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SCIENCE MEDICINES HEALTH

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Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Minutes of the meeting on 11-14 December 2017

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

Health and safety information

In accordance with the Agency's health and safety policy, delegates are to be briefed on health, safety and emergency information and procedures prior to the start of the meeting.

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

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



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1. Introduction

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

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified as included in the list of participants and restrictions. See (current) December 2017 CHMP minutes for the list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session held 11-14 December 2017 (to be published post January 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.

The CHMP noted the new alternate member Maria Orfanou from Greece replacing Maria Dimokleia Ziotopoulou and noted the new alternate member Elena Kaisi from Cyprus replacing Panayiotis Triantafyllis.

1.2. Adoption of agenda

CHMP agenda for 11-14 December 2017

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 6-9 November 2017

The CHMP adopted the CHMP minutes for 6-9 November 2017. The Minutes of the December 2017 CHMP ORGAM meeting held on 4 December 2017, together with all decisions taken at that meeting, were adopted.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

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

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

Scope: Oral explanation

Action: Oral explanation to be held on 12 December 2017 at time 11:00

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

Oral explanation was held on 07.11.2017. List of Outstanding Issues adopted on 14.09.2017. List of Questions adopted on 23.02.2017.

An oral explanation was held on 12 December 2017 at time 11:45.

See 3.1

2.1.2. enclomifene - EMEA/H/C/004198

treatment of hypogonadotropic hypogonadism

Scope: Oral explanation

Action: Oral explanation to be held on 13 December 2017 at time 09:00

List of Outstanding Issues adopted on 12.10.2017. List of Questions adopted on 26.01.2017.

An oral explanation was held on 13 December 2017 at time 09:00.

2.1.3. 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: Oral explanation

Action: Oral explanation to be held on 12 December 2017 at time 14:00

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

The CHMP agreed that an oral explanation is not needed at this time.

See 3.2.

2.1.4. human herpesvirus 3 - EMEA/H/C/004336

prevention of herpes zoster (HZ) and HZ-related complications

Scope: Oral explanation

Action: Oral explanation to be held on 12 December 2017 at time 16:00

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

The CHMP agreed that oral explanation is not needed this time. The Committee discussed the wording of the indication.

See 3.2

2.1.5. abaloparatide - EMEA/H/C/004157

treatment of osteoporosis

Scope: Oral explanation

Action: Oral explanation to be held on 13 December 2017 at time 11:30

List of Outstanding Issues adopted on 20.07.2017, 15.12.2016. List of Questions adopted on 01.04.2016.

An oral explanation was held on 13 December 2017 at time 11:30.

See 3.2

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

2.3.1. Opdivo - nivolumab - EMEA/H/C/003985/II/0030

Bristol-Myers Squibb Pharma EEIG

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

Scope: Oral explanation/Opinion

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

Request for Supplementary Information adopted on 22.06.2017, 23.03.2017.

An oral explanation was held on 11 December 2017 at time 16:00. The oral explanation focussed on validity of study populations and survival benefit.

The CHMP noted that the applicant withdrew the application.

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Alkindi - hydrocortisone - PUMA - EMEA/H/C/004416

Diurnal Ltd; treatment of adrenal insufficiency

Scope: Opinion

Action: For adoption

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

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

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

The Committee adopted a positive opinion recommending the granting of a paediatric use 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 18 December 2017.

3.1.2. Alofisel - darvadstrocel - Orphan - ATMP - EMEA/H/C/004258

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

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 13.11.2017 via written procedure. List of Outstanding Issues adopted on 17.02.2017. List of Questions adopted on 15.07.2016.

The CHMP noted the discussion and draft opinion taken by the CAT at their December meeting.

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

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (22 out of 27 votes) together with the CHMP assessment report and translation timetable.

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

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation. The divergent position (Alar Irs, Alexandre Moreau, Johann Lodewijk Hillege, Greg Markey, Robert James Hemmings) was appended to the opinion. The legal status was agreed as medicinal product subject to restricted medical prescription. The summary of opinion was circulated for information.

3.1.3. [Anagrelide Mylan - anagrelide - EMEA/H/C/004585](#)

Mylan S.A.S; reduction of elevated platelet counts in at risk essential thrombocythaemia patients

Scope: Opinion

Action: For adoption

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

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

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

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

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation. The legal status was agreed as medicinal product subject to restricted medical prescription. The summary of opinion was circulated for information.

3.1.4. [Aplidin - plitidepsin - Orphan - EMEA/H/C/004354](#)

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

Scope: Opinion/Oral explanation

Action: For adoption

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

Oral explanation was held on 07.11.2017. List of Outstanding Issues adopted on 14.09.2017. List of Questions adopted on 23.02.2017.

See 2.1

An oral explanation was held on 12 December 2017 at time 11:45.

The CHMP noted the answers from BSWP.

The CHMP was concerned that the data from the main study showed only a modest increase of around one month in the time patients given Aplidin lived without their disease getting worse, compared with those treated with dexamethasone alone. In addition, improvement in overall survival was not sufficiently demonstrated. Regarding safety, severe side effects were reported more frequently with the combination of Aplidin and dexamethasone than

with dexamethasone alone.

Based on the above, the CHMP was of the opinion that the benefits of Aplidin did not outweigh its risks and recommended that it be refused marketing authorisation.

The CHMP adopted a negative opinion by majority (21 out of 25 votes), recommending the refusal of the marketing authorisation application. The CHMP adopted the assessment report.

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

The divergent opinion (Bart van der Schueren, Concepcion Prieto Yerro, Koenraad Norga, Sol Ruiz, Svein Rune Andersen) was appended to the opinion.

The summary of opinion was circulated for information.

The refusal question and answers document was circulated for information.

Post-meeting note: the applicant submitted the request for re-examination on 03.01.2018 and has requested a SAG oncology to take place as part of this re-examination procedure.

3.1.5. [Crysvita - burosumab - Orphan - EMEA/H/C/004275](#)

Kyowa Kirin Limited; treatment of X-linked hypophosphataemia (XLH)

Scope: Opinion

Action: For adoption

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

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

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

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

Furthermore, the CHMP considered that burosumab 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 CHMP noted the letter of recommendation dated 14 December 2017.

The summary of opinion was circulated for information.

3.1.6. [Efavirenz/Emtricitabine/Tenofovir disoproxil Krka - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/004274](#)

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

Scope: Opinion

Action: For adoption

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

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 recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

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

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

The CHMP noted the letter of recommendation dated 13 December 2017.

The summary of opinion was circulated for information.

3.1.7. Herzuma - trastuzumab - EMEA/H/C/002575

Celltrion Healthcare Hungary Kft.; treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 09.11.2017. 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 restricted medical prescription.

The summary of opinion was circulated for information.

3.1.8. Ozempic - semaglutide - EMEA/H/C/004174

Novo Nordisk A/S; to improve glycaemic control in adults with type 2 diabetes and to prevent cardiovascular events

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, 14.09.2017. List of Questions adopted on 21.04.2017.

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

addressed.

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

Furthermore, the CHMP considered that semaglutide 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. glibenclamide - Orphan - EMEA/H/C/004379

Ammtek; treatment of neonatal diabetes

Scope: 2nd day 180 list of outstanding issue.

Action: For adoption

List of Outstanding Issues adopted on 22.06.2017. List of Questions adopted on 24.01.2017.

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. betrixaban - EMEA/H/C/004309

treatment of prophylaxis of venous thromboembolism (VTE)

Scope: 2nd day 180 list of outstanding issue. List of expert to SAG CVS adopted by written procedure on 5 December 2017. Report from SAG CVS.

Action: For adoption

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

The CHMP noted the report from SAG CVS.

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.

Post meeting note: a revised 2nd list of outstanding issues was adopted after the Plenary on 22.12.2017 via written procedure.

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

AVI Biopharma International Ltd; treatment of Duchenne muscular dystrophy

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.04.2017.

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.

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

3.2.4. emicizumab - EMEA/H/C/004406

Accelerated assessment

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: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 10.10.2017.

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.

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

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

Scope: Oral explanation, Day 180 list of outstanding issue

Action: Oral explanation to be held on 12 December 2017 at time 14:00

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

The CHMP agreed that an oral explanation is not needed this time.

The CHMP noted the answers from the ad hoc expert group meeting. The experts were of the view that the treatment is considered efficacious in (part of) patients with alpha-mannosidosis. The treatment was not considered effective in neurological manifestations and currently young patients with severe manifestations should be excluded from treatment. The expert group highlighted the importance of establishing a disease registry to collect further data in this rare disease setting.

The Committee adopted a 2nd Day 180 list of outstanding issues with a specific timetable.

3.2.6. [metreleptin - Orphan - EMEA/H/C/004218](#)

Aegerion Pharmaceuticals Limited; treatment of leptin deficiency (lipodystrophy)

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 18.05.2017.

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

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

3.2.7. [gemtuzumab ozogamicin - Orphan - EMEA/H/C/004204](#)

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

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 21.04.2017.

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.

3.2.8. [prasugrel - EMEA/H/C/004644](#)

prevention of atherothrombotic events

Scope: Day 180 list of outstanding issue

Action: For adoption

List of Questions adopted on 14.09.2017.

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.

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

Clovis Oncology UK Ltd; treatment of ovarian cancer

Scope: Day 180 list of outstanding issue

Action: For adoption

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

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

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

The CHMP agreed to consult a SAG.

3.2.10. human herpesvirus 3 - EMEA/H/C/004336

prevention of herpes zoster (HZ) and HZ-related complications

Scope: Oral explanation

Action: Oral explanation to be held on 12 December 2017 at time 16:00

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

The CHMP agreed that oral explanation is not needed this time. The Committee discussed the wording of the indication.

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

3.2.11. abaloparatide - EMEA/H/C/004157

treatment of osteoporosis

Scope: Oral explanation

Action: Oral explanation to be held on 13 December 2017 at time 11:30

List of Outstanding Issues adopted on 20.07.2017, 15.12.2016. List of Questions adopted on 01.04.2016.

An oral explanation was held on 13 December 2017 at time 11:30.

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

The CHMP agreed to consult an ad-hoc expert group.

3.2.12. pegfilgrastim - EMEA/H/C/004413

treatment of neutropenia

Scope: Day 180 list of outstanding issue, request for extension of clock stop to respond to List of outstanding issue to be adopted in December 2017

Action: For adoption

List of Questions adopted on 23.03.2017.

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

The Committee adopted a list of outstanding issues.

The Committee agreed to the extension of clock stop to respond to List of outstanding issue.

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

3.3.1. binimetinib - EMEA/H/C/004579

in combination with encorafenib is indicated for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation

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. encorafenib - EMEA/H/C/004580

in combination with binimetinib is indicated for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation

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. gefitinib - EMEA/H/C/004826

treatment of non-small cell lung cancer

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. vigabatrin - PUMA - EMEA/H/C/004534

Treatment in monotherapy of infantile spasms (West's syndrome) and resistant partial epilepsy in infants and children

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.5. lenalidomide - EMEA/H/C/004857

treatment of multiple myeloma

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.6. voretigene neparvovec - Orphan - ATMP - EMEA/H/C/004451

Spark Therapeutics Ireland Ltd; treatment of patients with vision loss due to Leber congenital amaurosis or retinitis pigmentosa inherited retinal dystrophy

Scope: Day 120 list of questions

Action: For information

The Committee discussed the issues identified in this application. The CHMP was updated on discussions at the CAT during their December 2017 meeting.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions as agreed by CAT.

3.3.7. mexiletine hydrochloride - Orphan - EMEA/H/C/004584

Lupin (Europe) Limited; Treatment of myotonic disorders

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.8. paclitaxel - EMEA/H/C/004441

treatment of metastatic breast cancer

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.9. tezacaftor / ivacaftor - Orphan - EMEA/H/C/004682

Vertex Pharmaceuticals (Europe) Ltd.; treatment of cystic fibrosis

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

The CHMP adopted the similarity assessment report.

3.3.10. abemaciclib - EMEA/H/C/004302

treatment of hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer

Scope: Day 120 list of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.11. 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: 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.

3.3.12. eravacycline - EMEA/H/C/004237

treatment of complicated intra-abdominal infections (cIAI) in adults

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.

3.3.13. axicabtagene ciloleucel - Orphan - ATMP - EMEA/H/C/004480

Accelerated assessment

Kite Pharma EU B.V.; treatment of diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL) and transformed follicular lymphoma (TFL)

Scope: Day 120 list of questions

Action: For information

The Committee discussed the issues identified in this application. The CHMP was updated on discussions at the CAT during their December 2017 meeting.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions as agreed by CAT. The CHMP agreed to revert back to a standard timetable for the assessment.

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

3.4.1. ropeginterferon alfa-2b - Orphan - EMEA/H/C/004128

AOP Orphan Pharmaceuticals AG; treatment of polycythemia vera

Scope: Request for an extension to the clock stop to respond to the list of questions adopted on 22.06.2017.

Action: For adoption

List of Questions adopted on 22.06.2017.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted on 22.06.2017.

3.4.2. carmustine - EMEA/H/C/004326

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

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

Action: For adoption

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

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

3.4.3. [adalimumab - EMEA/H/C/004429](#)

treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis

Scope: Request for extension of clock stop to respond to Day 120 list of questions adopted on 14.09.2017

Action: For adoption

List of Questions adopted on 14.09.2017.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to Day 120 list of questions adopted on 14.09.2017

3.4.4. [tildrakizumab - EMEA/H/C/004514](#)

treatment of adults with moderate-to-severe plaque psoriasis

Scope: Request for extension of clock stop to respond to List of Questions adopted on 27.07.2017

Action: For information

List of Questions adopted on 27.07.2017.

The CHMP agreed to the request by the applicant for an extension of clock stop by written procedure on 22.11.2017.

3.4.5. [pegfilgrastim - EMEA/H/C/003961](#)

treatment of neutropenia

Scope: Request by the applicant for an extension to the clock stop to respond to the list of questions adopted on 14.09.2017.

Action: For adoption

List of Questions adopted on 14.09.2017.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted on 14.09.2017.

3.4.6. [rotigotine - EMEA/H/C/004286](#)

treatment of idiopathic Restless Legs Syndrome and Parkinson's disease

Scope: Request by the applicant dated 30 November 2017 requesting an extension of clock

stop to respond to the List of Questions adopted on 21 April 2017.

Action: For adoption

The CHMP did not agree to the request by the applicant for an extension of clock stop to respond to the List of Questions adopted on 21 April 2017.

Post-meeting note: the applicant withdrew the application for initial marketing authorisation.

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

No items

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

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

No items

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

AstraZeneca AB

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Extension application to add a new strength of 250 µg in a PVC/PVDC/Alu blister of 28 tablets."

Action: For adoption

List of Questions adopted on 20.07.2017.

The Committee discussed the issues identified in this application. The issues related to pharmacokinetics and the wording of some SmPC sections.

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

4.2.2. [Daxas - roflumilast - EMEA/H/C/001179/X/0035](#)

AstraZeneca AB

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Extension application to add a new strength of 250 µg in a PVC/PVDC/Alu blister of 28 tablets."

Action: For adoption

List of Questions adopted on 20.07.2017.

The Committee discussed the issues identified in this application. The issues related to pharmacokinetics and the wording of some SmPC sections.

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

4.2.3. [Libertek - roflumilast - EMEA/H/C/002399/X/0032](#)

AstraZeneca AB

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Dolores Montero Corominas

Scope: "Extension application to add a new strength of 250 µg in a PVC/PVDC/Alu blister of 28 tablets."

Action: For adoption

List of Questions adopted on 20.07.2017.

The Committee discussed the issues identified in this application.

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

4.2.4. [Lynparza - olaparib - Orphan - EMEA/H/C/003726/X/0016/G](#)

AstraZeneca AB

Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Carmela Macchiarulo

Scope: "Extension application to add a new pharmaceutical form associated with a new strength (100mg and 150 mg film-coated tablets) including an extension of the indication to treat patients with platinum-sensitive relapsed ovarian tumours. The extension application is grouped with a type II variation to align the PI for the currently authorised capsule

licence with the safety updates proposed for the tablet formulation.”

Action: For adoption

List of Questions adopted on 14.09.2017.

The Committee discussed the issues identified in this application.

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

4.2.5. Nuwiq - simoctocog alfa - EMEA/H/C/002813/X/0020

Octapharma AB

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wandel 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 Questions adopted on 14.09.2017.

The Committee discussed the issues identified in this application, related to the quality part of the dossier.

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

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

4.3.1. Bosulif - bosutinib - Orphan - EMEA/H/C/002373/X/0026

Pfizer Limited

Rapporteur: Harald Enzmann

Scope: “Extension application to add a new strength of 400mg film-coated tablets.”

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.

4.3.2. [Inhixa - enoxaparin sodium - EMEA/H/C/004264/X/0018](#)

Techdow Europe AB

Rapporteur: Andrea Laslop, PRAC Rapporteur: Menno van der Elst

Scope: "Extension application to add two new strengths of 12,000 IU (120 mg)/0.8 mL and 15,000 IU (150 mg)/1 mL for enoxaparin sodium solution for injection in pre-filled syringe, for subcutaneous, extracorporeal and intravenous administration."

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.

4.3.3. [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'"

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.

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

No items

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

No items

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

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

5.1.1. Blincyto - blinatumomab - Orphan - EMEA/H/C/003731/II/0011

Amgen Europe B.V.

Rapporteur: Alexandre Moreau, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Eva Jirsová

Scope: "Extension of Indication to include the treatment of adults with minimal residual disease (MRD) positive B-cell precursor acute lymphoblastic leukaemia (ALL) for BLINCYTO; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, and to update the safety information. The Labelling is updated in accordance.

RMP version 4.0 is included in this submission". Report from SAG Oncology.

Action: For adoption

Request for Supplementary Information adopted on 22.06.2017.

The CHMP noted the report from the SAG Oncology. According to the experts, persistent MRD-positivity in adult patients after induction therapy and/or consolidation therapy in complete haematological remission (e.g. CR1) was considered an unmet medical need. However, MRD-negativity has not been validated as a surrogate endpoint for important clinical outcomes for blinatumumab or indeed any other agents. All these considerations make MRD a reasonably likely surrogate endpoint for clinical benefit but cannot be considered as a validated surrogate endpoint. In conclusion, MRD-negativity is a useful endpoint for benefit-risk decisions to accelerate regulatory approval in areas of high unmet need such as the indication applied for. However, confirmation should be provided prospectively in terms of important clinical endpoints.

The Committee discussed the issues identified in this application. The Committee noted that robust, high quality and long-term efficacy/safety data from randomized trials with validated, well-defined clinical endpoints and careful post-HSCT follow-up are needed to address the uncertainties in the broad indication. The available data was considered too limited to allow for a clear B/R assessment in the Ph+ MRD+ ALL population.

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

5.1.2. Cabometyx - cabozantinib - EMEA/H/C/004163/II/0003

Ipsen Pharma

Rapporteur: Robert James Hemmings, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur:

Sabine Straus

Scope: "Extension of indication to include for the treatment of advanced renal cell carcinoma the 'treatment-naïve adults with intermediate or poor risk per IMDC criteria' for CABOMETYX; as a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated in order to add a warning on dose reductions and dose interruptions and to update the safety information. The final report of the randomised phase II study comparing cabozantinib with commercially supplied sunitinib in subjects with previously untreated locally advanced or metastatic renal cell carcinoma (study A031203) is submitted in support of this application. The Package Leaflet is updated accordingly. The risk management plan (version 3.0) is also submitted.

In addition, the Marketing authorisation holder (MAH) took the opportunity to make some editorial changes in the product information."

Action: For adoption

The Committee discussed the issues identified in this application.

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

5.1.3. [Feraccru - ferric maltol - EMEA/H/C/002733/II/0010](#)

Shield TX (UK) Ltd

Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Harald Enzmann, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension of indication to widen the indication for Feraccru from the treatment "in adults with Iron deficiency anaemia in patients with IBD" to the treatment of "adults with Iron deficiency"; As a consequence, sections 4.1, 4, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet has been updated accordingly.

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

Action: For adoption

The Committee discussed the issues identified in this application, mainly relating to the wording of the indication and the possible effect in patients with iron deficiency without anaemia.

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

5.1.4. [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 for the treatment of patients with chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy to prevent relapse of neuromuscular disability and impairment. 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 is updated (v. 4.0)”

Action: For adoption

Request for Supplementary Information adopted on 12.10.2017.

The Committee discussed the issues identified in this application. The discussions focused on the posology and the wording of different sections of the SmPC.

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

5.1.5. Inovelon - rufinamide - Orphan - EMEA/H/C/000660/II/0045

Eisai Ltd

Rapporteur: Alexandre Moreau, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Ghania Chamouni

Scope: “Extension of indication to include the treatment of seizures associated with Lennox Gastaut syndrome in patients 1 year of age and older as adjunctive therapy. As a consequence sections 4.1, 4.2, 4.5, 5.1 and 5.2. The Package Leaflet and the RMP (version 10.0) are updated accordingly. In addition the Marketing Authorisation Holder (MAH) took the opportunity to make small corrections with the Product Information and to update the name and contact details of the local representative in Belgium and Luxembourg. Furthermore, the Product Information is brought in line with the latest QRD template version 10.”

Action: For adoption

The Committee discussed the issues identified in this application.

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

5.1.6. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/II/0063/G

Vertex Pharmaceuticals (Europe) Ltd.

Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Dolores Montero Corominas

Scope: “1) C.I.6.a (type II) - Extension of Indication to include the combination regimen of the ivacaftor 150 mg evening dose and Symkevi (tezacaftor/ivacaftor);
2) B.IIe.5.a.2 (type IB) - to add a blister card pack presentation containing 28-tablets for the 150 mg film-coated tablets (EU/1/12/782/005);
3) B.IIe.5.a.2 (type IB) - to add a blister pack presentation containing 28-tablets for the 150 mg film-coated tablets (EU/1/12/782/006).

As a consequence, section 4.1, 4.2, 4.4, 4.5, 4.8, 6.5 and 8 of the SmPC are updated.

Annex A, the Package Leaflet and Labelling are updated in accordance.

An updated RMP (version 6.0) is included.”

Action: For adoption

The Committee discussed the issues identified in this application.

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

The CHMP adopted the similarity assessment report.

5.1.7. Opdivo - nivolumab - EMEA/H/C/003985/II/0039

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include treatment of adult patients with advanced or recurrent gastric or gastroesophageal junction (GEJ) cancer after two or more prior systemic therapies, based on data from study ONO-4538-12. As a consequence, sections 4.1, 4.4, 4.8, and 5.1 of the SmPC are updated. The Annex II and Package Leaflet are updated in accordance. The RMP version version 11.0 has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application

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

5.1.8. Perjeta - pertuzumab - EMEA/H/C/002547/II/0034

Roche Registration Limited

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Doris Stenver

Scope: "Extension of Indication for Perjeta in combination with trastuzumab and chemotherapy for the adjuvant treatment of adult patients with HER2-positive early breast cancer. The submission is based on the primary analysis of efficacy and safety data from the pivotal Phase III study BIG-4-11/BO25126/TOC4939g (APHINITY). With the submission of the APHINITY data, the MAH also aims to fulfil the Annex IID obligation from the approval of the neoadjuvant indication of Perjeta granted in 2015. Sections 4.2, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. Annex II and the Package Leaflet have been updated accordingly.

The RMP version 10.0 has also been submitted." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004).

Action: For adoption

The Committee discussed the issues identified in this application.

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

5.1.9. Repatha - evolocumab - EMEA/H/C/003766/II/0017/G

Amgen Europe B.V.

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension of Indication to include reduction of atherosclerotic cardiovascular disease risk in adults with high cardiovascular risk for Repatha based on the results from Study 20110118 (a category 3 PV activity in the Risk Management Plan, MEA 004); as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 5.1 of the SmPC to include important mechanistic information for healthcare professionals based on Study 20120153 (a category 3 PV activity, MEA 006).

Submission of an updated RMP version 2.0 in order to add two category 3 studies in the RMP (Study 20160250 and Study 20150338), as well as to update the milestones of five category 3 studies (20110110, 20110271, 20120138, 20130286, 20130295)"

Action: For adoption

Request for Supplementary Information adopted on 14.09.2017.

The Committee discussed the issues identified in this application.

The Committee adopted a 2nd request for supplementary information with a specific timetable via written procedure on 21.12.2017.

5.1.10. Taltz - ixekizumab - EMEA/H/C/003943/II/0009

Eli Lilly Nederland B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include Ixekizumab alone or in combination with methotrexate, the treatment of active psoriatic arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drug (DMARD) therapies. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, and 5.2 of the SmPC are updated to reflect the new safety and efficacy information. The Package Leaflet and RMP (v.5.1) have been updated accordingly.

The variation leads to amendments to the Summary of Product Characteristics and Package Leaflet.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 14.09.2017.

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

The MAH submitted at the start of the procedure a request for consideration that the new indication brings significant benefit in comparison to existing therapies in accordance with Article 14(11) of Regulation (EC) 726/2004 - one year of market protection for a new indication. During the assessment, the CHMP raised questions concerning the significant benefit. Prior to the adoption of the CHMP opinion, the company withdrew its request for additional market protection. As a result of the MAH withdrawal of this ancillary request, no opinion on the additional market protection is adopted by CHMP.

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.

5.1.11. Translarna - ataluren - Orphan - EMEA/H/C/002720/II/0037

PTC Therapeutics International Limited

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include a new population (children from 2 to less than 5 years of age) for Translarna; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and RMP (version 7.1) is updated in accordance."

Action: For adoption

The Committee discussed the issues identified in this application.

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

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

Gilead Sciences International Limited

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

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

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

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

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

Action: For adoption

Request for Supplementary Information adopted on 14.09.2017, 18.05.2017.

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.

The summary of opinion was circulated for information.

5.1.13. [Xeljanz - tofacitinib - EMEA/H/C/004214/II/0006](#)

Pfizer Limited

Rapporteur: Robert James Hemmings, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include treatment of adult patients with active psoriatic arthritis who have had an inadequate response or who have been intolerant to a prior disease-modifying anti-rheumatic drug (DMARD) therapy, based on data from studies A3921091, A3921092, A3921125. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the Annex II with minor editorial changes. The RMP version 3.0 has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application.

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

5.1.14. [Yervoy - ipilimumab - EMEA/H/C/002213/II/0044](#)

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of indication to include the treatment of advanced (unresectable or metastatic) melanoma in children and adolescents 12 years of age and older for Yervoy. As a consequence sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 15) are updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 14.09.2017, 22.06.2017.

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

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

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

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

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

Scope: List of questions for the SAG planned in January 2018

Action: For adoption

Opinion adopted on 27.09.2017

The CHMP adopted the list of questions to the SAG to take place on 12 January 2018.

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

No items

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 7 recommendations for eligibility to PRIME: 7 were denied. The individual outcomes are listed in PRIME Monthly Report on EMA website.

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Blincyto - blinatumomab - Orphan - EMEA/H/C/003731/II/0009

Amgen Europe B.V.

Rapporteur: Alexandre Moreau

Scope: "Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to update the safety information with the data from the study 103311. This study is fulfilling the specific obligation for the conditional MA. The SO is removed from annex II. The Package Leaflet is updated accordingly.

The MAH takes this opportunity to amend the format of the preparation instructions to improve clarity. The content is not impacted."

Action: For adoption

Request for Supplementary Information adopted on 20.07.2017, 26.01.2017.

A Scientific Advisory Group consultation took place on 22nd November 2017. SAG experts were of the opinion that patients with relapsed/refractory Acute Lymphoblastic Leukemia (R/R ALL) could in theory benefit from alloHSCT. However, the mortality increase signal associated with the blinatumomab arm was not clearly understood. The presented data were unfortunately not sufficient to make any solid recommendation or thoughts around the identification of the population for blinatumomab treatment.

It was clear for the SAG experts that blinatumomab likely adds some value for the

treatment of R/R ALL patients as a window of the opportunity to lead patients to the unique curative therapy which is the transplantation. However, due to the too early close of Study follow-up, data from this prospective and randomised phase 3 study were considered too limited to draw any firm conclusions on the B/R balance of Blincyto. Also, additional efficacy and safety data in transplant recipients after blinatumomab could be still necessary.

The Committee discussed the issues identified in this application.

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

9.1.2. [Blincyto - blinatumomab - Orphan - EMEA/H/C/003731/R/0013](#)

Amgen Europe B.V.

Rapporteur: Alexandre Moreau, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Eva Jirsová

Scope: "Renewal"

Action: For adoption

The Committee discussed the renewal and feasibility of specific obligations related to this.

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

9.1.3. [Enbrel – etanercept - EMEA/H/C/000262 – WS1190 - 0210/G and Lifmior - EMEA/H/C/004167 - WS1190 - 0009/G](#)

Pfizer Limited

Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Patrick Batty

Action: For discussion

Request for Supplementary Information adopted on 30.11.2017, 28.09.2017.

The Committee discussed the issues identified in this application.

The Committee adopted a 3rd request for supplementary information with a specific timetable by written procedure on 20 December 2017.

9.1.4. [Keytruda - pembrolizumab - EMEA/H/C/003820/LEG/016](#)

Merck Sharp & Dohme Limited

Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus

Scope: Studies Keynote-183 and -185 - Halted clinical trials for Keytruda in combination with dexamethasone and an immunomodulatory (IMiD) agent (lenalidomide or pomalidomide) for the treatment of patients with multiple myeloma.

Action: For discussion

The CHMP was updated on the KN183 and KN185 studies. Both studies were halted because

of concerns about the safety of participants.

The CHMP agreed that results from these studies do not affect Keytruda's marketing authorisation in the EU, because the authorised uses of Keytruda do not involve the combination of medicines used in the two trials and Keytruda is not authorised for treating multiple myeloma.

9.1.5. [Ontruzant - trastuzumab - EMEA/H/C/004323](#)

Samsung Bioepis UK Limited (SBUK); treatment of breast cancer and metastatic gastric cancer

Scope: EPAR

Action: For adoption

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

Opinion adopted on 14.09.2017. List of Outstanding Issues adopted on 20.07.2017. List of Questions adopted on 26.01.2017.

The CHMP discussed the EPAR and agreed on the wording. The CHMP adopted the EPAR.

9.1.6. [Opdivo - nivolumab - EMEA/H/C/003985/LEG/025](#)

Bristol-Myers Squibb Pharma EEIG

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

Scope: MAH is requested to submit all relevant background information/documentation and a discussion of the impact of the data (efficacy and safety) from CA209-039, CA209-602 and CA204-142 on the Opdivo benefit/risk balance in the currently authorised indications in the EU (safety, efficacy and impact on overall benefit/risk).

Action: For discussion

The Committee discussed the issues identified in this application.

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

9.1.7. [Xofigo - radium-223 - EMEA/H/C/002653](#)

Bayer AG

Rapporteur: Harald Enzmann

Scope: Due to of the increased risk of death and fractures potentially arising from the use of radium-223 dichloride in combination with abiraterone acetate and prednisone/ prednisolone, the PRAC has agreed that the MAH should distribute a DHPC for radium-223 dichloride (Xofigo) regarding its concomitant use with abiraterone and strongly advising against the use of this combination.

Action: DHPC adopted by written procedure on 4 December 2017

The CHMP noted the DHPC and ongoing discussions at PRAC.

Roche Registration Limited

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver

Scope: From PSUSA/00002652/201611: Lymphopenia and CD4 depletion: The MAH is requested to provide a cumulative review of T lymphocyte decrease overall as well as CD4+ and CD8+ lymphocyte decrease addressing all relevant data (spontaneous reports, clinical trials, literature) split by indication. The review should focus on data in which rituximab was used as mono-therapy and include a discussion on biological plausibility. Due to the infections associated with low T-lymphocyte counts, it is requested that CD4 and CD8 depletions are described separately, with data presented in lymphocyte absolute counts as well as in percentage. The MAH should discuss the impact of this review on the benefit-risk balance of the product and make any relevant proposals to update the SmPC. PML: 1. The MAH is requested to review the incidence of PML in rituximab treated patients stratified by indication and clinical setting (backbone, pre-treatment or not etc.), using all available information. This should include all available literature data. Based on the outcome of the review, the MAH should discuss the need to amend the SmPC. 2. The MAH should provide an in-depth review of all risk factors for PML in rituximab treated patients and discuss the need for PML risk stratification strategies and make a proposal for a risk stratification algorithm. In particular, the MAH should discuss the usefulness of JCV diagnostic assays; duration of treatment; and prior immunosuppressant use as part of risk stratification. The discussion on JCV diagnostic assays should include analysis of the positive predictive value, sensitivity, specificity and any other information relevant to clinical utility of the assays as a risk stratification tool. The MAH should propose measures to minimise the risk depending on the level of risk.

Action: For information

The CHMP was informed about the PRAC conclusions.

Based on the PRAC review of available data on CD4 depletion and risk of PML in relation to rituximab treatment, and following advice from the SAG Oncology, the PRAC agreed that the risk-benefit balance of rituximab remains unchanged and that no variation of the marketing authorisation is warranted. The PRAC agreed that no changes to the current risk management of PML in patients treated with rituximab can be recommended based on the available evidence.

In future PSURs the MAH is requested to report any new significant findings which may emerge from ongoing clinical trials and basic research regarding association between rituximab treatment, as monotherapy or in combination with other anti-cancer agents, and depletion within T-cell (sub-) populations and about the pathophysiology and risk factors for PML in the context of anti-CD-20 treatment.

The CHMP adopted the assessment report with the final conclusions of the PRAC.

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

10.8.1. Hydroxyethyl starch (HES)

Fresenius Kabi Deutschland GmbH (Volulyte, Voluven),
B. Braun Melsungen AG (Tetraspan, Venofundin),
Seruwerk Bernburg AG (Hesra); various

PRAC Rapporteur: Patrick Batty; PRAC Co-rapporteur: Ulla Wändel Liminga

Scope: List of expert for Art 107i ad hoc expert group meeting on 18 December 2017.

Action: For adoption

Review of the benefit-risk balance following notification by Sweden of a referral under Article 107i of Directive 2001/83/EC, based on pharmacovigilance data

The CHMP adopted the list of experts.

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

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

Action: For information

The CHMP noted the information.

12. Inspections

12.1. GMP inspections

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

Impact of Brexit on manufacturing and supply

Action: For information

The CHMP noted the information.

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

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. Area of expertise of co-opted member

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

Scope: Discussion on area of expertise

Action: For adoption

The CHMP agreed on the following area of expertise: quality of non-biologicals and pharmacokinetics expertise. Nominations should be sent by February 14th 2018, end of business.

The election will take place during the February CHMP.

14.1.2. First experiences working with HTA bodies at the time of Market Entry

Action: For discussion

Postponed to the January CHMP meeting

14.1.3. Seating plan for CHMP under Bulgarian EU Presidency, 1 January – 30 June 2018

CHMP Seating Plan 1 January – 30 June 2018, under Bulgarian EU presidency

Action: For information

The CHMP noted the seating plan for the first half of 2018 under the Bulgarian presidency.

14.1.4. CHMP ORGAM meeting dates for 2018

There are additional ORGAM meetings scheduled for January and April and slight change in date for May (May ORGAM is moved to 22 May) during 2018.

Action: For information

The CHMP agreed to the additional ORGAM meetings for 2018.

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 27-30 November 2017

Action: For information

The CHMP noted the Summary of recommendations and advice.

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

Action: For adoption

The CHMP noted the information.

14.2.2. [Committee for Advanced Therapies \(CAT\)](#)

CAT draft minutes of meeting held on 6-8 December 2017

Action: For information

The CHMP noted the draft minutes.

14.2.3. [Committee for Herbal Medicinal Products \(HMPC\)](#)

Report from the HMPC meeting held on 20-21 November 2017

Action: For information

The CHMP noted the report.

14.2.4. [Paediatric Committee \(PDCO\)](#)

PIPs reaching D30 at December 2017 PDCO

Action: For information

The CHMP noted the information.

Report from the PDCO meeting held on 12-15 December 2017

Action: For information

The CHMP noted the information.

Joint CHMP/PDCO session

Agenda for joint session

Action: For discussion

The CHMP and PDCO joint discussion was held.

14.2.5. [Committee for Orphan Medicinal Products \(COMP\)](#)

Report from the COMP meeting held on 5-7 December 2017

Action: For information

The CHMP noted the report.

14.2.6. [Coordination Group for Mutual Recognition and Decentralised Procedures – Human \(CMDh\)](#)

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 11-13 December 2017

Action: For information

The CHMP noted the report.

14.2.7. Procedural advice on the evaluation of advanced therapy medicinal product in accordance with Article 8 of Regulation (EC) No 1394/2007

Scope: Present and adopt the final updated procedural advice for ATMP

Action: For adoption

The document was presented. Main updates concern the aligned processes for LoQ and LoOI between CHMP and CAT, simplification of oral explanation at CAT and CHMP, CHMP OE is exceptional. Also the role of PRAC in ATMP evaluation is now reflected in the advice document. Other updates concerned the committees' collaboration. The CAT is the lead in the assessment and re-examination needs to be based on CAT draft opinion. CAT and PRAC already adopted the document. The CHMP adopted the advice document. The next step is that the guidance will be published.

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 27-30 November 2017. Table of conclusions

Action: For information

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

The CHMP noted the report.

Re-nomination of the SAWP members

Action: For adoption

The CHMP re-appointed the SAWP members.

Mandate of the Scientific Advice Working Party (EMEA/CHMP/SAWP/69686/04 rev 12)

Action: For adoption

The CHMP adopted the mandate.

14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 22 November 2017.

Action: For adoption

The CHMP adopted the document.

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP December 2017 meeting to CHMP for adoption:

- 13 reports on products in scientific advice and protocol assistance

- 11 reports on products in pre-authorisation procedures
- 00 reports on products in post-authorisation procedures
- 06 reports on products in plasma master file

Action: For adoption

The CHMP adopted the BWP reports.

Work plan for the Biologics Working Party (BWP) for 2018 (EMA/CHMP/BWP/400117/2017)

Action: For adoption

The CHMP adopted the Work plan for the Biologics Working Party (BWP) for 2018.

14.3.4. Cardiovascular Working Party (CVSWP)

Chair: Pieter de Graeff/Kristina Dunder

Election of CVSWP Chair following resignation of Pieter de Graeff

Action: For adoption

The CHMP elected Kristina Dunder (SE) as CVSWP Chair.

Work plan for the Cardiovascular Working Party (CVSWP) for 2018
(EMA/CHMP/365586/2017)

Action: For adoption

The CHMP adopted the CVS Work Plan 2018.

14.3.5. Biostatistics Working Party (BSWP)

Chair: Anja Schiel/Thomas Lang

Call for nominations for BSWP Vice-Chair.

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

Action: For information

The CHMP noted the call.

Work plan for the Biostatistics Working Party (BSWP) for 2018 (EMA/CHMP/333668/2017)

Action: For adoption

The CHMP adopted the BSWP Work Plan 2018.

14.3.6. Safety Working Party (SWP)

Chair: Jan Willem Van der Laan

Work plan for the Safety Working Party (SWP) for 2018 (EMA/CHMP/SWP/420217/2017)

Action: For adoption

The CHMP adopted the SWP Work Plan 2018.

14.3.7. Quality Working Party (QWP)

Chair: Keith Pugh

Work plan for the Quality Working Party (QWP) for 2018
(EMA/CHMP/CVMP/QWP/504882/2017)

Action: For adoption

The CHMP adopted the QWP Work Plan 2018.

14.3.8. Biosimilar Medicinal Product Working Party (BMWP)

Chair: Elena Wolff-Holz/Niklas Ekman

Work plan for the Biosimilar Medicinal Product Working Party (BMWP) for 2018
(EMA/CHMP/BMWP/420509/2017)

Action: For adoption

The CHMP adopted the BMWP Work Plan 2018.

14.3.9. Vaccines Working Party (VWP)

Chair: Mair Powell/Svein Rune Andersen

Work plan for the Vaccines Working Party (VWP) for 2018 (EMA/CHMP/VWP/515395/2017)

Action: For adoption

The CHMP adopted the VWP Work Plan 2018.

14.3.10. Blood Products Working Party (BPWP)

Chair: Jacqueline Kerr

Work plan for the Blood Products Working Party (BPWP) for 2018
(EMA/CHMP/BPWP/399637/2017)

Action: For adoption

The CHMP adopted the BPWP Work Plan 2018.

14.3.11. Pharmacogenomics Working Party (PGWP)

Chair: Krishna Prasad/Markus Paulmichl

Work plan for the Pharmacogenomics Working Party (PGWP) for 2018
(EMA/CHMP/370931/2017)

Action: For adoption

The CHMP adopted the PGWP Work Plan 2018.

14.3.12. Infectious Diseases Working Party (IDWP)

Chair: Maria Jesus Fernandez Cortizo

Work plan for the Infectious Diseases Working Party (IDWP) for 2018 (EMA/517878/2017)

Action: For adoption

The CHMP adopted the IDWP Work Plan 2018.

14.3.13. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink/Henrike Potthast

Work plan for the Pharmacokinetics Working Party (PKWP) for 2018
(EMA/CHMP/365756/2017)

Action: For adoption

The CHMP adopted the PKWP Work Plan 2018.

Reflection paper on investigation of pharmacokinetics and pharmacodynamics in the obese population

Action: For adoption for 6 months public consultation

Postponed to January ORGAM

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

Action: For information

Postponed to January ORGAM

14.3.14. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus

Work plan for the Rheumatology/Immunology Working Party (RIWP) for 2018
(EMA/799178/2017)

Action: For adoption

The CHMP adopted the RIWP Work Plan 2018.

Guideline on clinical investigation of medicinal products for the treatment of rheumatoid arthritis (CPMP/EWP/556/95 Rev. 2)

Action: For adoption

The CHMP adopted the guideline.

14.3.15. Oncology Working Party (ONCWP)

Chair: Pierre Demolis/Paolo Foggi

Work plan for the Oncology Working Party (ONCWP) for 2018 (EMA/413341/2017)

Action: For adoption

The CHMP adopted the ONCWP Work Plan 2018.

14.3.16. Central Nervous System Working Party (CNSWP)

Chair: Karl Broich/André Elferink

Work plan for the Central Nervous System Working Party (CNSWP) for 2018 (EMA/625937/2017)

Action: For adoption

The CHMP adopted the CNSWP Work Plan 2018.

14.3.17. Gastroenterology Drafting Group (GDG)

Chair: Elmer Schabel

Work Plan for the Gastroenterology Drafting Group (GDG) for 2018 (EMA/CHMP/350919/2017)

Action: For adoption

The CHMP adopted the GDG Work Plan 2018.

14.3.18. Respiratory Drafting Group (RDG)

Chair: Karolina Törneke

Work plan for the Respiratory Drafting Group (RDG) for 2018 (EMA/CHMP/383892/2017)

Action: For adoption

The CHMP adopted the RDG Work Plan 2018.

14.3.19. Excipients Drafting Group (ExcpDG)

Chair: Dominique Masset

Work plan for the CHMP Excipients Drafting Group (ExcpDG) for the revision of the EC guideline 'Excipients in the labelling and package leaflet of medicinal products for human use' for 2018 (EMA/CHMP/672198/2017)

Action: For adoption

The CHMP adopted the ExcpDG Work Plan 2018.

14.3.20. Modelling and Simulation Working Group (MSWG)

Work plan for the Modelling and Simulation Working Group (MSWG) for 2018 (EMA/710355/2017)

Action: For adoption

The CHMP adopted the MSWG work plan 2018.

14.4. Cooperation within the EU regulatory network

14.4.1. Draft Commission Regulation amending Regulation (EC) No 847/2000 as regards the definition of the concept 'similar medicinal product'

Letter from the European Commission

Action: For information

Postponed.

14.5. The final amendment will be adopted via written procedure. Post-meeting note: the proposal was adopted via written procedure on 8th January 2018. Cooperation with International Regulators

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

ICH report to CHMP

Presentation

Action: For information

The CHMP noted the ICH report.

Scope: ICH guideline E17 - Step 5 -: general principles for planning and design of multi-regional clinical trials (EMA/CHMP/ICH/453276/2016)

Action: For adoption

The CHMP adopted the ICH guideline E17 - Step 5.

Scope: S3A Q&A - Step 5 - Note for guidance on toxicokinetics the assessment of systemic exposure in toxicity studies - questions and answers (EMA/CHMP/ICH/320985/2016)

Action: For adoption

The CHMP adopted the S3A Q&A - Step 5.

Scope: Q12 draft Guideline 'Technical and regulatory considerations for pharmaceutical product lifecycle management' – Step 2 - (EMA/804273/2017)

Action: For adoption for 12 months public consultation

The CHMP adopted the Q12 draft Guideline – Step 2 for 12 months public consultation.

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 discussion

The CHMP discussed the work plan. An adoption is envisaged during the January 2018 meeting. Please send any comments by 10 January 2018.

14.8. Planning and reporting

14.8.1. New marketing authorisation applications for 2017 with and without appointed rapporteurs

Action: For information

The CHMP noted the 2017 forecast.

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.

15.1.2. EC Consultation on Pharmaceuticals in the Environment

Scope: Update on consultation procedure

Action: For information

The CHMP noted the update on the consultation procedure. Furthermore, it was asked to send any comments from CHMP members to SWP. The deadline for responses to the targeted questionnaire is 21 January 2018 but an extension to 28 January will be requested to the Commission to allow adoption of the SWP response at the January CHMP.

15.1.3. Workshop on CAR-T cell registries

Action: For information

The CHMP noted the information on the workshop, to take place on 9 February 2018.

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 11-14 December 2017 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Tomas Salmonson	Chair	Sweden	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Milena Stain	Alternate	Austria	No interests declared	
Bart Van der Schueren	Member	Belgium	No interests declared	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Katarina Vučić	Member	Croatia	No interests declared	
Emilia Mavrokordatou	Member	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
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	
Harald Enzmann	Member (Vice-Chair)	Germany	No interests declared	
Eleftheria Nikolaidi	Member	Greece	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
			declared	
Agnes Gyurasics	Member	Hungary	No interests declared	
Kolbeinn Gudmundsson	Member	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	
Natalja Karpova	Alternate	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No participation in final deliberations and voting on:	3.2.4. emicizumab - EMEA/H/C/004406 5.1.8. Perjeta - pertuzumab - EMEA/H/C/002547/II/0034 9.1.12. Mabthera – Rituximab - EMEA/H/C/000165/LEG/096
Jacqueline Genoux-Hames	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	
Svein Rune Andersen	Member	Norway	No interests declared	
Bjorg Bolstad	Alternate	Norway	No participation in discussion, final deliberations and voting on:	9.1.10. Xofigo - radium-223 - EMEA/H/C/002653
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Aldona Paluchowska	Alternate	Poland	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Bruno Sepodes	Member	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meeting	
Simona Badoi	Member	Romania	No interests declared	
Francisek Drafi	Member	Slovakia	No interests declared	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member	Spain	No interests declared	
Jorge Camarero Jiménez	Alternate	Spain	No participation in final deliberations and voting on:	3.2.4. emicizumab - EMEA/H/C/004406 5.1.8. Perjeta - pertuzumab - EMEA/H/C/002547/II/0034 9.1.12. Mabthera – Rituximab - EMEA/H/C/000165/LEG/096
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Greg Markey	Member	United Kingdom	No interests declared	
Nithyanandan Nagercoil	Alternate	United Kingdom	No restrictions applicable to this meeting	
Robert James Hemmings	Co-opted member	United Kingdom	No restrictions applicable to this meeting	
Koenraad Norga	Co-opted member	Belgium	No participation in final deliberations and voting on:	2.1.4, 3.2.10. human herpesvirus 3 - EMEA/H/C/004336
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Jean-Louis Robert	Co-opted member	Luxembourg	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Ralf Meyer	Expert - in person*	Germany	No interests declared	
Nele Berthels	Expert - in person*	Belgium	No interests declared	
Ole Weis Bjerrum	Expert - via telephone*	Denmark	No restrictions applicable to this meeting	
Doris Johanna Hovgaard	Expert - via telephone*	Denmark	No interests declared	
Mats Welin	Expert - via telephone*	Sweden	No interests declared	
Martin Gore	Expert - via telephone*	United Kingdom	No restrictions applicable to this meeting	
Barbara Spruce	Expert - via telephone*	United Kingdom	No restrictions applicable to this meeting	
Yuansheng Sun	Expert - via telephone*	Germany	No interests declared	
Annette Lommel	Expert - via telephone*	Germany	No interests declared	
Monique van Raamsdonk	Expert - via telephone*	Netherlands	No interests declared	
Franz Xaver Kleber	Expert - via telephone*	Germany	No interests declared	
Elina Rönnemaa	Expert - via telephone*	Sweden	No interests declared	
Ingrid Lund	Expert - via telephone*	Norway	No interests declared	
Ingrid Wang	Expert - via telephone*	Norway	No interests declared	
Jan Span	Expert - via telephone*	Netherlands	No interests declared	
Lida Spruijt	Expert - via telephone*	Netherlands	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Nele Berthels	Expert - via telephone*	Belgium	No interests declared	
Johanna de Groot	Expert - via telephone*	Netherlands	No interests declared	
Muriel Uzzan	Expert - via telephone*	France	No interests declared	
Elisabeth Johanne Rook	Expert - via telephone*	Netherlands	No interests declared	
Jonas Bergh	Expert - via telephone*	Sweden	No restrictions applicable to this meeting	
Shirley Hopper	Expert - in person*	United Kingdom	No interests declared	
Anne Isabel Roth	Expert - via Adobe*	Germany	No interests declared	
Olga Kholmanskikh	Expert - via Adobe*	Belgium	No interests declared	
Milena Peraita Ezcurra	Expert - via Adobe*	Spain	No interests declared	
Representative from the European Commission attended the meeting				
Meeting was 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 *(section 5.3)*

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 Pharmacovigilance 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/



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A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

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

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

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

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

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

**ATryn - antithrombin alfa -
EMA/H/C/000587/S/0030**

MAH: Laboratoire Francais du Fractionnement et des Biotechnologies, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Caroline Laborde

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.

**Strensiq - asfotase alfa -
EMA/H/C/003794/S/0024, Orphan**

MAH: Alexion Europe SAS, Rapporteur: Greg Markey, PRAC Rapporteur: Almath Spooner

Positive Opinion adopted by consensus together with the CHMP assessment report.

The Marketing Authorisation remains under exceptional circumstances.

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

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

B.2.2. Renewals of Marketing Authorisations for unlimited validity

**Thalidomide Celgene - thalidomide -
EMA/H/C/000823/R/0054, Orphan**

MAH: Celgene Europe Limited, Rapporteur: Alexandre Moreau, Co-Rapporteur: Filip

Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.

Based on the review of the available

<p>Josephson, PRAC Rapporteur: Ghania Chamouni Request for Supplementary Information adopted on 12.10.2017.</p>	<p>information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.</p>
<p>Iclusig - ponatinib - EMA/H/C/002695/R/0042, Orphan MAH: Incyte Biosciences UK Ltd, Rapporteur: Greg Markey, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.</p> <p>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.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.</p>
<p>Memantine ratiopharm - memantine - EMA/H/C/002671/R/0011 MAH: ratiopharm GmbH, Generic, Generic of Ebixa, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Dolores Montero Corominas Request for Supplementary Information adopted on 14.12.2017.</p>	<p>Request for Supplementary Information adopted</p>
<p>Mycamine - micafungin - EMA/H/C/000734/R/0034 MAH: Astellas Pharma Europe B.V., Rapporteur: Harald Enzmann, Co-Rapporteur: Koenraad Norga, PRAC Rapporteur: Martin Huber Request for Supplementary Information adopted on 12.10.2017.</p>	<p>Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.</p> <p>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.</p> <p>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.</p>
<p>Spedra - avanafil - EMA/H/C/002581/R/0029 MAH: Menarini International Operations Luxembourg S.A., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Dolores Montero Corominas Request for Supplementary Information adopted on 14.12.2017.</p>	<p>Request for Supplementary Information adopted</p>
<p>Stribild - elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil - EMA/H/C/002574/R/0086 MAH: Gilead Sciences International Limited, Rapporteur: Robert James Hemmings, Co-Rapporteur: Joseph Emmerich, PRAC Rapporteur: Julie Williams</p>	<p>Request for Supplementary Information adopted</p>

Request for Supplementary Information adopted on 14.12.2017.

Voriconazole Accord - voriconazole - EMEA/H/C/002669/R/0017
MAH: Accord Healthcare Limited, Generic, Generic of Vfend, Rapporteur: John Joseph Borg, PRAC Rapporteur: Menno van der Elst

Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.

Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.

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

Xtandi - enzalutamide - EMEA/H/C/002639/R/0037
MAH: Astellas Pharma Europe B.V., Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Eva A. Segovia

Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.

Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.

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

B.2.3. Renewals of Conditional Marketing Authorisations

Blinicyto - 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.

See 9.1 in main agenda

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

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.

Caprelsa - vandetanib - EMEA/H/C/002315/R/0027
MAH: Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

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

Request for Supplementary Information adopted on 09.11.2017.	be granted. The Marketing Authorisation remains conditional. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
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B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

<p>Esbriet (CAP) - EMEA/H/C/PSR/S/0011 (pirfenidone)</p> <p>PRAC Rapporteur: Julie Williams</p> <p>Final study report for an imposed PASS: a prospective observational registry to evaluate the long-term safety of Esbriet (pirfenidone) in a real-world setting (passport)</p> <p>Action: For adoption</p>	<p>The CHMP, having considered in accordance with Article 28b(2) of Regulation (EC) No 726/2004 the results of the study on the basis of the PRAC recommendation and the PRAC assessment report as appended, is of the opinion by consensus that the terms of the marketing authorisation(s) for the above mentioned medicinal product(s) should be varied with the change(s).</p> <p>In addition, as this imposed PASS is the only criteria for additional monitoring, the deletion of the black symbol and the related statement in the product information is warranted.</p> <p>The Icelandic and the Norwegian CHMP member(s) agree(s) with the above-mentioned opinion of the CHMP.</p>
<p>Signal detection</p> <p>PRAC recommendations on signals adopted at the PRAC meeting held on 27-30 November 2017 PRAC:</p>	<p>Noted</p>

Insulin^[1]: insulin aspart – NOVOMIX, NOVORAPID; insulin bovine; insulin degludec – TRESIBA; insulin degludec, insulin aspart – RYZODEG, insulin degludec, liraglutide – XULTOPHY; insulin detemir – LEVEMIR; insulin glargine – ABASAGLAR, LANTUS, LUSDUNA, TOUJEO; insulin glulisine – APIDRA; insulin human (rDNA) – ACTRAPHANE, ACTRAPID, INSULATARD, INSULIN HUMAN WINTHROP, INSUMAN, MIXTARD, PROTAPHANE; insulin human, insulin isophane (NAP); insulin lispro – HUMALOG, LIPROLOG; insulin porcine (NAP) – Signal of potential increased risk of medication error associated with withdrawing insulin from pre-filled pens and cartridges, leading to dysglycaemia – PRAC recommendation on a variation

^[1] Pre-filled pens and cartridges

**Signal of angioedema -
Xeljanz - Tofacitinib Citrate –
EMA/H/C/004214**

MAH: Pfizer Limited, Rapporteur: Robert James Hemmings, Co-Rapporteur: Daniela Melchiorri,

Signal of fractures and fatal cases in chemotherapy-naïve patients

**Xofigo - Radium Ra 223 Dichloride -
EMA/H/C/002653**

MAH: Bayer AG, Rapporteur: Harald Enzmann, Co-Rapporteur: Daniela Melchiorri,

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

EMA/H/C/PSUSA/00001353/201704
(febuxostat)

CAPS:

Adenuric (EMA/H/C/000777) (febuxostat), MAH: Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop, PRAC Rapporteur: Jan Neuhauser, "21 Apr 2016 - 20 Apr 2017"

The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):

Update of section 4.8 of the SmPC to add the adverse reaction agranulocytosis with a frequency rare.

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

EMA/H/C/PSUSA/00002029/201705
(methylthioninium chloride)

CAPS:

Methylthioninium chloride Proveblue (EMA/H/C/002108) (methylthioninium chloride), MAH: Provepharm SAS, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "06/05/2016 - 05/05/2017"

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 sections 4.4, 4.5 and 4.8 of the SmPC to add the adverse reaction serotonin syndrome with concomitant use of serotonergic drugs with a frequency not known. Update of sections 4.4 and 4.8 of the SmPC to the adverse reaction photosensitivity with a frequency not known. The Package leaflet is updated accordingly.

The Icelandic and the Norwegian CHMP

	members agree with the above-mentioned recommendation of the CHMP.
<p>EMA/H/C/PSUSA/0002772/201703 (somatropin) CAPS: NutropinAq (EMA/H/C/000315) (somatropin), MAH: Ipsen Pharma, Rapporteur: Hanne Lomholt Larsen Omnitrope (EMA/H/C/000607) (somatropin), MAH: Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege Somatropin Biopartners (EMA/H/C/002196) (somatropin), MAH: BioPartners GmbH, Rapporteur: Martina Weise NAPS: NAPS - EU , PRAC Rapporteur: Doris Stenver, "01/10/2015 - 31/03/2017"</p>	<p>The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended , recommends by consensus the variation to the terms of the marketing authorisation(s) for the medicinal products containing the above referred active substance(s) , concerning the following change(s): Update of sections 4.2, 4.4 and 4.5 of the SmPC to add new information on possible need for dose optimisation of somatropin in women and a warning about the concomitant use of oral oestrogen therapy and somatropin. The Package Leaflet is updated accordingly. Update of section 4.4 and 4.5 of the SmPC to add a warning on possible need for dose adjustment of glucocorticoid replacement therapy and to add information on interactions between somatropin and glucocorticoids. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.</p>
<p>EMA/H/C/PSUSA/00009261/201705 (pixantrone) CAPS: Pixuvri (EMA/H/C/002055) (pixantrone), MAH: CTI Life Sciences Limited, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, "11-Nov-2016 to 10-May-2017"</p>	<p>The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended recommends by consensus the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change: Update of section 4.8 of the SmPC to add the adverse reaction 'Sepsis' 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.</p>
<p>EMA/H/C/PSUSA/00010186/201705 (vedolizumab) CAPS: Entyvio (EMA/H/C/002782) (vedolizumab), MAH: Takeda Pharma A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Adam Przybylkowski, "20Nov2016 – 19May2017"</p>	<p>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</p>

	<p>medicinal product(s), concerning the following change(s):</p> <p>Update of section 4.8 of the SmPC to add pneumonia and blurred vision with a frequency very rare. The Package leaflet is updated accordingly.</p>
<p>EMEA/H/C/PSUSA/00010255/201705 (simeprevir) CAPS: Olysio (EMEA/H/C/002777) (simeprevir), MAH: Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Julie Williams, “22 November 2016 – 21 May 2017”</p>	<p>The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change:</p> <p>The update of section 4.4 and 4.8 of the SmPC to reflect the post-marketing experience on photosensitivity reactions and additionally strengthen the wording on sun protective measures to be considered during treatment with Olysio.</p> <p>The Icelandic and the Norwegian CHMP members agree with the above mentioned recommendation of CHMP</p>
<p>EMEA/H/C/PSUSA/00010301/201705 (ibrutinib) CAPS: Imbruvica (EMEA/H/C/003791) (ibrutinib), MAH: Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, “13 May 2016 to 12 November 2016”</p>	<p>The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change:</p> <p>Update of section 4.8 of the SmPC to add: ‘panniculitis’ with frequency ‘uncommon’</p> <p>The Package leaflet is updated accordingly.</p> <p>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.</p>
<p>EMEA/H/C/PSUSA/00010455/201705 (lumacaftor / ivacaftor) CAPS: Orkambi (EMEA/H/C/003954) (lumacaftor / ivacaftor), MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Almath Spooner, “20 Nov 16 to 19 May 2017”</p>	<p>The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following change:</p> <p>Update of section 4.8 of the SmPC to add ‘Blood creatine phosphokinase increased’ with frequency ‘common’. The Package leaflet is updated accordingly.</p>

<p>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</p> <p>PRAC Rapporteur: Patrick Batty, "3 May 2016 - 2 May 2017"</p>	<p>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.</p>
	<p>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 sections 4.4 and 4.6 of the SmPC to update information on teratogenic effects and pregnancy and the contraception recommendations based on the current available data. The Package leaflet is updated accordingly. The educational materials were also updated.</p>
	<p>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.</p>

B.4. EPARs / WPARs

<p>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)</p>	<p>adopted.</p>
<p>Darunavir Krka - darunavir - EMEA/H/C/004273 Applicant: KRKA, d.d., Novo mesto, treatment of HIV-1 infection, Generic, Generic of Prezista, Generic application (Article 10(1) of Directive No 2001/83/EC)</p>	<p>adopted.</p>
<p>Darunavir Krka d.d. - darunavir - EMEA/H/C/004891 Applicant: KRKA, d.d., Novo mesto, treatment of HIV-1 infection, Generic, Duplicate, Generic of Prezista, Duplicate of Darunavir Krka, Generic application (Article 10(1) of Directive No 2001/83/EC)</p>	<p>adopted.</p>
<p>Fanaptum - iloperidone - EMEA/H/C/004149 Applicant: Vanda Pharmaceuticals Ltd.,</p>	<p>adopted.</p>

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

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

Applicant: AstraZeneca AB, treatment of severe asthma with an eosinophilic phenotype, New active substance (Article 8(3) of Directive No 2001/83/EC)

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

Applicant: Mylan S.A.S, treatment of breast cancer, Generic, Generic of Faslodex, Generic application (Article 10(1) of Directive No 2001/83/EC)

Infinia - alpha-1-antitrypsin - Orphan - EMEA/H/C/003934 adopted.

Applicant: Kamada BioPharma Limited at Fieldfisher LLP, Known active substance (Article 8(3) of Directive No 2001/83/EC)

WPAR

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

Applicant: Endoceutics Limited, treatment of vulvovaginal atrophy, New active substance (Article 8(3) of Directive No 2001/83/EC)

Jorveza - budesonide - EMEA/H/C/004655, Orphan adopted.

Applicant: Dr. Falk Pharma GmbH, treatment of eosinophilic esophagitis (EoE), Known active substance (Article 8(3) of Directive No 2001/83/EC)

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

Applicant: Amgen Europe B.V., treatment of metastatic breast cancer, unresectable advanced, metastatic or recurrent non-small cell lung cancer, unresectable advanced metastatic or recurrent non-squamous non-small cell lung cancer, advanced and/or metastatic renal cell cancer, advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer, platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer, Duplicate, Duplicate of KYOMARC, Similar biological application (Article 10(4) of Directive No 2001/83/EC)

Ocrevus - ocrelizumab - adopted.

EMA/H/C/004043

Applicant: Roche Registration Limited,
treatment of multiple sclerosis
treatment of multiple sclerosis, New active
substance (Article 8(3) of Directive No
2001/83/EC)

Onzeald - etirinotecan pegol - adopted.
EMA/H/C/003874

Applicant: Nektar Therapeutics UK Limited,
treatment of breast cancer with brain
metastases, New active substance (Article 8(3)
of Directive No 2001/83/EC)

Plivensia - sirukumab - EMA/H/C/004165 adopted.

Applicant: Janssen-Cilag International NV,
treatment of rheumatoid arthritis, Rapporteur:
Kristina Dunder, Co-Rapporteur: Johann
Lodewijk Hillege, PRAC Rapporteur: Kimmo
Jaakkola, New active substance (Article 8(3) of
Directive No 2001/83/EC)

WPAR

Prevymis - letermovir - adopted.
EMA/H/C/004536, Orphan

Applicant: Merck Sharp & Dohme Limited,
prophylaxis of cytomegalovirus (CMV)
reactivation and disease, New active substance
(Article 8(3) of Directive No 2001/83/EC)

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

Avastin - bevacizumab - Positive Opinion adopted by consensus on
EMA/H/C/000582/II/0098 23.11.2017. The Icelandic and Norwegian CHMP
MAH: Roche Registration Limited, Rapporteur: Members were in agreement with the CHMP
Sinan B. Sarac recommendation.
Opinion adopted on 23.11.2017.
Request for Supplementary Information adopted
on 12.10.2017.

Axumin - fluciclovine (18F) - Request for Supplementary Information adopted
EMA/H/C/004197/II/0001/G
MAH: Blue Earth Diagnostics Ltd, Rapporteur:
Harald Enzmann
Request for Supplementary Information adopted
on 14.12.2017.

<p>Axumin - fluciclovine (18F) - EMEA/H/C/004197/II/0002/G MAH: Blue Earth Diagnostics Ltd, Rapporteur: Harald Enzmann</p>	<p>Request for Supplementary Information adopted</p>
<p>Request for Supplementary Information adopted on 14.12.2017.</p>	
<p>Blincyto - blinatumomab - EMEA/H/C/003731/II/0020/G, Orphan MAH: Amgen Europe B.V., Rapporteur: Alexandre Moreau Opinion adopted on 14.12.2017.</p>	<p>Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Brineura - cerliponase alfa - EMEA/H/C/004065/II/0001/G, Orphan MAH: BioMarin International Limited, Rapporteur: Martina Weise Opinion adopted on 07.12.2017.</p>	<p>Positive Opinion adopted by consensus on 07.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Request for Supplementary Information adopted on 12.10.2017.</p>	
<p>Daptomycin Hospira - daptomycin - EMEA/H/C/004310/II/0003 MAH: Hospira UK Limited, Generic, Generic of Cubicin, Rapporteur: Kolbeinn Gudmundsson Opinion adopted on 07.12.2017.</p>	<p>Positive Opinion adopted by consensus on 07.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Request for Supplementary Information adopted on 19.10.2017.</p>	
<p>DuoTrav - travoprost / timolol - EMEA/H/C/000665/II/0051 MAH: Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro Opinion adopted on 23.11.2017.</p>	<p>Positive Opinion adopted by consensus on 23.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Elaprase - idursulfase - EMEA/H/C/000700/II/0071/G MAH: Shire Human Genetic Therapies AB, Rapporteur: Greg Markey Opinion adopted on 07.12.2017.</p>	<p>Positive Opinion adopted by consensus on 07.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Request for Supplementary Information adopted on 26.10.2017.</p>	
<p>Eliquis - apixaban - EMEA/H/C/002148/II/0049/G MAH: Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 16.11.2017.</p>	<p>Positive Opinion adopted by consensus on 16.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Elocta - efmoroctocog alfa - EMEA/H/C/003964/II/0016/G MAH: Swedish Orphan Biovitrum AB (publ), Rapporteur: Jan Mueller-Berghaus</p>	<p>Positive Opinion adopted by consensus on 16.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>

Opinion adopted on 16.11.2017.
Request for Supplementary Information adopted
on 14.09.2017.

**Elonva - corifollitropin alfa -
EMA/H/C/001106/II/0037/G**
MAH: Merck Sharp & Dohme Limited,
Rapporteur: Paula Boudewina van Hennik.
Opinion adopted on 14.12.2017.
Request for Supplementary Information adopted
on 19.10.2017.

Positive Opinion adopted by consensus on
14.12.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Envarsus - tacrolimus -
EMA/H/C/002655/II/0008/G**
MAH: Chiesi Farmaceutici S.p.A., Rapporteur:
John Joseph Borg
Opinion adopted on 14.12.2017.
Request for Supplementary Information adopted
on 20.07.2017, 16.03.2017.

Positive Opinion adopted by consensus on
14.12.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

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

Positive Opinion adopted by consensus on
14.12.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

Opinion adopted on 14.12.2017.

**Fotivda - tivozanib -
EMA/H/C/004131/II/0001**
MAH: EUSA Pharma (UK) Limited, Rapporteur:
Bruno Sepodes

Positive Opinion adopted by consensus on
07.12.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

Opinion adopted on 07.12.2017.

**Hizentra - human normal immunoglobulin -
EMA/H/C/002127/II/0089**
MAH: CSL Behring GmbH, Rapporteur: Jan
Mueller-Berghaus
Opinion adopted on 30.11.2017.
Request for Supplementary Information adopted
on 05.10.2017.

Positive Opinion adopted by consensus on
30.11.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

**Hizentra - human normal immunoglobulin -
EMA/H/C/002127/II/0091**
MAH: CSL Behring GmbH, Rapporteur: Jan
Mueller-Berghaus
Request for Supplementary Information adopted
on 14.12.2017.

Request for Supplementary Information adopted

**Kevzara - sarilumab -
EMA/H/C/004254/II/0003/G**
MAH: sanofi-aventis groupe, Rapporteur: Jan
Mueller-Berghaus

Positive Opinion adopted by consensus on
23.11.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

Opinion adopted on 23.11.2017.

Kevzara - sarilumab -

EMA/H/C/004254/II/0004

MAH: sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus

Opinion adopted on 07.12.2017.

Positive Opinion adopted by consensus on 07.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Kineret - anakinra -

EMA/H/C/000363/II/0058

MAH: Swedish Orphan Biovitrum AB (publ), Rapporteur: Sinan B. Sarac

Opinion adopted on 07.12.2017.

Positive Opinion adopted by consensus on 07.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Kyprolis - carfilzomib -

EMA/H/C/003790/II/0020, Orphan

MAH: Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez

Opinion adopted on 23.11.2017.

Positive Opinion adopted by consensus on 23.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Kyprolis - carfilzomib -

EMA/H/C/003790/II/0022/G, Orphan

MAH: Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez

Opinion adopted on 14.12.2017.

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) -

EMA/H/W/002300/II/0025/G

MAH: GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus

Opinion adopted on 14.12.2017.

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Natpar - parathyroid hormone -

EMA/H/C/003861/II/0004/G, Orphan

MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Bart Van der Schueren

Opinion adopted on 14.12.2017.

Request for Supplementary Information adopted on 02.11.2017.

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine -

EMA/H/C/002226/II/0069

MAH: Pfizer Limited, Rapporteur: Greg Markey
Request for Supplementary Information adopted on 16.11.2017.

Request for Supplementary Information adopted

NovoEight - turoctocog alfa -

EMA/H/C/002719/II/0021/G

MAH: Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus

Request for Supplementary Information adopted

Request for Supplementary Information adopted on 14.12.2017.

**Nucala - mepolizumab -
EMA/H/C/003860/II/0011**

MAH: GlaxoSmithKline Trading Services Limited,
Rapporteur: Nithyanandan Nagercoil
Request for Supplementary Information adopted on 23.11.2017.

Request for Supplementary Information adopted

**NutropinAq - somatropin -
EMA/H/C/000315/II/0068/G**

MAH: Ipsen Pharma, Rapporteur: Hanne Lomholt Larsen
Opinion adopted on 23.11.2017.

Positive Opinion adopted by consensus on 23.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Opdivo - nivolumab -
EMA/H/C/003985/II/0037/G**

MAH: Bristol-Myers Squibb Pharma EEIG,
Rapporteur: Jorge Camarero Jiménez
Opinion adopted on 14.12.2017.
Request for Supplementary Information adopted on 14.09.2017.

Positive Opinion adopted by consensus on 14.12.2017. 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) -
EMA/H/C/003963/II/0009/G**

MAH: AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus
Request for Supplementary Information adopted on 14.12.2017.

Request for Supplementary Information adopted

**Pixuvri - pixantrone -
EMA/H/C/002055/II/0040**

MAH: CTI Life Sciences Limited, Rapporteur: Greg Markey
Opinion adopted on 07.12.2017.

Positive Opinion adopted by consensus on 07.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Praluent - alirocumab -
EMA/H/C/003882/II/0028/G**

MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege
Opinion adopted on 16.11.2017.
Request for Supplementary Information adopted on 21.09.2017.

Positive Opinion adopted by consensus on 16.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Praluent - alirocumab -
EMA/H/C/003882/II/0030**

MAH: sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege
Opinion adopted on 23.11.2017.

Positive Opinion adopted by consensus on 23.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

<p>Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0127 MAH: CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 14.12.2017.</p>	<p>Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Scenesse - afamelanotide - EMEA/H/C/002548/II/0017, Orphan MAH: Clinuvel (UK) Limited, Rapporteur: Harald Enzmann Request for Supplementary Information adopted on 30.11.2017.</p>	<p>Request for Supplementary Information adopted</p>
<p>Strensiq - asfotase alfa - EMEA/H/C/003794/II/0026/G, Orphan MAH: Alexion Europe SAS, Rapporteur: Greg Markey Opinion adopted on 23.11.2017.</p>	<p>Positive Opinion adopted by consensus on 23.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>TachoSil - human thrombin / human fibrinogen - EMEA/H/C/000505/II/0081 MAH: Takeda Austria GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 16.11.2017. Request for Supplementary Information adopted on 21.09.2017.</p>	<p>Positive Opinion adopted by consensus on 16.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Tecentriq - atezolizumab - EMEA/H/C/004143/II/0001 MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac Opinion adopted on 14.12.2017.</p>	<p>Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Travatan - travoprost - EMEA/H/C/000390/II/0057 MAH: Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro Opinion adopted on 23.11.2017.</p>	<p>Positive Opinion adopted by consensus on 23.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Trulicity - dulaglutide - EMEA/H/C/002825/II/0021 MAH: Eli Lilly Nederland B.V., Rapporteur: Greg Markey Request for Supplementary Information adopted on 23.11.2017, 19.10.2017.</p>	<p>Request for Supplementary Information adopted</p>
<p>Vimizim - elosulfase alfa - EMEA/H/C/002779/II/0021/G, Orphan MAH: BioMarin Europe Ltd, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 16.11.2017. Request for Supplementary Information adopted on 21.09.2017.</p>	<p>Positive Opinion adopted by consensus on 16.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>

<p>Xofigo - radium-223 - EMA/H/C/002653/II/0027 MAH: Bayer AG, Rapporteur: Harald Enzmann Opinion adopted on 30.11.2017.</p>	<p>Positive Opinion adopted by consensus on 30.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>Zaltrap - aflibercept - EMA/H/C/002532/II/0040 MAH: sanofi-aventis groupe, Rapporteur: Filip Josephson Opinion adopted on 07.12.2017.</p>	<p>Positive Opinion adopted by consensus on 07.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>WS1232 Infanrix hexa- EMA/H/C/000296/WS1232/0232 MAH: GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Request for Supplementary Information adopted on 14.12.2017.</p>	<p>Request for Supplementary Information adopted</p>
<p>WS1233/G Hexacima- EMA/H/C/002702/WS1233/0070/G Hexaxim- EMA/H/W/002495/WS1233/0075/G Hexyon- EMA/H/C/002796/WS1233/0074/G MAH: Sanofi Pasteur SA, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 16.11.2017.</p>	<p>Request for Supplementary Information adopted</p>
<p>WS1254/G Hirobriz Breezhaler- EMA/H/C/001211/WS1254/0042/G Onbrez Breezhaler- EMA/H/C/001114/WS1254/0041/G Oslif Breezhaler- EMA/H/C/001210/WS1254/0041/G Ultibro Breezhaler- EMA/H/C/002679/WS1254/0017/G Ulunar Breezhaler- EMA/H/C/003875/WS1254/0017/G Xoterna Breezhaler- EMA/H/C/003755/WS1254/0020/G MAH: Novartis Europharm Limited, Lead Rapporteur: Hanne Lomholt Larsen Opinion adopted on 14.12.2017. Request for Supplementary Information adopted on 19.10.2017.</p>	<p>Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>WS1262 Cerezyme-</p>	<p>Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP</p>

EMEA/H/C/000157/WS1262/0106

Fabrazyme-

EMEA/H/C/000370/WS1262/0101

Myozyme-

EMEA/H/C/000636/WS1262/0067

Thyrogen-

EMEA/H/C/000220/WS1262/0093

MAH: Genzyme Europe BV, Lead Rapporteur:

Johann Lodewijk Hillege

Opinion adopted on 14.12.2017.

Members were in agreement with the CHMP recommendation.

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

Afstyla - lonoctocog alfa -

EMEA/H/C/004075/II/0007

MAH: CSL Behring GmbH, Rapporteur: Jan

Mueller-Berghaus, "Update of section 4.8 of the SmPC in order to include information on

inhibitor development in Previously Untreated Patients (PUPs), based on the ongoing Phase III

study CSL627_3001 which aims to evaluate the long-term safety and efficacy of rVIII-Single

Chain for routine prophylaxis and on-demand

treatment of bleeding episodes in children,

adolescents and adults with severe hemophilia A (ie, FVIII activity of $\leq 1\%$). The Package Leaflet

is updated accordingly.

In addition, the Marketing authorisation holder

(MAH) took the opportunity to make editorial

changes related to the secondary packaging in

section 6.5 and 6.6 of the SmPC, in section 4 of

the Labelling and sections 3 and 6 of the

Package leaflet.

Moreover, the MAH took the opportunity to

update the list of local representatives (for

Bulgaria) in the Package Leaflet."

Request for Supplementary Information adopted

on 14.12.2017.

Request for Supplementary Information adopted

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 in order to update the

safety information with the data from the study

103311. This study is fulfilling the specific

obligation for the conditional MA. The SO is

removed from annex II. The Package Leaflet is

updated accordingly.

The MAH takes this opportunity to amend the

format of the preparation instructions to

See 9.1 in main agenda

improve clarity. The content is not impacted.”
Request for Supplementary Information adopted
on 20.07.2017, 26.01.2017.

**Buccolam - midazolam -
EMA/H/C/002267/II/0035**

Request for Supplementary Information adopted

MAH: Shire Services BVBA, Rapporteur: Johann Lodewijk Hillege, “Update of SmPC sections 4.4 and 4.5 to strengthen the warning regarding concomitant administration of benzodiazepines and opioids following a recent review of the MAH’s safety databases and literature. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to align the annexes with the latest QRD template and to update the contact details of the MAH in the Package Leaflet.”

Request for Supplementary Information adopted
on 23.11.2017.

**CellCept - mycophenolate mofetil -
EMA/H/C/000082/II/0136**

Positive Opinion adopted by consensus on
23.11.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

MAH: Roche Registration Limited, Rapporteur: Greg Markey, “Update of sections 4.4 and 4.5 of the SmPC of all pharmaceutical forms, in order to update information regarding potential interactions with antibiotics and drugs interfering with glucuronidation pathway, based on a review of published literature. The Package Leaflet is updated accordingly. In addition, update of section 6.6 of the SmPC and section 3 of the package leaflet to improve the recommendations regarding safe handling of the powder for oral suspension formulation as well as other minor editorial changes.”
Opinion adopted on 23.11.2017.

**DuoTrav - travoprost / timolol -
EMA/H/C/000665/II/0052**

Request for Supplementary Information adopted

MAH: Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, “Update of sections 4.8 of the SmPC in order to add “lid sulcus deepened” and “iris hyperpigmentation” as new adverse drug reactions and to upgrade the frequency of “skin hyperpigmentation (periocular)” from rare to uncommon based on the post-approval review of the safety data. In addition, section 4.8 of SmPC has been updated to align Adverse Drug Reactions table for the travoprost monotherapy.
Based on the same safety review, section 4.6 of SmPC has been updated with dose margin

estimates.

In addition, the MAH took the opportunity to align the Product information with the currently approved travoprost EU SmPC and QRD version 10 and to update the list of local representatives."

Request for Supplementary Information adopted on 14.12.2017.

**Epivir - lamivudine -
EMA/H/C/000107/II/0104**

Request for Supplementary Information adopted

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."

Request for Supplementary Information adopted on 14.12.2017, 21.09.2017, 05.05.2017.

**Humira - adalimumab -
EMA/H/C/000481/II/0170**

Request for Supplementary Information adopted

MAH: AbbVie Limited, Rapporteur: Kristina Dunder, "Update of section 4.6 of the SmPC in order to update information on pregnancy and lactation based on results from pregnancy registry (OTIS; study number M03-604) and supported by relevant published literature. The Package Leaflet is updated accordingly."

Request for Supplementary Information adopted on 30.11.2017.

**Ibrance - palbociclib -
EMA/H/C/003853/II/0006**

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

MAH: Pfizer Limited, Rapporteur: Filip Josephson, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to reflect independently-reviewed PFS results of study A5481008 (PALOMA-2) and of the Phase 2 portion of the A5481010 single-arm study; the information on

ethnicity was also updated in Section 5.2 of the SmPC based on the results of the A5481010 study in Japanese patients.”
Opinion adopted on 14.12.2017.
Request for Supplementary Information adopted on 12.10.2017, 22.06.2017.

**Iclusig - ponatinib -
EMA/H/C/002695/II/0041, Orphan**
MAH: Incyte Biosciences UK Ltd, Rapporteur: Greg Markey, “Update of section 4.8 of the SmPC in order to include a paragraph regarding severe cutaneous adverse reactions (SCARs) reported in the post-marketing setting. The Package Leaflet is updated accordingly. In addition, discrepancies between the SmPC and the Package Leaflet are being corrected in order to align the safety information in the Package Leaflet with the SmPC.”
Opinion adopted on 07.12.2017.
Request for Supplementary Information adopted on 12.10.2017.

Positive Opinion adopted by consensus on 07.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Invirase - saquinavir -
EMA/H/C/000113/II/0122**
MAH: Roche Registration Limited, Rapporteur: Milena Stain, “Update of sections 4.2, 4.3, and 4.5 of the SmPC following an update to the Company Core Data Sheet in order to include a cross-reference to a new contraindication against switching from rilpivirine to invirase/ritonavir (section 4.2), to include lurasidone in the contraindications section (section 4.3) and to add information on additional interactions regarding lurasidone, rilpivirine, dasatinib, and sunitinib (section 4.5). The existing information regarding the interaction with alfuzosin has been updated to include a warning that co-administration may also cause potentially life-threatening cardiac arrhythmia. The existing information regarding interaction with medicines listed in the section ‘neuroleptics’ has been moved to the section ‘antipsychotics’ (section 4.5). The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity the PI to correct formatting and minor typographical errors.”
Request for Supplementary Information adopted on 07.12.2017.

Request for Supplementary Information adopted

Isentress - raltegravir -

Request for Supplementary Information adopted

EMA/H/C/000860/II/0069

MAH: Merck Sharp & Dohme Limited,
Rapporteur: Greg Markey, "Update of sections 4.8 and 5.1 of the SmPC based on the final results (i.e. through 96 weeks) from study PN292 (ONCEMRK), the pivotal Phase 3 study evaluating the safety and efficacy of raltegravir 1200 mg QD (2 x 600 mg tablets) versus raltegravir 400 mg BID, each in combination with emtricitabine / tenofovir disoproxil fumarate in treatment-naïve HIV-1 infected adult subjects. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC."

Request for Supplementary Information adopted on 07.12.2017.

Izba - travoprost -

Request for Supplementary Information adopted

EMA/H/C/002738/II/0008

MAH: Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information in line with Travoprost 40 µg/mL Eye Drops PI, based on the review of clinical trial and post-marketing data along with literature references.

The package leaflet section 4 is updated accordingly."

Request for Supplementary Information adopted on 07.12.2017, 05.10.2017.

Jevtana - cabazitaxel -

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

EMA/H/C/002018/II/0038

MAH: sanofi-aventis groupe, Rapporteur: Alexandre Moreau, "Submission of the final PK analysis report with data from studies EFC11784, EFC11785, TCD11068, and TCD 11870 to provide information on relationship between allelic variants of genes coding for CY3A4 enzyme and cabazitaxel. No changes to the PI are proposed."

Opinion adopted on 14.12.2017.

Maviret - glecaprevir / pibrentasvir -

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

EMA/H/C/004430/II/0002

MAH: AbbVie Limited, Rapporteur: Joseph Emmerich, "Update of sections 4.8 and 5.1 of the SmPC in order to add information on clinical efficacy and safety in HCV/HIV-1 co-infected subjects, based on new clinical data from Study M14-730 (EXPEDITION-2), a post-registrational Phase 3 study which evaluated the efficacy and

safety of the glecaprevir/pibrentasvir regimen in chronic HCV GT1-GT6/HIV-1 co-infected subjects who were HCV treatment-naïve or treatment-experienced. In addition, the SmPC was revised to make minor grammatical and formatting amendments and to correct errors in section 5.2."

Opinion adopted on 14.12.2017.

**Maviret - glecaprevir / pibrentasvir -
EMA/H/C/004430/II/0003**

Request for Supplementary Information adopted

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

Request for Supplementary Information adopted on 14.12.2017.

**Mysimba - naltrexone hydrochloride /
bupropion hydrochloride -
EMA/H/C/003687/II/0023**

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Opinion adopted on 14.12.2017.

**Natpar - parathyroid hormone -
EMA/H/C/003861/II/0006, Orphan**

Positive Opinion adopted by consensus on 30.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

MAH: Shire Pharmaceuticals Ireland Ltd, Rapporteur: Bart Van der Schueren, "Submission of the final report from studies

(R7661M-SHP634 and R7673M-SHP634) listed as a category 3 studies in the RMP.

Study R7661M-SHP634 is a Comparison of the Effects of Once- versus Twice-Daily Dosing with NPSP558 (Recombinant Human Parathyroid Hormone (1-84)) on Osteoblast Proliferation and Bone Formation in the Male Fischer 344 Rats.

Study R7673M-SHP634 is A 13-Week Subcutaneous Injection Study of NPSP558 (Recombinant Human PTH (1-84)) with an 8-Week Recovery Period in Juvenile Rats.”
Opinion adopted on 30.11.2017.

Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0071

Request for Supplementary Information adopted

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

The Package Leaflet is updated accordingly. Annex II is also updated to take into account that the 1 year timeline was fulfilled in ANX 13.3.”

Request for Supplementary Information adopted on 14.12.2017.

Rapiscan - regadenoson - EMEA/H/C/001176/II/0026

Positive Opinion adopted by consensus on 07.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

MAH: GE Healthcare AS, Rapporteur: Greg Markey, “Update of section 4.5 of the SmPC in order to add further information on molecular transporters based 5 non-clinical studies:

Study-OPT-2016-045, Study-OPT-2016-046, Study-OPT-2016-099, Study-OPT-2016-100 and Study-OPT-2016-101.”
Opinion adopted on 07.12.2017. Request for Supplementary Information adopted on 12.10.2017.

Roteas - edoxaban -

EMA/H/C/004339/II/0003

MAH: Daiichi Sankyo Europe GmbH, Rapporteur: Concepcion Prieto Yerro, “Update of sections 4.2 and 5.1 of the SmPC in line with changes already introduced to Lixiana (EMA/H/C/002629/II/0012) in order to add information deriving from clinical data for the use of edoxaban as anticoagulant therapy for patients with non-valvular atrial fibrillation undergoing cardioversion. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.8 of the SmPC as per the requirement of the finalised PSUSA/00010387/201610 procedure to include headache, abdominal pain and dizziness with a common frequency as new adverse drug reactions. The MAH also took the opportunity to bring the PI in line with the latest QRD template version 10.0 and to introduce some editorial changes and minor corrections.”
Opinion adopted on 30.11.2017.

Positive Opinion adopted by consensus on 30.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Simponi - golimumab -

EMA/H/C/000992/II/0078/G

MAH: Janssen Biologics B.V., Rapporteur: Kristina Dunder, “Update of sections 4.4 and 4.8 of the SmPC in order to add a warning on agranulocytosis and update neutropenia from uncommon to common based on new safety information in the Company Core Data Sheet (CCDS).

The Marketing Authorisation Holder has taken the opportunity to include the safety data from the intravenous (IV) psoriatic arthritis (PsA), and IV ankylosing spondylitis (AS) studies that were recently included in the CCDS.

The Package Leaflet is updated accordingly.”
Request for Supplementary Information adopted on 14.12.2017.

Request for Supplementary Information adopted

Starlix - nateglinide -

EMA/H/C/000335/II/0033

MAH: Novartis Europharm Limited, Rapporteur:

Request for Supplementary Information adopted

Greg Markey, "Update of section 5.2 of the SmPC to add information on the accumulation of M1 metabolite in diabetic patients with end-stage renal disease (ESRD), based on the review of the Core Data Sheet. This information is reflected in section 4.4 of the SmPC. The Package Leaflet and Labelling are updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with QRD template 10, combine the three SmPC into a single SmPC, align sections 1 and 2 of the package leaflet with the SmPC, and correct the name of the local representatives for Latvia and Bulgaria."

Request for Supplementary Information adopted on 07.12.2017.

Sutent - sunitinib -

EMA/H/C/000687/II/0067

MAH: Pfizer Limited, Rapporteur: Daniela Melchiorri, "Update of sections 4.5 and 5.2 of the SmPC in order to include information regarding a possible interaction between sunitinib and other medicinal products that are inhibitors of the efflux transporter breast cancer resistance protein (BCRP) following assessment of PAM (REC 052)."

Opinion adopted on 07.12.2017.

Positive Opinion adopted by consensus on 07.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Tafinlar - dabrafenib -

EMA/H/C/002604/II/0027

MAH: Novartis Europharm Limited, Rapporteur: Filip Josephson, "Submission of the final report from study BRF113683 (BREAK-3) listed as a category 3 study in the RMP. This is a phase III, randomised, two-arm, open label study comparing dabrafenib to dacarbazine (DTIC) in previously untreated patients with BRAF mutation positive advanced (stage III) or metastatic (stage IV) melanoma. This study is aimed to confirm the superior efficacy of dabrafenib compared to DTIC."

Opinion adopted on 14.12.2017.

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Torisel - temsirolimus -

EMA/H/C/000799/II/0069, Orphan

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

Request for Supplementary Information adopted

MAH took the opportunity to make minor editorial changes in the Package Leaflet.”
Request for Supplementary Information adopted on 14.12.2017.

Translarna - ataluren -

Request for Supplementary Information adopted

EMA/H/C/002720/II/0039, Orphan

MAH: PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.2, 4.4, and 5.2 of the SmPC to include new clinical information based on final results from study PTC124-GD-033-HV (Study 033) listed as a category 3 study in the RMP (MEA009); this is a Safety and PK study in patients with moderate to severe hepatic impairment; the Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0 and to implement some editorial changes.”

Request for Supplementary Information adopted on 14.12.2017.

Trumenba - meningococcal group B vaccine (recombinant, adsorbed) -

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

EMA/H/C/004051/II/0002/G

MAH: Pfizer Limited, Rapporteur: Johann Lodewijk Hillege, “Update of section 4.4 of the SmPC in order to add a warning on syncope based on review of post-marketing data. Update of section 4.8 of the SmPC in order to update the safety information regarding booster vaccination based a review of adverse events data reported in the interim clinical study report (B1971033). The package leaflet is updated accordingly. In addition, the MAH took the opportunity to make a clarification on interchangeability of Trumenba in section 4.2 of the SmPC and to update the list of local representatives in the package leaflet.”

Opinion adopted on 14.12.2017.

Vectibix - panitumumab -

Request for Supplementary Information adopted

EMA/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.”

Request for Supplementary Information adopted on 07.12.2017.

Velphoro - mixture of polynuclear iron(III)-oxyhydroxide, sucrose and starches - EMEA/H/C/002705/II/0012

MAH: Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Johann Lodewijk Hillege, “Update of section 4.4 of the SmPC in order to remove a warning related to allergy to gluten. The Package Leaflet has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor corrections in the SmPC in line with the Company Core Data Sheet (CCDS). Moreover, the MAH took the opportunity to bring the Annex IIIA in line with the latest QRD template version 10.”

Opinion adopted on 16.11.2017.

Positive Opinion adopted by consensus on 16.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Venclyxto - venetoclax - EMEA/H/C/004106/II/0007/G, Orphan

MAH: AbbVie Limited, Rapporteur: Filip Josephson, “Update of section 4.5 of the SmPC in order to update the drug-drug interaction between venetoclax and digoxin based on final results from study M16-042; this is study to assess the effect of venetoclax on the pharmacokinetics of digoxin in healthy female subjects.

Update of section 4.5 of the SmPC in order to update the drug-drug interaction between venetoclax and ritonavir, based on final results from study M15-719; this is study to assess the effect of ritonavir on the pharmacokinetics of venetoclax in healthy female subjects of non-childbearing potential.

Update of section 4.5 of the SmPC in order to update the drug-drug interaction between venetoclax and azithromycin, based on final results from study M16-068; this is study to assess effect of azithromycin on the pharmacokinetics of venetoclax in healthy female subjects.

The MAH took the opportunity to update the Product Information with minor editorial and QRD updates.”

Request for Supplementary Information adopted

Request for Supplementary Information adopted

on 14.12.2017.

Xeljanz - tofacitinib -

EMA/H/C/004214/II/0003

MAH: Pfizer Limited, Rapporteur: Robert James Hemmings, "Update of section 4.5 and 5.2 of the SmPC to add results of in vitro transporter inhibition studies evaluating tofacitinib for its potential to inhibit organic anion transporter (OAT1, OAT3) and to interact with MRP2 Transporter, in order to fulfil a CHMP recommendation."

Opinion adopted on 07.12.2017.

Request for Supplementary Information adopted on 14.09.2017.

Positive Opinion adopted by consensus on 07.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Zeffix - lamivudine -

EMA/H/C/000242/II/0069

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

Request for Supplementary Information adopted on 14.12.2017, 21.09.2017, 05.05.2017.

Request for Supplementary Information adopted

Zostavax - shingles (herpes zoster) vaccine (live) - EMA/H/C/000674/II/0115

MAH: MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, "Update section 4.4 of the SmPC to complement the safety information regarding the vaccination of contraindicated immunodeficient individuals based on three post-marketing reports."

In addition, the MAH took the opportunity to make some editorial changes to the English product information and to following linguistic versions of the product information: Dutch, Czech, Greek, Spanish, Italian, Norwegian, Polish, Portuguese, Swedish, Slovenian, Slovak, Croatian, Hungarian and Finish."

Opinion adopted on 23.11.2017.

Positive Opinion adopted by consensus on 23.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Zykadia - ceritinib -

EMA/H/C/003819/II/0016

MAH: Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.2, 4.4, 4.8 and 5.2 of the SmPC in order to

Request for Supplementary Information adopted

include amendments to the posology in hepatically impaired patients and update the safety information, respectively. The updates are based on the results from the hepatic function Study CLDK378A2110 which evaluated the PK, safety and tolerability of a single oral dose of ceritinib in subjects with varying degrees of impaired hepatic function and results from physiology-based pharmacokinetic (PBPK) modeling at steady-state.

Submission of the Report for Study A2110 fulfils MEA 001 for Zykadia."

Request for Supplementary Information adopted on 14.12.2017, 09.11.2017, 14.09.2017.

WS1137

**Lyrice-EMEA/H/C/000546/WS1137/0087
Pregabalin Pfizer-**

EMEA/H/C/003880/WS1137/0017

MAH: Pfizer Limited, Lead Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect final results from paediatric study A0081041: "A Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study of the Efficacy and Safety of Pregabalin as Adjunctive Therapy in Children 4-16 Years of Age with Partial Onset Seizures"."

Opinion adopted on 16.11.2017.

Request for Supplementary Information adopted on 14.09.2017, 08.05.2017.

Positive Opinion adopted by consensus on 16.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1156

Combivir-

EMEA/H/C/000190/WS1156/0090

Kivexa-EMEA/H/C/000581/WS1156/0072

Triumeq-

EMEA/H/C/002754/WS1156/0042

Trizivir-EMEA/H/C/000338/WS1156/0104

MAH: ViiV Healthcare UK Limited, Lead Rapporteur: Joseph Emmerich, "Update of section 4.5 of the SmPC to add information regarding the potential interaction between lamivudine and sorbitol based on the results of Study 204857. The Package Leaflet has been updated accordingly. Further, a minor amendment has been implemented throughout the SmPC in order to update the clinical terminology of Pneumocystis carinii pneumonia to Pneumocystis jiroveci pneumonia. In addition, the MAH takes the opportunity to make minor editorial changes, to align the

Request for Supplementary Information adopted

annexes with the QRD template version 10 and to update the contact details of the local representative in Norway in the Package Leaflet.”

Request for Supplementary Information adopted on 14.12.2017, 21.09.2017, 05.05.2017.

WS1210/G

Request for Supplementary Information adopted

Mekinist-

EMA/H/C/002643/WS1210/0021/G

Tafinlar-

EMA/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.” Request for Supplementary Information adopted on 30.11.2017, 05.10.2017.

WS1219

Positive Opinion adopted by consensus on 16.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Brimica Genuair-

EMA/H/C/003969/WS1219/0014

Duaklir Genuair-

EMA/H/C/003745/WS1219/0014

MAH: AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, “Update of section 5.2 of the SmPC in order to update information based on results from study KRP-AB1102F-302 [KRP-AB1102F Phase II Clinical Pharmacology Study - An Investigation into the Pharmacokinetics upon Repeated Administration of KRP-AB1102F to COPD Patients as Subjects]. In addition, the Worksharing applicant (WSA) took the opportunity to update footnotes of the table in section 4.8 as requested during PSUR procedure EMA/H/C/PSUSA/00010307/201511 and to amend annex II following request from

procedure EMEA/H/C/PSA/S/0017.”
Opinion adopted on 16.11.2017.
Request for Supplementary Information adopted
on 14.09.2017.

B.5.3. CHMP-PRAC assessed procedures

Caprelsa - vandetanib -

Request for Supplementary Information adopted

EMEA/H/C/002315/II/0028

MAH: Genzyme Europe BV, Rapporteur:
Alexandre Moreau, PRAC Rapporteur: Ghania
Chamouni, “Update of sections 4.1, 4.4 and 5.1
of the SmPC in order to delete the information
regarding Rearranged during Transfection (RET)
mutation. The application addresses SOB 001
and the MAH proposes to revert from
conditional marketing authorisation to standard
marketing authorisation. Annex II and Package
Leaflet are updated accordingly. The RMP
version 12.2 has also been submitted. In
addition, the MAH took the opportunity to bring
the PI in line with the latest QRD template
version 10.”

Request for Supplementary Information adopted
on 14.12.2017.

Cerdelga - eliglustat -

Request for Supplementary Information adopted

EMEA/H/C/003724/II/0015/G, Orphan

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

Request for Supplementary Information adopted
on 14.12.2017.

Cimzia - certolizumab pegol -

Positive Opinion adopted by consensus on

EMEA/H/C/001037/II/0060

14.12.2017. The Icelandic and Norwegian CHMP

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

Members were in agreement with the CHMP

Dunder, PRAC Rapporteur: Ulla Wändel Liminga, recommendation.

“Update of sections 4.6 and 5.3 of the SmPC in order to update the information on pregnancy and lactation based on two pharmacokinetics studies evaluation the transfer of Cimzia into breastmilk and via the placenta (UP0016 and UP0017). The Package Leaflet is updated accordingly. The RMP version 12.1 has also been agreed.”

Opinion adopted on 14.12.2017.

Request for Supplementary Information adopted on 09.11.2017, 14.09.2017, 22.06.2017.

Defitelio - defibrotide -

Request for Supplementary Information adopted

EMA/H/C/002393/II/0026, Orphan

MAH: Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams,

“Update of sections 4.8 and 5.1 of the SmPC in order to update the frequencies of adverse reactions included in the tabulated list of adverse reactions and to update the clinical efficacy and safety information based on the results from study 2006-05 listed as category 3 in the RMP. This is a phase 3, open-label expanded access study designed to provide access to defibrotide as an investigational new drug to patients with severe hepatic veno-occlusive disease. The final study report is being submitted together with the revised risk management plan (version 3.0). The package leaflet is also being updated accordingly. In addition, the MAH took the opportunity to bring the SmPC in line with the latest QRD template (version 10), to update the list of local representatives in the package leaflet and to correct a translation error in the Polish, Finnish, Danish and Latvian languages.”

Request for Supplementary Information adopted on 30.11.2017, 28.09.2017.

Dificlir - fidaxomicin -

Request for Supplementary Information adopted

EMA/H/C/002087/II/0032/G

MAH: Astellas Pharma Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Qun-Ying Yue, “C.I.11.b)

Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to update the safety information following final results from the drug utilisation study ANEMONE listed as an additional pharmacovigilance activity in the RMP. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder

(MAH) took the opportunity to update the list of local representatives in the Package Leaflet.

C.1.3

Update of sections 4.4 and 5.2 of the SmPC in order to update the safety information based on results from the PROFILE study, an open label study designed to evaluate the pharmacokinetics of fidaxomicin in IBD subjects with CD. The Package Leaflet is updated accordingly.

The RMP version 9.0 has also been submitted.”
Request for Supplementary Information adopted on 30.11.2017.

**Ibrance - palbociclib -
EMA/H/C/003853/II/0007**

MAH: Pfizer Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver, “Update of sections 4.2, 4.4 and 5.2 of the SmPC to reflect the results of PK studies on the impact of hepatic impairment (Study A5481013) and the impact of renal impairment (Study A5481014). The RMP (version 1.4) is amended to reflect the completion of these studies.”
Opinion adopted on 14.12.2017.
Request for Supplementary Information adopted on 14.09.2017.

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Imraldi - adalimumab -
EMA/H/C/004279/II/0002/G**

MAH: Samsung Bioepis UK Limited (SBUK), Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Ulla Wändel Liminga
Request for Supplementary Information adopted on 30.11.2017.

Request for Supplementary Information adopted

**INOmax - nitric oxide -
EMA/H/C/000337/II/0051**

MAH: Linde Healthcare AB, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams
Request for Supplementary Information adopted on 14.12.2017, 12.10.2017.

Request for Supplementary Information adopted

**Keytruda - pembrolizumab -
EMA/H/C/003820/II/0037/G**

MAH: Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus, “Update of sections 4.4 and 4.8 of the SmPC to add information regarding the risks of encephalitis, sarcoidosis

Request for Supplementary Information adopted

and graft versus host disease (GVHD) that have been reported in patients treated with pembrolizumab. The Package Leaflet and the 'additional risk minimization measures' section (educational material) in the Annex II have been updated accordingly. In addition, the MAH has implemented minor changes in the SmPC section 5.1 and editorial changes in the Package Leaflet.

An updated RMP version 13.0 was provided as part of the application."

Request for Supplementary Information adopted on 14.12.2017.

Kuvan - sapropterin -

Request for Supplementary Information adopted

EMA/H/C/000943/II/0052, Orphan

MAH: BioMarin International Limited,

Rapporteur: Peter Kiely, PRAC Rapporteur:

Almath Spooner, "Based on a review of the post-marketing experience and in order to harmonize the safety information with the CCDS, update of section 4.4 of the Kuvan SmPC to add a warning regarding gastritis and update of section 4.8 to add the following adverse events regarding gastrointestinal tract and respiratory irritation: oropharyngeal pain, oesophageal pain, dyspepsia, nausea, gastritis and pharyngitis.

The Package Leaflet is updated accordingly. The RMP version 13.0 has also been submitted."

Request for Supplementary Information adopted on 30.11.2017.

Kyprolis - carfilzomib -

Request for Supplementary Information adopted

EMA/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 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.” Request for Supplementary Information adopted on 14.12.2017, 12.10.2017.

**Neulasta - pegfilgrastim -
EMA/H/C/000420/II/0093/G**

Request for Supplementary Information adopted

MAH: Amgen Europe B.V., Rapporteur: Robert James Hemmings, PRAC Rapporteur: Patrick Batty
Request for Supplementary Information adopted on 14.12.2017, 14.09.2017, 22.06.2017.

**Olumiant - baricitinib -
EMA/H/C/004085/II/0003**

Request for Supplementary Information adopted

MAH: Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Patrick Batty, “Update of section 4.4 of the SmPC in order to include results of a vaccination sub-study of the long term extension study I4V-MC-JADY (I4V-MC-JADY: ‘A Phase 3, Multicenter Study to Evaluate the Long-Term Safety and Efficacy of Baricitinib in Patients with Rheumatoid Arthritis’). In addition, the updated RMP version 4.0 has been submitted as part of this application.” Request for Supplementary Information adopted on 14.12.2017.

**Orkambi - lumacaftor / ivacaftor -
EMA/H/C/003954/II/0017**

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

MAH: Vertex Pharmaceuticals (Europe) Ltd., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Almath Spooner, “Updates of sections 4.8 and 5.1 of the SmPC in order to reflect the long-term safety and efficacy data from Study VX12 809 105. Study VX12 809 105 was a Phase 3, rollover study to evaluate the safety and efficacy of long term treatment with LUM/IVA in subjects aged 12 years and older with cystic fibrosis, homozygous or heterozygous for the F508del CFTR mutation (MEA 001). A new version of the RMP (ver. 3.5) included in this submission has been updated to include the final data from Study 105. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10 and to make editorial corrections.”

Opinion adopted on 14.12.2017.

Request for Supplementary Information adopted on 12.10.2017, 18.05.2017, 23.02.2017.

**Sivextro - tedizolid phosphate -
EMA/H/C/002846/II/0019**

MAH: Merck Sharp & Dohme Limited,
Rapporteur: Bruno Sepodes, PRAC Rapporteur:
Dolores Montero Corominas, "Update of section 4.8 of the SmPC of the concentrate for solution for infusion formulation, in order to add information from BAY119-2631/16121, a Phase 3 randomized, double-blind, multi-centre study comparing the efficacy and safety of intravenous to oral 6-day tedizolid phosphate and intravenous to oral 10 day linezolid for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and change the reported expected frequency of the adverse reaction "infusion site phlebitis" from "uncommon" to "common". The Package Leaflet is updated accordingly. An updated RMP (version 3.2) has also been submitted, proposing to collect safety information regarding tedizolid phosphate by conducting three investigator initiated studies and deleting the original proposed long term safety study. The MAH also took the opportunity to make minor editorial corrections throughout the product information."

Opinion adopted on 30.11.2017.

Request for Supplementary Information adopted on 28.09.2017, 06.07.2017.

Positive Opinion adopted by consensus on 30.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Soliris - eculizumab -
EMA/H/C/000791/II/0098, Orphan**

MAH: Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia, "Update of sections 4.6 and 5.3 of the SmPC in order to update the safety information related to pregnancy, lactation and fertility following the review of data in PSUR 13 and 14. Annex II and the Package Leaflet are updated accordingly. In addition, Annex IIIA is updated to introduce headers for the unique identifier-2D barcode and human readable data. The RMP version 17.2 has been submitted with updated information on pregnancy and lactation and fertility."

Opinion adopted on 14.12.2017.

Request for Supplementary Information adopted

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 14.09.2017.

Sylvant - siltuximab -

Request for Supplementary Information adopted

EMA/H/C/003708/II/0026/G, Orphan

MAH: Janssen-Cilag International NV,
Rapporteur: Concepcion Prieto Yerro, PRAC
Rapporteur: Brigitte Keller-Stanislawski,
"Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to update the product information following final results from studies CNTO328MCD2001 and CNTO328MCD2002 listed as imposed obligation in the Annex II. The Package Leaflet are updated accordingly. The RMP version 4.0 has also been submitted."
Request for Supplementary Information adopted on 30.11.2017.

Letter from the applicant dated 18.12.2017 requesting a clock stop extension.

Tecentriq - atezolizumab -

Request for Supplementary Information adopted

EMA/H/C/004143/II/0002/G

MAH: Roche Registration Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Grouped variations consisting of: 1) update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add myocarditis as a new adverse reaction based on the results of a cumulative review of cases of suspected myocarditis. As a consequence, the information regarding the posology and special warnings have been updated. Annex II, the Package Leaflet and the RMP (version 2.0) have been updated accordingly; 2) update of the RMP to add haemolytic anaemia as a new important identified potential risk"

Request for Supplementary Information adopted on 14.12.2017.

Trulicity - dulaglutide -

Request for Supplementary Information adopted

EMA/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." Request for Supplementary Information adopted on 30.11.2017.

**Xalkori - crizotinib -
EMA/H/C/002489/II/0050**

MAH: Pfizer Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of sections 4.2, 4.3, 4.4, 4.8 and 5.2 of the SmPC in order to update the information about hepatic impairment based on the results of study (A8081012) which evaluated the effect of hepatic impairment on the pharmacokinetics and safety of crizotinib in advanced cancer patients. The package leaflet is updated accordingly. In addition, the final study report of study (A8081012) and an updated RMP version 7.4 are also being submitted."

Opinion adopted on 14.12.2017.

Request for Supplementary Information adopted on 12.10.2017.

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Zydelig - idelalisib -
EMA/H/C/003843/II/0035/G**

MAH: Gilead Sciences International Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, "Update of section 5.3 of the SmPC in order to revise the carcinogenicity information for idelalisib based on final results from two long term carcinogenicity studies (TX-312-2017, TX-312-2019). The RMP version 2.3 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0."

Opinion adopted on 30.11.2017.

Request for Supplementary Information adopted on 28.09.2017.

Positive Opinion adopted by consensus on 30.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

**Zydelig - idelalisib -
EMA/H/C/003843/II/0038**

MAH: Gilead Sciences International Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to reflect information from a recent cumulative safety review of cases of organising pneumonia. The safety review

Request for Supplementary Information adopted

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.”.”
Request for Supplementary Information adopted on 14.12.2017.

**Zykadia - ceritinib -
EMA/H/C/003819/II/0015**

Request for Supplementary Information adopted

MAH: Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Ulla Wändel Liminga, “Update of sections 4.2, 4.4, 4.5, 4.8 and 5.2 of the SmPC in order to update the safety information based on based on the primary PK and preliminary safety results of the food effect study CLDK378A2112. The Package Leaflet is updated accordingly.

The RMP version 9.0 has also been submitted.”
Request for Supplementary Information adopted on 14.12.2017, 12.10.2017, 22.06.2017.

**WS1026
Rasilez-EMA/H/C/000780/WS1026/0110
Rasilez HCT-
EMA/H/C/000964/WS1026/0080**

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

MAH: Noden Pharma DAC, Lead Rapporteur: Daniela Melchiorri, Lead PRAC Rapporteur: Carmela Macchiarulo, “Update of section 5.1 of the SmPC in order to reflect the results of study SPP100F2301 (ATMOSPHERE) a multicenter, randomized, doubleblind, parallel group, active-controlled study to evaluate the efficacy and safety of both aliskiren monotherapy and aliskiren/enalapril combination therapy compared to enalapril monotherapy, on morbidity and mortality in patients with chronic heart failure (NYHA Class II - IV).

The RMP (v 13.2) has also been updated to reflect the study results.”
Opinion adopted on 14.12.2017.
Request for Supplementary Information adopted on 09.11.2017, 14.09.2017, 22.06.2017, 21.04.2017, 15.12.2016.

**WS1190/G
Enbrel-
EMA/H/C/000262/WS1190/0210/G**

See 9.1 in main agenda

LIFMIOR-**EMA/H/C/004167/WS1190/0009/G**

MAH: Pfizer Limited, Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Patrick Batty

Request for Supplementary Information adopted on 30.11.2017, 28.09.2017.

WS1248/G**Blitzima-****EMA/H/C/004723/WS1248/0002/G****Ritemvia-****EMA/H/C/004725/WS1248/0002/G****Rituzena-****EMA/H/C/004724/WS1248/0003/G**

MAH: Celltrion Healthcare Hungary Kft., Duplicate, Duplicate of Truxima, Lead Rapporteur: Sol Ruiz, Lead PRAC Rapporteur: Doris Stenver

Opinion adopted on 30.11.2017.

Positive Opinion adopted by consensus on 30.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1292**Evotaz-EMA/H/C/003904/WS1292/0019****Reyataz-****EMA/H/C/000494/WS1292/0114**

MAH: Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Joseph Emmerich, Lead PRAC Rapporteur: Caroline Laborde, "Update of section 4.3 and 4.5 of the SmPC in order to add a contraindication with lurasidone to reflect this interaction based on literature data. The Package Leaflet is updated accordingly. The RMP of Reyataz/Evotaz versions 14 and 6 respectively have been submitted."

Request for Supplementary Information adopted on 14.12.2017.

Request for Supplementary Information adopted

B.5.4. PRAC assessed procedures

PRAC Led

Arzerra - ofatumumab -**EMA/H/C/001131/II/0054, Orphan**

MAH: Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Update of the RMP (version 14.1) in order to amend the study milestones for two studies:
- study OMB112517, a phase III, open label, randomized, multicentre trial of ofatumumab maintenance treatment versus no further treatment in subjects with relapsed CLL who

Positive Opinion adopted by consensus on 30.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

have responded to induction therapy: final study report to be submitted by 30 June 2019 - study OMB110913, a phase III, open label, randomized trial of ofatumumab added to fludarabine-cyclophosphamide versus fludarabine-cyclophosphamide combination in subjects with relapsed CLL: final study report to be submitted by 30 June 2019.

In addition, changes have been implemented in the safety specifications as previously agreed during the last PSUR outcome (EMA/H/C/PSUSA/00002202/201610) to upgrade the potential risk of infections and progressive multifocal leukoencephalopathy from potential to an identified risk.”
Opinion adopted on 30.11.2017.

PRAC Led

Request for Supplementary Information adopted

**Betaferon - interferon beta-1b -
EMA/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.”
Request for Supplementary Information adopted on 30.11.2017.

PRAC Led

Positive Opinion adopted by consensus on 30.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Eliquis - apixaban -

EMA/H/C/002148/II/0048

MAH: Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of the final report from study (B0661073) listed as a category 4 study in the RMP. This is a non-interventional post-authorisation safety study (PASS) of the utilisation patterns of apixaban in Denmark. In addition, a revised RMP (version 18.0) is submitted.”
Opinion adopted on 30.11.2017.

PRAC Led

Request for Supplementary Information adopted

Eylea - aflibercept -

EMA/H/C/002392/II/0039

MAH: Bayer AG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, “Submission of

the final report from the post authorisation safety study 16526, listed as a category 3 study in the RMP. This is an observational study to evaluate the physician and patient knowledge of safety and safe use information for Aflibercept in Europe as stated in the EU Educational Material of Eylea.”

Request for Supplementary Information adopted on 30.11.2017.

PRAC Led

Request for Supplementary Information adopted

Nulojix - belatacept -

EMA/H/C/002098/II/0047/G

MAH: Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, “Submission of the final report from studies IM103061 and IM103089, listed as a category 3 studies in the RMP.

IM103061 is an epidemiological study on pregnancy outcome among belatacept users in the US.

IM103089 evaluates data retrospectively to assess the association between belatacept and the risk of PTDL in renal transplant recipients in Europe.

An updated RMP, reflecting completion of the two above studies is being submitted as part of this variation (Version 15).”

Request for Supplementary Information adopted on 30.11.2017.

PRAC Led

Request for Supplementary Information adopted

Sebivo - telbivudine -

EMA/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 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

Positive Opinion adopted by consensus on 30.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Xarelto - rivaroxaban -

EMA/H/C/000944/II/0055

MAH: Bayer AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final study report of a non-interventional PASS listed as a category 3 study in the RMP (MEA 019): An Observational Post-Authorization Safety Specialist Cohort Event Monitoring Study (SCEM) to Monitor the Safety and Utilization of Rivaroxaban (Xarelto) for the Prevention of Stroke in Patients with AF, Treatment of DVT and PE, and the Prevention of Recurrent DVT and PE in the Secondary Care Setting in England and Wales (The ROSE Study), study number 16171."
Opinion adopted on 30.11.2017.
Request for Supplementary Information adopted on 28.09.2017.

PRAC Led
WS1164
Glyxambi-
EMA/H/C/003833/WS1164/0008
Jardiance-
EMA/H/C/002677/WS1164/0033
Synjardy-
EMA/H/C/003770/WS1164/0030

MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Dolores Montero Corominas, PRAC-CHMP liaison: Concepcion Prieto Yerro, "C.I.11: Submission of an updated RMP for Jardiance (v12.1), for Synjardy (9.2) and for Glyxambi (v3.0) in order to address the PRAC recommendation concluded in the Article 20 referral for SGLT2 inhibitors on the important potential risk for lower limb amputation. Additionally, the PRAC request to include pancreatitis as important potential risk for empagliflozin-containing medicines following the conclusion adopted by the PRAC after the review of PSUSA/00010077/201603 (canagliflozin) is discussed."
Opinion adopted on 30.11.2017.
Request for Supplementary Information adopted on 28.09.2017.

PRAC Led
WS1207
Bretaris Genuair-
EMA/H/C/002706/WS1207/0034
Eklira Genuair-
EMA/H/C/002211/WS1207/0034

recommendation.

Positive Opinion adopted by consensus on 30.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Positive Opinion adopted by consensus on 30.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

MAH: AstraZeneca AB, Lead Rapporteur:
Nithyanandan Nagercoil, Lead PRAC Rapporteur:
Julie Williams, PRAC-CHMP liaison: Robert
James Hemmings, "Submission of the final
report from study D6560R00005, (Aclidinium
Bromide Drug Utilisation Post-Authorisation
Safety Studies (DUS 1) in the United Kingdom,
Denmark, and Germany) listed as a category 3
study in the RMP (MEA002). The updated RMP
version 6.0 has also been submitted."
Opinion adopted on 30.11.2017.
Request for Supplementary Information adopted
on 28.09.2017.

PRAC Led
WS1229
Ebymect-
EMA/H/C/004162/WS1229/0025
Edistride-
EMA/H/C/004161/WS1229/0019
Forxiga-
EMA/H/C/002322/WS1229/0039
Xigduo-EMA/H/C/002672/WS1229/0036

MAH: AstraZeneca AB, Lead Rapporteur:
Kristina Dunder, Lead PRAC Rapporteur: Qun-
Ying Yue, PRAC-CHMP liaison: Kristina Dunder,
"Submission of the final report from study
D1690R00013 listed as a category 3 study in
the RMP: Incidence of Diabetic Ketoacidosis
among Patients with Type 2 Diabetes in the
United States.
The RMP version 15 (Forxiga/Edistride) and
version 10 (Xigduo/Ebymect) have been
consequentially updated."
Opinion adopted on 30.11.2017.

Positive Opinion adopted by consensus on
30.11.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

PRAC Led
WS1256
Harvoni-
EMA/H/C/003850/WS1256/0059
Sovaldi-EMA/H/C/002798/WS1256/0044

MAH: Gilead Sciences International Limited,
Lead PRAC Rapporteur: Julie Williams, PRAC-
CHMP liaison: Greg Markey, "Submission of the
final report from study GS-EU-337-2030, listed
as a category 3 study in the RMP. This is an
observational, cross-sectional post-authorisation
safety study to assess healthcare provider
awareness of risks related to sofosbuvir and
ledipasvir/sofosbuvir."
Opinion adopted on 30.11.2017.

Positive Opinion adopted by consensus on
30.11.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

PRAC Led
WS1259
Ebymect-
EMA/H/C/004162/WS1259/0024
Edistride-
EMA/H/C/004161/WS1259/0018
Forxiga-
EMA/H/C/002322/WS1259/0038
Xigduo-EMA/H/C/002672/WS1259/0035
MAH: AstraZeneca AB, Lead Rapporteur:
Kristina Dunder, Lead PRAC Rapporteur: Qun-
Ying Yue, PRAC-CHMP liaison: Kristina Dunder,
"Submission of the final report for the Drug
Utilisation Study MB102-134 listed as a
category 3 study in the RMP: Observational
Single-cohort Data Base Study of Dapagliflozin
Utilization in Europe. The RMP version 15
(Forxiga/Edistride) and version 10
(Xigduo/Ebymect) have been consequentially
updated."
Opinion adopted on 30.11.2017.

Positive Opinion adopted by consensus on
30.11.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

PRAC Led
WS1264
Ariclaim-
EMA/H/C/000552/WS1264/0068
Cymbalta-
EMA/H/C/000572/WS1264/0072
Duloxetine Lilly-
EMA/H/C/004000/WS1264/0008
Xeristar-
EMA/H/C/000573/WS1264/0075
Yentreve-
EMA/H/C/000545/WS1264/0058
MAH: Eli Lilly Nederland B.V., Duplicate,
Duplicate of Yentreve, Lead Rapporteur:
Concepcion Prieto Yerro, Lead PRAC Rapporteur:
Dolores Montero Corominas, PRAC-CHMP
liaison: Concepcion Prieto Yerro, "Submission of
the final report from study F1J-MC-B056 listed
as a category 3 study in the RMP. This is a non-
interventional non-imposed study aimed to
investigate the association between duloxetine
exposure and suicide-related behaviours and
ideation in women with stress urinary
inconsistence (SUI). The RMP version 12.3 has
also been submitted."
Request for Supplementary Information adopted
on 30.11.2017.

Request for Supplementary Information adopted

PRAC Led
WS1294

Positive Opinion adopted by consensus on
14.12.2017. The Icelandic and Norwegian CHMP

Actos-EMEA/H/C/000285/WS1294/0078
Competact-
EMEA/H/C/000655/WS1294/0068
Glubrava-
EMEA/H/C/000893/WS1294/0055
Glustin-EMEA/H/C/000286/WS1294/0077
Tandemact-
EMEA/H/C/000680/WS1294/0056

Members were in agreement with the CHMP recommendation.

MAH: Takeda Pharma A/S, Informed Consent of Competact, Lead PRAC Rapporteur: Almath Spooner, PRAC-CHMP liaison: Peter Kiely, "To update the RMPs to version 24.0 for Actos & Glustin (pioglitazone), version 22.0 for Tandemact (pioglitazone/ glimepiride), and version 25.0 for Compeact & Glubrava (pioglitazone/metformin); the RMPs have been updated as follows:

- For all RMPs, addition of information regarding the effect of pioglitazone on bone mineral density and the increased risk of fractures from the study AD4833-402 addendum report as recommended in conclusion to the assessment of the following post-authorisation measures (PAM): Actos MEA 068.2, Glustin MEA 070.2, Competact MEA 029.2, Glubrava MEA 018.2, Tandemact MEA 027.2.

- For pioglitazone/metformin RMPs only, addition of lactic acidosis questionnaire as recommended in conclusion to the assessment of variation EMEA/H/C/WS0991.

The MAH also took the opportunity to make some general edits to all RMPs."

Opinion adopted on 14.12.2017.

B.5.5. CHMP-CAT assessed procedures

MACI - matrix applied characterised autologous cultured chondrocytes - EMEA/H/C/002522/II/0014/G, ATMP

MAH: Vericel Denmark ApS, Rapporteur: Christiane Niederlaender,

Request for Supplementary Information adopted on 08.12.2017.

Request for Supplementary Information adopted

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

WS1185/G

Hexacima-

EMA/H/C/002702/WS1185/0065/G

Hexaxim-

EMA/H/W/002495/WS1185/0071/G

Hexyon-

EMA/H/C/002796/WS1185/0069/G

MAH: Sanofi Pasteur Europe, Duplicate,
Duplicate of Hexacima, Lead Rapporteur: Jan
Mueller-Berghaus

Opinion adopted on 16.11.2017.

Request for Supplementary Information adopted
on 14.09.2017.

Positive Opinion adopted by consensus on
16.11.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

WS1199/G

ProQuad-

EMA/H/C/000622/WS1199/0120/G

Zostavax-

EMA/H/C/000674/WS1199/0114/G

MAH: MSD Vaccins, Lead Rapporteur: Jan
Mueller-Berghaus

Opinion adopted on 16.11.2017.

Positive Opinion adopted by consensus on
16.11.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

WS1202/G

Efficib-

EMA/H/C/000896/WS1202/0084/G

Janumet-

EMA/H/C/000861/WS1202/0084/G

Januvia-

EMA/H/C/000722/WS1202/0058/G

Ristaben-

EMA/H/C/001234/WS1202/0050/G

Ristfor-

EMA/H/C/001235/WS1202/0071/G

TESAVEL-

EMA/H/C/000910/WS1202/0058/G

Velmetia-

EMA/H/C/000862/WS1202/0087/G

Xelevia-

EMA/H/C/000762/WS1202/0062/G

MAH: Merck Sharp & Dohme Limited, Lead
Rapporteur: Johann Lodewijk Hillege,
Opinion adopted on 16.11.2017.

Request for Supplementary Information adopted

Positive Opinion adopted by consensus on
16.11.2017. The Icelandic and Norwegian CHMP
Members were in agreement with the CHMP
recommendation.

on 14.09.2017.

WS1245

Infanrix hexa-

EMA/H/C/000296/WS1245/0228

MAH: GlaxoSmithkline Biologicals SA, Lead

Rapporteur: Bart Van der Schueren

Opinion adopted on 30.11.2017.

Positive Opinion adopted by consensus on 30.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1246/G

Epclusa-

EMA/H/C/004210/WS1246/0017/G

Harvoni-

EMA/H/C/003850/WS1246/0060/G

Sovaldi-

EMA/H/C/002798/WS1246/0045/G

Vosevi-

EMA/H/C/004350/WS1246/0005/G

MAH: Gilead Sciences International Limited,

Lead Rapporteur: Filip Josephson,

Opinion adopted on 30.11.2017.

Positive Opinion adopted by consensus on 30.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1250/G

Infanrix hexa-

EMA/H/C/000296/WS1250/0230/G

MAH: GlaxoSmithkline Biologicals SA, Lead

Rapporteur: Bart Van der Schueren

Opinion adopted on 14.12.2017.

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1255

Infanrix hexa-

EMA/H/C/000296/WS1255/0231

MAH: GlaxoSmithkline Biologicals SA, Lead

Rapporteur: Bart Van der Schueren

Opinion adopted on 14.12.2017.

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1257

Infanrix hexa-

EMA/H/C/000296/WS1257/0229

MAH: GlaxoSmithkline Biologicals SA, Lead

Rapporteur: Bart Van der Schueren

Opinion adopted on 14.12.2017.

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1263/G

Avamys-

EMA/H/C/000770/WS1263/0035/G

Relvar Ellipta-

EMA/H/C/002673/WS1263/0034/G

Revinty Ellipta-

EMA/H/C/002745/WS1263/0030/G

MAH: Glaxo Group Ltd, Lead Rapporteur:

Concepcion Prieto Yerro

Opinion adopted on 16.11.2017.

Positive Opinion adopted by consensus on 16.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

<p>WS1271/G Ebymect- EMA/H/C/004162/WS1271/0028/G Qtern- EMA/H/C/004057/WS1271/0010/G Xigduo- EMA/H/C/002672/WS1271/0039/G MAH: AstraZeneca AB, Lead Rapporteur: Kristina Dunder Opinion adopted on 23.11.2017.</p>	<p>Positive Opinion adopted by consensus on 23.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>WS1279 Helixate NexGen- EMA/H/C/000276/WS1279/0193 KOGENATE Bayer- EMA/H/C/000275/WS1279/0201 MAH: Bayer AG, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 30.11.2017.</p>	<p>Positive Opinion adopted by consensus on 30.11.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>WS1280 Blitzima- EMA/H/C/004723/WS1280/0005 Ritemvia- EMA/H/C/004725/WS1280/0005 Rituzena- EMA/H/C/004724/WS1280/0006 MAH: Celltrion Healthcare Hungary Kft., Duplicate, Duplicate of Truxima, Lead Rapporteur: Sol Ruiz Opinion adopted on 07.12.2017.</p>	<p>Positive Opinion adopted by consensus on 07.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>WS1287 Abseamed- EMA/H/C/000727/WS1287/0066 Binocrit- EMA/H/C/000725/WS1287/0066 Epoetin alfa Hexal- EMA/H/C/000726/WS1287/0065 MAH: Sandoz GmbH, Lead Rapporteur: Alexandre Moreau Opinion adopted on 14.12.2017.</p>	<p>Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>
<p>WS1290 Abseamed- EMA/H/C/000727/WS1290/0067 Binocrit- EMA/H/C/000725/WS1290/0067 Epoetin alfa Hexal- EMA/H/C/000726/WS1290/0066 MAH: Sandoz GmbH, Lead Rapporteur: Alexandre Moreau</p>	<p>Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.</p>

Opinion adopted on 14.12.2017.

WS1313/G

Amgevita-

EMA/H/C/004212/WS1313/0003/G

SOLYMBIC-

EMA/H/C/004373/WS1313/0003/G

MAH: Amgen Europe B.V., Lead Rapporteur:

Kristina Dunder

Opinion adopted on 14.12.2017.

Positive Opinion adopted by consensus on 14.12.2017. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Raplixa - human fibrinogen / human thrombin - EMA/H/C/002807/II/0028/G

MAH: Mallinckrodt Pharmaceuticals Ireland

Limited, Rapporteur: Nithyanandan

NagercoilWithdrawal request submitted on

04.12.2017.

The MAH withdrew the procedure on 04.12.2017.

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

doravirine - EMA/H/C/004747

, treatment of adults infected with HIV-1 without past or present evidence of viral resistance to treatment of adults infected with HIV-1 without past or present evidence of viral resistance to doravirine

doravirine / lamivudine / tenofovir

disoproxil - EMA/H/C/004746

, treatment of adults infected with HIV-1 without past or present evidence of viral resistance to doravirine, lamivudine, or tenofovir

galcanezumab - EMA/H/C/004648,

prophylaxis of migraine

pegfilgrastim - EMA/H/C/004915,

treatment of neutropenia

pegfilgrastim - EMA/H/C/004556,

Reduction in the duration of neutropenia and the incidence of febrile neutropenia in adult patients

adalimumab - EMEA/H/C/004475

, treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis

inotersen - EMEA/H/C/004782, Orphan
, treatment of transthyretin amyloidosis (hATTR)

Accelerated review

tisagenlecleucel - EMEA/H/C/004090, Orphan, ATMP

, treatment of B cell acute lymphoblastic leukaemia (ALL) and diffuse large B cell lymphoma (DLBCL)

Accelerated review

macimorelin - EMEA/H/C/004660

, Diagnosis of Adult growth hormone deficiency (AGHD)

trastuzumab - EMEA/H/C/004916

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

buprenorphine - EMEA/H/C/004743

, Substitution treatment for opioid drug dependence

influenza vaccine surface antigen, inactivated, prepared in cell cultures - EMEA/H/C/004814,

, prophylaxis of influenza in adults and children from 4 years of age

human fibrinogen / human thrombin - EMEA/H/D/004308

, to support the endogenous clotting process and increase of haemostasis in surgical procedures

daunorubicin / cytarabine - EMEA/H/C/004282, Orphan

, treatment of adults with high-risk acute myeloid leukaemia (AML)

Accelerated review

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

fingolimod -

EMEA/H/C/002202/X/0044/G

enoxaparin sodium -

EMEA/H/C/004264/X/0026

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

bortezomib - EMEA/H/C/003984/X/0008

List of Questions adopted on 20.07.2017.

caplacizumab - EMEA/H/C/004426,

Orphan, indicated for the treatment of acquired thrombotic thrombocytopenic purpura (aTTP).

List of Questions adopted on 22.06.2017.

emicizumab - EMEA/H/C/004406

, 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.

List of Outstanding Issues adopted on 12.12.2017.

List of Questions adopted on 10.10.2017.

dolutegravir / rilpivirine -**EMEA/H/C/004427**

, treatment of HIV

List of Questions adopted on 12.10.2017.

pemetrexed - EMEA/H/C/003958

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

List of Questions adopted on 12.10.2017.

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

mecasermin - EMEA/H/C/000704/S/0050

susoctocog alfa -**EMEA/H/C/002792/S/0016**

cholic acid - EMEA/H/C/001250/S/0022,**Orphan**

MAH: Laboratoires CTRS

tocofersolan - EMEA/H/C/000920/S/0027

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

Atosiban SUN - atosiban -**EMEA/H/C/002329/R/0012**

MAH: Sun Pharmaceutical Industries Europe

B.V., Generic, Generic of Tractocile, Rapporteur:

John Joseph Borg, PRAC Rapporteur: Amelia

Cupelli

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

Imatinib medac - imatinib -**EMEA/H/C/002692/R/0008**

MAH: medac Gesellschaft für klinische
Spezialpräparate mbH, Generic, Generic of
Glivec, Rapporteur: John Joseph Borg, PRAC
Rapporteur: Eva A. Segovia

Imnovid - pomalidomide -**EMEA/H/C/002682/R/0028, Orphan**

MAH: Celgene Europe Limited, Rapporteur:
Robert James Hemmings, Co-Rapporteur: Jorge
Camarero Jiménez, PRAC Rapporteur: Patrick
Batty

Imvanex - modified vaccinia ankara virus -**EMEA/H/C/002596/R/0032**

MAH: Bavarian Nordic A/S, Rapporteur: Greg
Markey, Co-Rapporteur: Jan Mueller-Berghaus,
PRAC Rapporteur: Julie Williams

Inflectra - infliximab -**EMEA/H/C/002778/R/0056**

MAH: Hospira UK Limited, Duplicate, Duplicate
of Remsima, Rapporteur: Greg Markey, Co-
Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur:
Patrick Batty

Lojuxta - lomitapide -**EMEA/H/C/002578/R/0029**

MAH: Aegerion Pharmaceuticals Limited,
Rapporteur: Johann Lodewijk Hillege, Co-
Rapporteur: Robert James Hemmings, PRAC
Rapporteur: Menno van der Elst

Lonquex - lipegfilgrastim -**EMEA/H/C/002556/R/0039**

MAH: Sicor Biotech UAB, Rapporteur: Greg
Markey, Co-Rapporteur: Johann Lodewijk
Hillege, PRAC Rapporteur: Patrick Batty

Nexium Control - esomeprazole -**EMEA/H/C/002618/R/0021**

MAH: Pfizer Consumer Healthcare Limited,
Rapporteur: Romaldas Mačiulaitis, Co-
Rapporteur: Robert James Hemmings, PRAC
Rapporteur: Simona Kudeliene

Ovaleap - follitropin alfa -

EMEA/H/C/002608/R/0023

MAH: Teva B.V., Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Menno van der Elst

Pixuvri - pixantrone -**EMEA/H/C/002055/R/0042**

MAH: CTI Life Sciences Limited, Rapporteur: Greg Markey, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty

Remsima - infliximab -**EMEA/H/C/002576/R/0047**

MAH: Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Patrick Batty

Stivarga - regorafenib -**EMEA/H/C/002573/R/0025**

MAH: Bayer AG, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus

Tafinlar - dabrafenib -**EMEA/H/C/002604/R/0030**

MAH: Novartis Europharm Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ulla Wändel Liminga

Voncento - human coagulation factor VIII / human von willebrand factor -**EMEA/H/C/002493/R/0032**

MAH: CSL Behring GmbH, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Sabine Straus

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

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

Tagrisso - osimertinib -**EMEA/H/C/004124/II/0019**

MAH: AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Sabine Straus, "Extension of Indication to include first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer whose tumours have epidermal growth factor receptor exon 19 deletions or exon 21

(L858R) substitution mutations, based on data from the FLAURA study (D5160C00007); a phase III, double-blind, randomised study to assess the efficacy and safety of AZD9291 versus a standard of care epidermal growth factor receptor-Tyrosine Kinase Inhibitor as first-line treatment in patients with epidermal growth factor receptor mutation-positive, locally-advanced or metastatic non-small-cell lung cancer.

As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly.

In addition, the MAH took the opportunity to implement editorial changes in the SmPC and Package Leaflet.

As part of this application the MAH is requesting an additional year of market protection.

An updated RMP version 8 was submitted as part of the application.”

**Xarelto - rivaroxaban -
EMA/H/C/000944/II/0058**

MAH: Bayer AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, “Extension of Indication to include the prevention of stroke, myocardial infarction and cardiovascular death, and for the prevention of acute limb ischaemia and mortality in adult patients with coronary artery disease (CAD) or peripheral artery disease (PAD) for Xarelto 2.5 mg co-administered with acetylsalicylic acid; as a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance.

In addition, section 4.8 of the SmPC is updated for all other dose strengths (10/15/20 mg) of Xarelto with relevant exposure information based on the provided clinical data.

The updated RMP version 11.1 has also been submitted.”

**Xultophy - insulin degludec / liraglutide -
EMA/H/C/002647/II/0023**

MAH: Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, “Update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety information based on cardiovascular outcomes studies conducted a for each of the monocomponents

of Xultophy: LEADER (Liraglutide Cardiovascular Outcomes Trial) and DEVOTE (Insulin Degludec Cardiovascular Outcomes Trial).

The MAH is also proposing to reorganise parts of section 5.1 to improve the reader friendliness and to remove Xultophy from the list of medicines under additional monitoring.

The Package Leaflet is updated accordingly.

The RMP version 7.0 has also been submitted.”

WS1274

Mekinist-

EMA/H/C/002643/WS1274/0023

Tafinlar-

EMA/H/C/002604/WS1274/0031

MAH: Novartis Europharm Limited, Lead Rapporteur: Paula Boudewina van Hennik, Lead Co-Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ulla Wändel Liminga, “Extension of indication to include the combination adjuvant treatment with trametinib and dabrafenib of adult patients with stage III melanoma with a BRAF V600 mutation, following complete resection. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the Mekinist and Tafinlar SmPCs are updated. The Package Leaflet and the Risk Management plan (version 14.0 for Mekinist and version 9.0 for Tafinlar, according to GVP module V revision 2) are updated in accordance. In addition, the Worksharing applicant (WSA) took the opportunity to correct some typos throughout the Mekinist and Tafinlar product information, to include a cross reference to the Mekinist SmPC in section 4.6 of the Tafinlar SmPC regarding fertility, to update the list of local representatives for Bulgaria, Hungary, Estonia, Latvia and Lithuania in the Package Leaflet of both products.”

WS1278

Opdivo-EMA/H/C/003985/WS1278/0042

Yervoy-EMA/H/C/002213/WS1278/0053

MAH: Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Jorge Camarero Jiménez, Lead Co-Rapporteur: Paula Boudewina van Hennik, Lead PRAC Rapporteur: Brigitte Keller-Stanislawski, “Extension of indication to include the combination treatment with nivolumab and ipilimumab of adult patients with intermediate/poor-risk advanced renal cell

carcinoma. As a consequence sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the Opdivo and Yervoy SmPCs are updated. The Package Leaflet and the Risk Management Plan (version 19.0 for Yervoy and version 13.0 for Opdivo) are updated in accordance. In addition, the Worksharing applicant (WSA) took the opportunity to correct some typos throughout the Yervoy and Opdivo product information.”

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Bortezomib Accord - bortezomib -

EMA/H/C/003984/II/0012

MAH: Accord Healthcare Ltd, Generic, Generic of VELCADE, Rapporteur: Milena Stain

Cinryze - C1-esterase inhibitor, human -

EMA/H/C/001207/II/0058/G

MAH: Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus

Cosentyx - secukinumab -

EMA/H/C/003729/II/0031/G

MAH: Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen

Erelzi - etanercept -

EMA/H/C/004192/II/0005/G

MAH: Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege

Evicel - human fibrinogen / human thrombin - EMA/H/C/000898/II/0053

MAH: Omrix Biopharmaceuticals N. V., Rapporteur: Jan Mueller-Berghaus

Flixabi - infliximab -

EMA/H/C/004020/II/0020

MAH: Samsung Bioepis UK Limited, Rapporteur: Jan Mueller-Berghaus

Ilaris - canakinumab -

EMA/H/C/001109/II/0053/G

MAH: Novartis Europharm Limited, Rapporteur: Jan Mueller-Berghaus

Lojuxta - lomitapide -

EMA/H/C/002578/II/0028

MAH: Aegerion Pharmaceuticals Limited, Rapporteur: Johann Lodewijk Hillege

Memantine ratiopharm - memantine -

EMA/H/C/002671/II/0012

MAH: ratiopharm GmbH, Generic, Generic of
Ebixa, Rapporteur: Bart Van der Schueren

Nplate - romiplostim -
EMA/H/C/000942/II/0066, Orphan
MAH: Amgen Europe B.V., Rapporteur:
Concepcion Prieto Yerro

Nucala - mepolizumab -
EMA/H/C/003860/II/0012
MAH: GlaxoSmithKline Trading Services Limited,
Rapporteur: Nithyanandan Nagercoil

Opsumit - macitentan -
EMA/H/C/002697/II/0025/G, Orphan
MAH: Actelion Registration Limited, Rapporteur:
Concepcion Prieto Yerro

Oxervate - cenegermin -
EMA/H/C/004209/II/0002, Orphan
MAH: Dompe farmaceutici S.p.A., Rapporteur:
Concepcion Prieto Yerro

Plegridy - peginterferon beta-1a -
EMA/H/C/002827/II/0040
MAH: Biogen Idec Ltd, Rapporteur: Johann
Lodewijk Hillege

Praluent - alirocumab -
EMA/H/C/003882/II/0032/G
MAH: sanofi-aventis groupe, Rapporteur:
Johann Lodewijk Hillege

**Respreeza - human alpha1-proteinase
inhibitor - EMA/H/C/002739/II/0020**
MAH: CSL Behring GmbH, Rapporteur: Kristina
Dunder

Torisel - temsirolimus -
EMA/H/C/000799/II/0070/G, Orphan
MAH: Pfizer Limited, Rapporteur: Harald
Enzmann

Trulicity - dulaglutide -
EMA/H/C/002825/II/0023
MAH: Eli Lilly Nederland B.V., Rapporteur: Greg
Markey

Vpriv - velaglucerase alfa -
EMA/H/C/001249/II/0035, Orphan
MAH: Shire Pharmaceuticals Ireland Ltd,
Rapporteur: Harald Enzmann

WS1237/G
Ambirix-
EMA/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

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

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 SA, Lead Rapporteur: Jan
Mueller-Berghaus

WS1311/G
Aflunov-
EMEA/H/C/002094/WS1311/0040/G
Foclivia-
EMEA/H/C/001208/WS1311/0034/G
MAH: Seqirus S.r.l, Lead Rapporteur: Daniela
Melchiorri

WS1314
Abasaglar-
EMEA/H/C/002835/WS1314/0017
Humalog-
EMEA/H/C/000088/WS1314/0162
Liprolog-
EMEA/H/C/000393/WS1314/0124
MAH: Eli Lilly Regional Operations GmbH, Lead
Rapporteur: Robert James Hemmings

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-

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

Advate - octocog alfa -

EMA/H/C/000520/II/0088

MAH: Baxter AG, Rapporteur: Jan Mueller-Berghaus, "Submission of the final report from study O61301. This is an interventional, open-label study aimed to evaluate the efficacy and safety of Advate in the treatment of previously treated patients with haemophilia A."

Advate - octocog alfa -

EMA/H/C/000520/II/0090

MAH: Baxter AG, Rapporteur: Jan Mueller-Berghaus, "Submission of the final clinical study report from study O60402. 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."

CellCept - mycophenolate mofetil -

EMA/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 literature and clinical treatment guidelines. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct inconsistencies in the Package Leaflet."

PRAC Led

Cetrotide - cetorelix -

EMA/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."

Cubicin - daptomycin -**EMA/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)."

Descovy - emtricitabine / tenofovir**alafenamide - EMA/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 updates and Minor Linguistic Amendments to the Product Information."

Fluenz Tetra - influenza vaccine (live attenuated, nasal) -**EMA/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."

Glivec - imatinib -**EMA/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 Latvia in the Package Leaflet."

Humira - adalimumab -

EMA/H/C/000481/II/0172

MAH: AbbVie Limited, Rapporteur: Kristina Dunder, "Update of sections 5.1 and 5.2 of the SmPC for 40mg/0.8ml and 40mg/0.4 ml Prefilled pen and prefilled syringe in order to add information on non-radiographic axial spondyloarthritis following final results from Humira remission-withdrawal-retreatment study (M13-375) listed in the RMP."

Imbruvica - ibrutinib -

EMA/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."

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) - EMA/H/C/000296/II/0234

MAH: GlaxoSmithKline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of section 5.1 of the SmPC in order to update the safety information regarding the long term immunity persistence to Hepatitis B at 12/13 years based on the final study CSR DTPa-HBV-IPV-114 in the framework of art. 46 submission (procedure number EMA/H/C/000296/P46/117).

In addition, minor editorial updates are included in section 4.4 of the SmPC to improve clarity."

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/0235

MAH: GlaxoSmithkline Biologicals SA,
Rapporteur: Bart Van der Schueren, "Update of section 4.5 of the SmPC in order to update the interactions section with additional data on the co-administration with Meningococcal serogroup B vaccine (MenB) in order to facilitate the administration of Infanrix hexa and Bexsero to infants and toddlers based on final results from clinical studies V72P12, V72P13 and V72P16."

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 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."

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 of 4-30% total body surface area.”

Odefsey - emtricitabine / rilpivirine / tenofovir alafenamide -

EMA/H/C/004156/II/0027/G

MAH: Gilead Sciences International Limited, Rapporteur: Robert James Hemmings, “Update of sections 4.8 and 5.1 of the SmPC to provide the 96 weeks clinical study reports for two Odefsey switch studies (GS-US-366-1216 and GS-US-366-1160), listed as category 3 studies in the Risk Management Plan, in fulfilment of post-authorisation measures (PAM) MEA 1.1 and 2.1 respectively.

Study GS-US-366-1216: A Phase 3b, Randomized, Double-Blind Switch Study to Evaluate the Safety and Efficacy of Emtricitabine/Rilpivirine/Tenofovir Alafenamide (FTC/RPV/TAF) Fixed Dose Combination (FDC) in HIV-1 Positive Subjects who are Virologically Suppressed on Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate (FTC/RPV/TDF).

Study GS-US-366-1160: A Phase 3b, Randomized, Double-Blind Study to Evaluate Switching from a Regimen Consisting of Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate (EFV/FTC/TDF) Fixed Dose Combination (FDC) to Emtricitabine/Rilpivirine/Tenofovir Alafenamide (FTC/RPV/TAF) FDC in Virologically-Suppressed, HIV-1 Infected Subjects.

In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor administrative amendments in the Product Information and minor linguistic amendments to the DE, NO and SV languages.”

Reagila - cariprazine -

EMA/H/C/002770/II/0002

MAH: Gedeon Richter Plc., Rapporteur: Kristina Dunder, “Update of section 4.8 of the SmPC to add the new ADR Steven-Johnson syndrome with an unknown frequency. The Package Leaflet has been updated accordingly.”

Sirturo - bedaquiline -**EMA/H/C/002614/II/0026, Orphan**

MAH: Janssen-Cilag International NV,
Rapporteur: Filip Josephson, "Submission of the final report from study TMC207TBC3001 listed as a category 3 study in the RMP. This is an interventional, open-label, non-comparative, uncontrolled study without formal efficacy objectives and associated statistical analyses to provide early access to BDQ for subjects with pulmonary infection due to pre-XDR or XDR strains of M. tuberculosis."

Spinraza - nusinersen -**EMA/H/C/004312/II/0004, Orphan**

MAH: Biogen Idec Ltd, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Qun-Ying Yue, "Update of section 4.8 of the SmPC to include new safety information related to hydrocephalus. The PIL and the RMP (new version 7.0) are proposed to be updated accordingly. In addition, the MAH took the opportunity to correct some typographical errors in section 5.1 of the SmPC"

Stelara - ustekinumab -**EMA/H/C/000958/II/0060**

MAH: Janssen-Cilag International NV,
Rapporteur: Greg Markey, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update the efficacy data following completion of extension of study IM-UNITI - A Phase 3, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Safety and Efficacy of Ustekinumab Maintenance Therapy in Subjects with Moderately to Severely Active Crohns Disease.

In addition, the marketing authorisation holder took the opportunity to introduce editorial changes in the SmPC and PL."

Sutent - sunitinib -**EMA/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)."

Sycrest - asenapine -

EMA/H/C/001177/II/0030

MAH: N.V. Organon, Rapporteur: Greg Markey, "Update of sections 4.4 and 4.8 of the SmPC to add safety information regarding falls as a result of postmarketing reports and published literature review. The package leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Denmark, Norway, Slovenia and Slovakia in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.0."

Tafinlar - dabrafenib -**EMA/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 the results of non-clinical studies 2014N220059 and 2015N235499."

Viekirax - ombitasvir / paritaprevir / ritonavir - EMA/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."

Vokanamet - canagliflozin / metformin - EMA/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 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."

Votrient - pazopanib -

EMA/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, as noted by the MHRA, in sections 4.4, 4.5 and 4.8 of the SmPC. The PL is updated accordingly."

Xeloda - capecitabine -

EMA/H/C/000316/II/0074

MAH: Roche Registration Limited, Rapporteur: Harald Enzmann, "Update of section 4.4 of the SmPC with regards to DPD deficiency genotyping, following a request from the PRAC after assessment of LEG-33.1."

Zaltrap - aflibercept -

EMA/H/C/002532/II/0044

MAH: sanofi-aventis groupe, Rapporteur: Filip Josephson, "Submission of the final report from study EFC11338 / AFLAME, "A Multinational, Randomized, Double-Blind Study of Aflibercept Versus Placebo with Irinotecan/5-FU Combination (FOLFIRI) in Patients with Metastatic Colorectal Cancer (MCRC) After Failure of an Oxaliplatin Based Regimen""

WS1258

Clopidogrel Zentiva-

EMA/H/C/000975/WS1258/0059

Clopidogrel/Acetylsalicylic acid Zentiva-

EMA/H/C/001144/WS1258/0050

DuoPlavin-

EMA/H/C/001143/WS1258/0049

Iscover-

EMA/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 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."

WS1273/G**Effentora-****EMEA/H/C/000833/WS1273/0047/G**

MAH: Teva B.V., Lead Rapporteur: Martina Weise, "Update of sections 4.2 and 4.4 of the SmPC in order to add a warning on Hyperalgesia following an internal cumulative review. The Package Leaflet is updated accordingly.

Update of sections 4.4 and 4.45 of the SmPC in order to add a warning on the interaction of fentanyl with benzodiazepines or other CNS depressants including alcohol following an internal cumulative review. The Package Leaflet is updated accordingly.

In addition, the MAH took the opportunity to introduce editorial and format changes in the SmPC and PL."

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."

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."

WS1310

Descovy-

EMA/H/C/004094/WS1310/0026

Genvoya-

EMA/H/C/004042/WS1310/0040

Odefsey-

EMA/H/C/004156/WS1310/0026

Vemlidy-

EMA/H/C/004169/WS1310/0008

MAH: Gilead Sciences International Limited,
Lead Rapporteur: Robert James Hemmings,
"Update of section 4.5 of the Descovy, Genvoya, Odefsey and Vemlidy SmPCs in order to include some information on the drug-drug interaction with sofosbuvir/velpatasvir/voxilaprevir fixed dose combination based on the results of study GS-US0367-1657, listed as a category 3 in the Vemlidy RMP, in order to fulfil MEA 006 for Vemlidy. Study GS-US0367 is a phase I multiple dose study to evaluate the drug-drug interaction potential between sofosbuvir/velpatasvir/voxilaprevir fixed dose combination and HIV anti-retrovirals in healthy subjects. In addition, the Worksharing applicant (WSA) took the opportunity to make some small corrections to section 4.5 of the SmPC for Descovy, Genvoya, Odefsey and Vemlidy and to make corrections to the DE, ES, HU, IS, IT, LV, NO, PT, SL and SV translations for Vemlidy."

WS1316

Glyxambi-

EMA/H/C/003833/WS1316/0011

Jardiance-

EMA/H/C/002677/WS1316/0037

Synjardy-

EMA/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 heart 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.”

B.6.10. CHMP-PRAC assessed procedures

Amyvid - florbetapir (18F) - EMA/H/C/002422/II/0029

MAH: Eli Lilly Nederland B.V., Rapporteur: Harald Enzmann, PRAC Rapporteur: Valerie Strassmann, “Submission of the final report from study I6E-MC-AVBF listed as a category 3 study in the RMP. This is a non-interventional category 3 PASS: European Drug Usage Survey for Amyvid to assess the usage pattern of Amyvid in the EU.

Section 4.4 of SmPC has been reformatted as result of this study.

The RMP version 3.1 has also been submitted.”

Atripla - efavirenz / emtricitabine / tenofovir disoproxil - EMA/H/C/000797/II/0127/G

MAH: Bristol-Myers Squibb and Gilead Sciences Ltd., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, “Update of sections 4.3, 4.4, 4.5 and 5.1 of the Atripla SmPC to include the results of the final study report for Study AI266959,; this is an interventional study to determine the concentration-electrocardiographic effects of efavirenz in healthy subjects enriched for Cyp2b6 Polymorphism, to fulfill the legally binding measure (LEG) requested by the PRAC following to the conclusion of the PSUR (EMA/PRAC/679906/2016) for Sustiva.

Update of sections 4.4 and 4.8 of the Atripla SmPC to add catatonia as a Psychiatric symptom following an assessment of catatonia cases reported in the literature and via the United States (US) Food and Drug Administration Adverse Event Reporting System (FAERS).

Submission of an updated RMP v.17 to remove malignant neoplasms as a potential risk, in line with GVP Module V, and approved by PRAC following the conclusion of the latest annual report on malignancy events (MEA 039.6).

The MAH took the opportunity to implement minor editorial changes in the Product Information and minor linguistic amendments to the following languages: DA, DE, ES, FI, FR, HR, HU, IS, MT, NO, PT and SV"

**Benlysta - belimumab -
EMA/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 EMA/H/C/002015/MEA/006.4 and EMA/H/C/002015/MEA/006.5 for study BEL116027."

**Eliquis - apixaban -
EMA/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 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."

**Fotivda - tivozanib -
EMA/H/C/004131/II/0002**

MAH: EUSA Pharma (UK) Limited, Rapporteur:

Bruno Sepodes, PRAC Rapporteur: Jolanta Gulbinovic, "Update of the section 5.2 of the SmPC with additional information on transporter proteins based on the results of an in vitro interaction transporter study. The updated RMP version 2.0 was also submitted."

Giotrif - afatinib -

EMA/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. In addition, an updated RMP (version 6.0) has also been submitted."

Imnovid - pomalidomide -

EMA/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."

Invokana - canagliflozin -

EMA/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 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.”

Keppra - levetiracetam -

EMA/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.”

Maviret - glecaprevir / pibrentasvir -

EMA/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.”

Odomzo - sonidegib -

EMA/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 histological subtypes.”

Consequentially, the updated RMP version 7.0 was provided in order to reflect the changes following the fulfilment of Annex II condition.”

Ofev - nintedanib -

EMA/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 and 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.”

Raxone - idebenone -

EMA/H/C/003834/II/0008, Orphan

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 Leaflet 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.”

ReFacto AF - moroctocog alfa -

EMA/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).

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 hemophilia 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 PI is brought in line with the latest QRD template (version 10). An editorial change has been made to the Package Leaflets (CZ local representative 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.”

Remicade - infliximab -

EMA/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.”

**RoActemra - tocilizumab -
EMA/H/C/000955/II/0074/G**

MAH: Roche Registration Limited, Rapporteur:
Jan Mueller-Berghaus, PRAC Rapporteur:
Brigitte Keller-Stanislawski

**Stribild - elvitegravir / cobicistat /
emtricitabine / tenofovir disoproxil -
EMA/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
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.”

**Symtuza - darunavir / cobicistat /
emtricitabine / tenofovir alafenamide -
EMA/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.”

**Symtuza - darunavir / cobicistat /
emtricitabine / tenofovir alafenamide -
EMA/H/C/004391/II/0003/G**

MAH: Janssen-Cilag International N.V.,
Rapporteur: Johann Lodewijk Hillege, PRAC
Rapporteur: Julie Williams, “Update of sections

4.4, 4.8, 5.1 and 5.2 of the SmPC in order to reflect the week-48 results from 2 studies (TMC114FD2HTX3001 and TMC114IFD3013) listed as category 3 studies in the RMP; these are phase 3 studies to evaluate the efficacy and safety of D/C/F/TAF once daily fixed-dose combination regimen versus a regimen consisting of DRV/COBI FDC co-administered with FTC/TDF FDC in ARV treatment-naïve HIV-1 infected subjects (study TMC114FD2HTX3001) and to evaluate switching to a D/C/F/TAF once-daily single-tablet regimen versus continuing the current regimen consisting of a boosted protease inhibitor combined with FTC/TDF in virologically-suppressed, HIV-1 infected subjects (study TMC114IFD3013). The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to make minor editorial revision in the product information.”

Tyverb - lapatinib -

EMA/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).”

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.

The RMP version 2.2 has also been submitted.

In addition, the MAH took the opportunity to introduce editorial changes in Annex IIIa"

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 and to bring the PI in line with the latest QRD template version 10."

Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0002/G, Orphan

MAH: Ipsen Pharma, Rapporteur: Martina

Weise, PRAC Rapporteur: Adam Przybylkowski, "Submission of the final report from studies LX301 (pivotal phase III study) and LX303 (supportive phase III study) two randomised, multicentre, double-blind, placebo-controlled studies listed as category 3 studies in the RMP. The objective of study LX301 is to evaluate the efficacy and safety of telotristat etiprate in patients with carcinoid syndrome not adequately controlled by Somatostatin Analog (SSA) therapy; while the objective of study LX303 is to evaluate the safety and efficacy of telotristat etiprate in patients with carcinoid syndrome.

The MAH also took the opportunity to provide updated safety data from the long-term extension study LX302; a phase 3, multicentre, open-label study to further evaluate the safety and tolerability of telotristat. As a consequence, an updated RMP (version 3.0) was provided to reflect those safety data."

B.6.11. PRAC assessed procedures

PRAC Led

Advate - octocog alfa -

EMA/H/C/000520/11/0089

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."

PRAC Led

Baraclude - entecavir -

EMA/H/C/000623/11/0053

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."

PRAC Led

Fiasp - insulin aspart -**EMA/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."

PRAC Led

Mycamine - micafungin -**EMA/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."

PRAC Led

Orencia - abatacept -**EMA/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.”

PRAC Led

**ReFacto AF - moroctocog alfa -
EMA/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.”

PRAC Led

**Scenesse - afamelanotide -
EMA/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”
-

PRAC Led

**Synflorix - pneumococcal polysaccharide
conjugate vaccine (adsorbed) -
EMA/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."

PRAC Led

**Tecfidera - dimethyl fumarate -
EMEA/H/C/002601/II/0049**

MAH: Biogen Idec Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the final report from study 109MS409 listed as a category 3 study in the RMP. This is an observation study aimed to estimate the proportion of dimethyl fumarate use that is prescribed "on-label" versus "off-label" in Germany."

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). 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."

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 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.”

PRAC Led

WS1294

Actos-EMEA/H/C/000285/WS1294/0078

Competact-

EMEA/H/C/000655/WS1294/0068

Glubrava-

EMEA/H/C/000893/WS1294/0055

Glustin-EMEA/H/C/000286/WS1294/0077

Tandemact-

EMEA/H/C/000680/WS1294/0056

MAH: Takeda Pharma A/S, Informed Consent of Competact, Lead PRAC Rapporteur: Almath Spooner, PRAC-CHMP liaison: Peter Kiely, “To update the RMPs to version 24.0 for Actos & Glustin (pioglitazone), version 22.0 for Tandemact (pioglitazone/ glimepiride), and version 25.0 for Compeact & Glubrava (pioglitazone/metformin); the RMPs have been updated as follows:

- For all RMPs, addition of information regarding the effect of pioglitazone on bone mineral density and the increased risk of fractures from the study AD4833-402 addendum report as recommended in conclusion to the assessment of the following post-authorisation measures (PAM): Actos MEA 068.2, Glustin MEA 070.2, Competact MEA 029.2, Glubrava MEA 018.2, Tandemact MEA 027.2.
- For pioglitazone/metformin RMPs only, addition of lactic acidosis questionnaire as recommended in conclusion to the assessment of variation EMEA/H/C/WS0991.

The MAH also took the opportunity to make some general edits to all RMPs.”

Opinion adopted on 14.12.2017.

PRAC Led

WS1299

Enurev Breezhaler-

EMEA/H/C/002691/WS1299/0025

Seebri Breezhaler-

EMEA/H/C/002430/WS1299/0025

Tovanor Breezhaler-

EMEA/H/C/002690/WS1299/0028

MAH: Novartis Europharm Limited, Lead Rapporteur: Hanne Lomholt Larsen, Lead PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, “Submission of the final study

report of the Category 1 Post-Authorisation Safety Study (PASS) on cardio and cerebrovascular outcomes (Multinational, multidatabase cohort study to assess adverse cardiovascular and cerebrovascular outcomes and mortality in association with inhaled NVA237 in Europe / CNVA237A2402T) with subsequent update of Annex II. Consequently the deletion from the list of additional monitoring led to the update of Annex I and IIIB. The MAH also took this opportunity to update the local representatives. The RMP version 8 was submitted.”

PRAC Led

WS1340

Ultibro Breezhaler-

EMA/H/C/002679/WS1340/0022

Ulnar Breezhaler-

EMA/H/C/003875/WS1340/0022

Xoterna Breezhaler-

EMA/H/C/003755/WS1340/0025

MAH: Novartis Europharm Limited, Lead Rapporteur: Hanne Lomholt Larsen, Lead PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, “Submission of the final report of the multinational, multi-database drug utilization study of indacaterol/glycopyrronium bromide (QVA149) in Europe (CQVA149A2401) with the objective to estimate the use of QVA149 off-label and in the subpopulations with missing information mentioned in the risk management plan (RMP).”

PRAC Led

WS1342

Exviera-EMA/H/C/003837/WS1342/0034

Viekirax-

EMA/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 (EMA/H/C/PSUSA/00010363/201701 and EMA/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.

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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.”

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

WS1269

Rotarix-EMEA/H/C/000639/WS1269/0103

MAH: GlaxoSmithKline Biologicals S.A., Lead
Rapporteur: Bart Van der Schueren

WS1272

Epclusa-

EMEA/H/C/004210/WS1272/0020

Vosevi-EMEA/H/C/004350/WS1272/0007

MAH: Gilead Sciences International Limited,
Lead Rapporteur: Filip Josephson

WS1297

Infanrix hexa-

EMEA/H/C/000296/WS1297/0236

MAH: GlaxoSmithkline Biologicals SA, Lead
Rapporteur: Bart Van der Schueren

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

WS1309**HyQvia-EMEA/H/C/002491/WS1309/0039****Kiovig-EMEA/H/C/000628/WS1309/0081**

MAH: Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus

WS1313/G**Amgevita-****EMEA/H/C/004212/WS1313/0003/G****Solymbic-****EMEA/H/C/004373/WS1313/0003/G**

MAH: Amgen Europe B.V., Lead Rapporteur:

Kristina Dunder

Opinion adopted on 14.12.2017.

WS1318**Mirapexin-****EMEA/H/C/000134/WS1318/0086****Sifrol-EMEA/H/C/000133/WS1318/0077**

MAH: Boehringer Ingelheim International GmbH, Lead Rapporteur: Hanne Lomholt Larsen

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

WS1321**Exelon-EMEA/H/C/000169/WS1321/0116****Prometax-****EMEA/H/C/000255/WS1321/0116**

MAH: Novartis Europharm Limited, Lead Rapporteur: Alexandre Moreau

WS1323**Aflunov-****EMEA/H/C/002094/WS1323/0041****Foclivia-****EMEA/H/C/001208/WS1323/0035**

MAH: Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri

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

WS1327

Corbilta-

EMEA/H/C/002785/WS1327/0014

Levodopa/Carbidopa/Entacapone Orion-

EMEA/H/C/002441/WS1327/0024

Stalevo-EMEA/H/C/000511/WS1327/0084

MAH: Orion Corporation, Lead Rapporteur: Outi Mäki-Ikola

WS1328/G

Epclusa-

EMEA/H/C/004210/WS1328/0021/G

Harvoni-

EMEA/H/C/003850/WS1328/0063/G

Sovaldi-

EMEA/H/C/002798/WS1328/0047/G

Vosevi-

EMEA/H/C/004350/WS1328/0008/G

MAH: Gilead Sciences International Limited,
Lead Rapporteur: Filip Josephson

WS1331

Ariclaim-

EMEA/H/C/000552/WS1331/0070

Cymbalta-

EMEA/H/C/000572/WS1331/0074

Duloxetine Lilly-

EMEA/H/C/004000/WS1331/0010

Xeristar-

EMEA/H/C/000573/WS1331/0077

MAH: Eli Lilly Nederland B.V., Duplicate,
Duplicate of Ariclaim, Yentreve, Lead
Rapporteur: Concepcion Prieto Yerro

Hexacima-

EMEA/H/C/002702/WS1286/0075

Hexaxim-

EMEA/H/W/002495/WS1286/0080

Hexyon-

EMEA/H/C/002796/WS1286/0079

MAH: Sanofi Pasteur , Lead Rapporteur: Jan
Mueller-Berghaus

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

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 11-14 December 2017 CHMP plenary:

<i>Endocrinology-Gynaecology-Fertility-Metabolism</i>	
1. (SME), ATMP, Treatment and <i>prevention</i> of progression of Type I Diabetes Mellitus in paediatric patients	The CHMP denied eligibility to PRIME and adopted the critical summary report.
<i>Neurology</i>	
2. (SME), Treatment of acute sudden sensorineural hearing loss (ASNHL)	The CHMP denied eligibility to PRIME and adopted the critical summary report.
<i>Immunology-Rheumatology-Transplantation</i>	
3. (SME), Treatment of Pemphigus	The CHMP denied eligibility to PRIME and adopted the critical summary report.
<i>Oncology</i>	
4. (SME), Treatment of familial adenomatous polyposis	The CHMP denied eligibility to PRIME and adopted the critical summary report.
5. (SME), Treatment of acute myeloid leukaemia	The CHMP denied eligibility to PRIME and adopted the critical summary report.
6. Treatment of acute myeloid leukaemia	The CHMP denied eligibility to PRIME and adopted the critical summary report.
7. Treatment of patients with unresectable or <i>metastatic</i> tumours with gene fusion/translocation	The CHMP denied eligibility to PRIME and adopted the critical summary report.

G.3.2. List of procedures starting in December 2017 for January 2018 CHMP adoption of outcomes

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