study ELX-PH-08 listed as a category 3 study. This is an in vitro evaluation study aimed to investigate the effects on treating primary cultures of cryopreserved human hepatocytes with eluxadoline on the expression of cytochrome P450 (CYP) enzymes C.I.13: Submission of the final report from study 3030-102-002 listed as a category 3 study. This is a randomised, open label study aimed to evaluate the effect of eluxadoline as a potential time dependent inhibitor of CYP3A4 with the substrate midazolam. C.I.11.a: To update the RMP for Truberzi to version v2.0 to update the important identified risk from "SO spasm" to "SO spasm (Sphincter of Oddi dysfunction, SOD)" and to include pancreatitis as an important identified risks. This change has been agreed by the CHMP/PRAC in the outcome of EMEA/H/C/PSUSA/00010528/201703."	
Xgeva - denosumab - EMEA/H/C/002173/II/0059 MAH: Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information and to revise the special warnings, precautions for use and undesirable effects based on cases of clinically significant hypercalcemia following discontinuation of denosumab in patients with growing skeletons (ie, adolescent subject with GCTB in Study 20062004) and in postmarketing reports of pediatric patients treated with denosumab for GCTB or for unapproved indications was previously determined to be an important identified risk; the Package Leaflet are updated accordingly. Consequently the RMP	

version 30 has also been submitted."

WS1312
Prezista-
EMEA/H/C/000707/WS1312/0093
Rezolsta-
EMEA/H/C/002819/WS1312/0023
Symtuza-
EMEA/H/C/004391/WS1312/0005
MAH: Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.4, 4.6, 5.1 and 5.2 of the SmPCs for Prezista, Rezolsta and Symtuva to reflect the data of the category 3 study TMC114HIV3015 in HIV-1 infected pregnant women. The PL of Symtuza is also updated . Updated RMPs (version 25.3 for Prezista, 4.3 for Rezolsta and 2.1 for Symtuza) are proposed accordingly.
In addition, the MAH took the opportunity to implement the template version 2 for the Prezista and Rezolsta RMPs, removal of the fulfilled category 4 DAD study from the Prezista and Rezolsta RMPs, removal of observational study on growth in children and 'growth abnormalities in the paediatric population' as important potential risk in the Prezista RMP and addition of the missing information 'Safety in patients with cardiac conduction disorders' in the Rezolsta RMP (alignement with Tybost RMP)."

WS1333
Blitzima-
EMEA/H/C/004723/WS1333/0007
Ritemvia-
EMEA/H/C/004725/WS1333/0007
Rituzena-
EMEA/H/C/004724/WS1333/0008
Truxima-
EMEA/H/C/004112/WS1333/0008
MAH: Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz, Lead PRAC Rapporteur: Doris Stenver, "Submission of the clinical study report (CSR) of final results (up to 76 weeks) of Study CT-P10 3.2. In addition, results up to Week 24 of Study CT-P10 3.3 (corresponding CSR submitted in D180 update [SN0004] are updated in this variation."

B.6.11. PRAC assessed procedures

PRAC Led

Ecalta - anidulafungin -
EMEA/H/C/000788/II/0036

MAH: Pfizer Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "C.I.11: Submission of an updated RMP (version 12.1) in order to include new safety information, an update of incidence and prevalence of hepatotoxicity categorised as important identified risk and re-categorisation of convulsions from important potential risk to important identified risk based on ongoing study A8851008, PASS A8851030 study, the Global Antifungal Surveillance Program and the MAH's review and analysis of cumulative exposure data up to the DLP of 31 August 2017."

PRAC Led

Humira - adalimumab -
EMEA/H/C/000481/II/0173

MAH: AbbVie Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from study BSRBR-RA (British Society for Rheumatology Biologics Registers Rheumatoid Arthritis). This is a registry in the UK, evaluating the influence of TNF inhibitor treatment on cancer incidence in RA patients with a history of malignancy. No changes to the PI are proposed."

PRAC Led

Imbruvica - ibrutinib -
EMEA/H/C/003791/II/0040/G, Orphan

MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "C.I.11 (type II): Submission of an updated RMP version 9.1 in order to :
- Include a feasibility assessment of experiments and/or studies to further understand the effect of ibrutinib on various components and functions of the adaptive and humoral immune system;
- Include the completed non-clinical in vitro rabbit ventricular and atrial wedge study (under review in Procedure EMEA/H/C/003791/IB/0039) in the table of completed studies in the RMP annex;

- Include a targeted follow-up questionnaire for cardiac arrhythmias as part of routine pharmacovigilance activities;
- Update the text for clarification purposes, to modify the important potential risk of "Infections (excluding PML)" to "Infections (including viral reactivation)". PML is already listed as a separate important potential risk.

C.I.11.z (type IB): To replace the 3 PAMs for Studies PCYC-1103-CA, PCI32765CAN3001 and PCYC-1116-CA related to long-term safety (> 2 years) of ibrutinib, with a single long-term safety PAM (Study 3038-1)."

PRAC Led

Otezla - apremilast - EMEA/H/C/003746/II/0018

MAH: Celgene Europe Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Concepcion Prieto Yerro, "Submission of an updated RMP version 10.0 in order to introduce changes on the pharmacovigilance activities related to the use of apremilast in pregnancy, to remove "use in patients of different racial origin" from the safety concerns."

PRAC Led

Saxenda - liraglutide - EMEA/H/C/003780/II/0016

MAH: Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report from study NN8022-4192, listed as a category 3 study in the RMP. This is a randomised, placebo-controlled trial on subjects with obesity or overweight who were otherwise healthy, to compare the effect of liraglutide 3.0 mg with placebo on postprandial gallbladder dynamics after 12 weeks of treatment.

This variation fulfils post-authorisation measure MEA 009.2 for Saxenda.

RMP version 29 was submitted, updated to reflect the completion of this additional pharmacovigilance activity."

PRAC Led

Thymanax - agomelatine - EMEA/H/C/000916/II/0037

MAH: Servier (Ireland) Industries Ltd.,

Duplicate, Duplicate of Valdoxan, Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Kristin Thorseng Kvande, PRAC-CHMP liaison: Svein Rune Andersen, "Submission of the final report from the Post-Authorisation Safety Study (PASS) of Agromelatine and the Risk of Hospitalisation for Acute Liver Injury CLE-20098-094. This is a large, multinational, retrospective longitudinal cohort and nested case-control study to compares the risk of Acute Liver Injury (ACI) in patients initiating treatment with agomelatine and other antidepressants with the risk in patients initiating treatment with citalopram."

PRAC Led

Valdoxan - agomelatine - EMEA/H/C/000915/II/0038

MAH: Les Laboratoires Servier, Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Kristin Thorseng Kvande, PRAC-CHMP liaison: Svein Rune Andersen, "Submission of the final report from the Post-Authorisation Safety Study (PASS) of Agromelatine and the Risk of Hospitalisation for Acute Liver Injury CLE-20098-094. This is a large, multinational, retrospective longitudinal cohort and nested case-control study to compares the risk of Acute Liver Injury (ALI) in patients initiating treatment with agomelatine and other antidepressants with the risk in patients initiating treatment with citalopram."

PRAC Led

Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0036

MAH: Pfizer Ireland Pharmaceuticals, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "Update of the RMP (verson 16) to implement changes from variations II/22 and II/29, as requested by PRAC following the PSUSA assessment."

PRAC Led

WS1326

Truvada-EMEA/H/C/000594/WS1326/0145

Viread-EMEA/H/C/000419/WS1326/0184

MAH: Gilead Sciences International Limited, Lead Rapporteur: Joseph Emmerich, Lead PRAC Rapporteur: Caroline Laborde, PRAC-CHMP

liaison: Joseph Emmerich, "Submission of the final report from study GS-EU-104-0433, listed as a category 3 study in the RMP. This is an observational, drug utilisation study of Viread in children and adolescents with HIV-1 infection, in fulfilment of a post-authorisation measure (PAM) for Viread (MEA 46) and Truvada (MEA 276)."

B.6.12. CHMP-CAT assessed procedures

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

WS1284 **Kalydeco-** **EMEA/H/C/002494/WS1284/0068** **Orkambi-** **EMEA/H/C/003954/WS1284/0029** MAH: Vertex Pharmaceuticals (Europe) Ltd., Lead Rapporteur: Concepcion Prieto Yerro
WS1291/G **Copalia-** **EMEA/H/C/000774/WS1291/0095/G** **Copalia HCT-** **EMEA/H/C/001159/WS1291/0064/G** **Dafiro-** **EMEA/H/C/000776/WS1291/0097/G** **Dafiro HCT-** **EMEA/H/C/001160/WS1291/0065/G** **Exforge-** **EMEA/H/C/000716/WS1291/0094/G** **Exforge HCT-** **EMEA/H/C/001068/WS1291/0063/G** MAH: Novartis Europharm Limited, Lead Rapporteur: Hanne Lomholt Larsen
WS1334/G **Combivir-** **EMEA/H/C/000190/WS1334/0091/G** **Epivir-** **EMEA/H/C/000107/WS1334/0105/G** **Kivexa-** **EMEA/H/C/000581/WS1334/0074/G** **Trizivir-** **EMEA/H/C/000338/WS1334/0106/G**

MAH: ViiV Healthcare UK Limited, Lead Rapporteur: Joseph Emmerich

WS1336/G
Entresto-
EMEA/H/C/004062/WS1336/0017/G
Neparvis-
EMEA/H/C/004343/WS1336/0015/G
MAH: Novartis Europharm Limited, Lead Rapporteur: Johann Lodewijk Hillege

Hexacima-
EMEA/H/C/002702/WS1304/0076
Hexaxim-
EMEA/H/W/002495/WS1304/0081
Hexyon-
EMEA/H/C/002796/WS1304/0080
MAH: Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

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 22-25 January 2018 CHMP plenary:

Oncology	
1. ATMP;Treatment of patients with newly diagnosed advanced ovarian cancer	The CHMP denied eligibility to PRIME and adopted the critical summary report.
2. ATMP;Treatment of patients with first recurrence of advanced ovarian cancer	The CHMP denied eligibility to PRIME and adopted the critical summary report.
3. Treatment of glioblastoma multiforme	The CHMP denied eligibility to PRIME and adopted the critical summary report.
4. Treatment of patients with relapsed or refractory	The CHMP denied eligibility to PRIME and

diffuse Large B-Cell *Lymphoma* (DLBCL) who are not eligible for high-dose chemotherapy and autologous stem-cell transplantation	adopted the critical summary report.
Gastroenterology-Hepatology	
5. Treatment of idiopathic gastroparesis	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Immunology-Rheumatology-Transplantation	
6. Treatment of lupus nephritis	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Neonatology-Paediatric Intensive Care	
7. Prevention of chronic lung disease in extremely premature infants (<28 weeks gestational age)	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Ophthalmology	
8. Treatment of Retinal Dystrophy associated with defects in RPE65 (LCA2)	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Other	
9. Treatment of Proteus Syndrome	The CHMP denied eligibility to PRIME and adopted the critical summary report.

G.3.2. List of procedures starting in January 2018 for February 2018 CHMP adoption of outcomes

Timetable for assessment:

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