19 November 2019
EMA/CHMP/599241/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Final Minutes for the meeting on 16-19 September 2019

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

Disclaimers

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

Of note, the minutes are a working document primarily designed for CHMP members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the minutes 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 the restricted involvement of some meeting participants in upcoming discussions as included in the pre-meeting list of participants and restrictions. See (current) September 2019 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 16-19 September 2019 (to be published post October 2019 CHMP meeting).

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

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

1.2. Adoption of agenda

CHMP agenda for 16-19 September 2019

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 22-25 July 2019

CHMP minutes for August written procedure

CHMP ORGAM minutes for 09 September 2019

The CHMP minutes for 22-25 July 2019 and for the August written procedure were adopted.

The Minutes of the September 2019 CHMP ORGAM meeting held on 09 September 2019, together with all decisions taken at that meeting, were adopted.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. sodium oxybate - EMEA/H/C/004962

medium to long-term maintenance of alcohol abstinence and treatment of mild to moderate alcohol withdrawal syndrome

Scope: Oral explanation

Action: Oral explanation to be held on Monday, 16 September 2019 at time 11:00

List of Outstanding Issues adopted on 26.04.2019. List of Questions adopted on 15.11.2018.

An oral explanation was held on Monday, 16 September 2019. The presentation by the applicant focused on efficacy data in the two indications and the feasibility of a PAES.

2.1.2. fostamatinib - EMEA/H/C/005012

indicated for the treatment of thrombocytopenia

Scope: Possible oral explanation

Action: Possible oral explanation to be held on Thursday, 19 September 2019 at time 16:00

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 31.01.2019.

The CHMP agreed that no oral explanation is needed this time.

See 3.2

2.1.3. enasidenib - Orphan - EMEA/H/C/004324

Celgene Europe BV; treatment of acute myeloid leukaemia (AML)

Scope: Possible oral explanation

Request by the applicant dated 12 September 2019 to postpone the oral explanation

SAG Oncology report from meeting held on 18 June 2019

Action: Possible oral explanation to be held on Tuesday, 17 September 2019 at time 14:00

List of Outstanding Issues adopted on 26.04.2019. List of Questions adopted on 18.10.2018.

The CHMP agreed the request by the applicant for a postponement of the oral explanation.

See 3.2

2.1.4. siponimod - EMEA/H/C/004712

treatment of secondary progressive multiple sclerosis (SPMS)

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday, 18 September 2019 at time 16:00

List of Outstanding Issues adopted on 29.05.2019. List of Questions adopted on 31.01.2019.

An oral explanation was held on Wednesday, 18 September 2019. The presentation by the

applicant focused on efficacy data in different subgroups.

See 3.2

2.1.5. omadacycline tosilate - EMEA/H/C/004715

treatment of community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI) in adults

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday, 18 September 2019 at time 14:00

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 31.01.2019.

An oral explanation was held on Wednesday, 18 September 2019. The presentation by the applicant focused on efficacy and safety data in the two indications and the feasibility of a PAES.

See 3.2

2.1.6. polatuzumab vedotin - Orphan - EMEA/H/C/004870

Roche Registration GmbH; Treatment of mature B cell lymphomas

Scope: Oral explanation/Opinion

List of experts to the SAG meeting was adopted via written procedure on 12 September 2019 Report from SAG Oncology held on 13 September 2019

Action: Oral explanation to be held on Monday, 16 September 2019 at time 14:00

List of Outstanding Issues adopted on 25.07.2019, 25.06.2019. List of Questions adopted on 24.04.2019.

An oral explanation was held on Monday, 16 September 2019. The presentation by the applicant focused on efficacy and safety data in different subgroups and possible post-approval studies.

See 3.2

2.1.7. Rhokiinsa - netarsudil - EMEA/H/C/004583

Aerie Pharmaceuticals Ireland Ltd; indicated for the reduction of elevated intraocular pressure (IOP) in adults with open-angle glaucoma or ocular hypertension.

Scope: Possible oral explanation

Action: Possible oral explanation to be held on Tuesday, 17 September 2019 at time 16:00

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

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 31.01.2019.

The CHMP agreed that no oral explanation is needed this time.

See 3.1

2.1.8. quizartinib - Orphan - EMEA/H/C/004468

Daiichi Sankyo Europe GmbH; treatment of acute myeloid leukaemia

Scope: Oral explanation

Action: Oral explanation to be held on Tuesday 17 September 2019 at time 11:00

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 29.01.2019.

An oral explanation was held on Tuesday 17 September 2019. The presentation of the applicant focused on efficacy data in different subgroups.

2.1.9. XOSPATA - gilteritinib - Orphan - EMEA/H/C/004752

Accelerated assessment

Astellas Pharma Europe B.V.; treatment of patients who have relapsed or refractory acute myeloid leukemia (AML) with a FLT3 mutation

Scope: Oral explanation

Action: Oral explanation to be held on Thursday 19 September 2019 at time 09:00

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

List of Questions adopted on 27.05.2019.

An oral explanation was held on Thursday 19 September 2019. The presentation by the applicant focused on clinical data supporting the indication wording with regard to prior treatment lines.

See 3.1

2.2. Re-examination procedure oral explanations

2.2.1. Xyndari - glutamine - Orphan - EMEA/H/C/004734

Emmaus Medical Europe Ltd; treatment of sickle cell disease

Scope: Oral Explanation

List of experts for the ad hoc expert group meeting was adopted via written procedure on 09 September 2019

Report from ad hoc expert group meeting held on 11 September 2019

Action: Oral explanation to be held on Wednesday, 18 September 2019 at time 11:00

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

Opinion adopted on 29.05.2019. List of Outstanding Issues adopted on 31.01.2019. List of Questions adopted on 28.06.2018.

An oral explanation was held on Wednesday, 18 September 2019. The presentation by the applicant focused on efficacy data in different subgroups.

The CHMP noted that the applicant withdrew the request for re-examination. Therefore the negative opinion by consensus adopted in May 2019 recommending the refusal of the marketing authorisation application becomes the final opinion.

2.3. Post-authorisation procedure oral explanations

2.3.1. WS1501
Anoro Ellipta - umeclidinium / vilanterol - EMEA/H/C/002751/WS1501/0024
Laventair Ellipta - umeclidinium / vilanterol - EMEA/H/C/003754/WS1501/0027

GlaxoSmithKline (Ireland) Limited

Lead Rapporteur: Peter Kiely, Lead Co-Rapporteur: Ewa Balkowiec Iskra

Scope: "Update of a section 5.1 of the SmPC in order to add efficacy information based on the 52-week study CTT116855; a 52-week study designed to evaluate the efficacy of FF/UMEC/VI 100/62.5/25 compared with dual therapy of FF/VI 100/25 or UMEC/VI 62.5/25 in subjects with COPD. In addition, clarification on information related to the 24 week study submitted at time of initial authorisation is introduced in section 5.1. The worksharing procedure leads to amendments to the Summary of Product Characteristics."

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday, 18 September 2019 at time 9:00 (joint OE for WS1501 and WS1505)

Request for Supplementary Information adopted on 29.05.2019, 31.01.2019.

An oral explanation was held on Wednesday, 18 September 2019. The presentation by the applicant focused on the wording in section 5.1 of the SmPC with supporting clinical data.

See 5.1

2.3.2. WS1505
Incruse Ellipta - umeclidinium bromide - EMEA/H/C/002809/WS1505/0023
Rolufta Ellipta - umeclidinium - EMEA/H/C/004654/WS1505/0008

GlaxoSmithKline (Ireland) Limited

Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead Co-Rapporteur: Peter Kiely

Scope: "Update of section 5.1 of the SmPC to add efficacy information based on the 52-week study CTT116855; a 52-week study designed to evaluate the efficacy of FF/UMEC/VI 100/62.5/25 compared with dual therapy of FF/VI 100/25 or UMEC/VI 62.5/25 in subjects with COPD. In addition, clarification on information related to the 24 week study submitted at time of initial authorisation is introduced in section 5.1. Update of section 4.8 of the SmPC to update the frequency of constipation from 'uncommon' to 'common'. The Package Leaflet is updated in accordance."

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday, 18 September 2019 at time 9:00 (joint OE for WS1501 and WS1505)

Request for Supplementary Information adopted on 29.05.2019, 31.01.2019.

An oral explanation was held on Wednesday, 18 September 2019. The presentation by the applicant focused on the wording in section 5.1 of the SmPC with supporting clinical data.

See 5.1

2.3.3. Xeljanz - tofacitinib - EMEA/H/C/004214/X/0012

Pfizer Europe MA EEIG

Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Extension application to introduce a new pharmaceutical form (prolonged-release tablet) associated with a new strength (11 mg), and presented in pack sizes of 28, 30, 90 and 91 tablets. The extension application includes a change in pharmacokinetics. An updated RMP (version 4.0) has been provided."

Possible oral explanation/list of outstanding issues

Action: Possible oral explanation to be held on Thursday, 19 September 2019 at time 11:00

List of Outstanding Issues adopted on 27.06.2019, 31.01.2019. List of Questions adopted on 26.07.2018.

The CHMP agreed that no oral explanation is needed this time.

See 4.2

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Arsenic trioxide Accord - arsenic trioxide - EMEA/H/C/005175

Accord Healthcare S.L.U.; treatment of relapsed acute promyelocytic leukaemia (APL)

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 25.07.2019. List of Questions adopted on 26.04.2019.

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

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

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

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

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report for Arsenic trioxide Accord.

3.1.2. Bortezomib Fresenius Kabi - bortezomib - EMEA/H/C/005074

Fresenius Kabi Deutschland GmbH; treatment of multiple myeloma

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 31.01.2019.

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

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

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

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

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report for Bortezomib Fresenius Kabi.

3.1.3. Ivozall - clofarabine - EMEA/H/C/005039

ORPHELIA Pharma SAS; treatment of acute lymphoblastic leukaemia

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 25.07.2019. List of Questions adopted on 31.01.2019.

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 17 September 2019.

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report for Ivozall.

3.1.4. Qtrilmet - dapagliflozin / saxagliptin / metformin hydrochloride - EMEA/H/C/004910

AstraZeneca AB; - to improve glycaemic control when metformin with or without sulphonylurea (SU) does not provide adequate glycaemic control and where simultaneous addition of dapagliflozin and saxagliptin is considered necessary - to improve glycaemic control when metformin with or without sulphonylurea (SU) and either dapagliflozin or

saxagliptin does not provide adequate glycaemic control - when already being treated with dapagliflozin and saxagliptin and metformin.

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 29.05.2019. List of Questions adopted on 15.11.2018.

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

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

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

The CHMP noted the letter of recommendation dated 12 September 2019.

The summary of opinion was circulated for information.

3.1.5. Rhokiinsa - netarsudil - EMEA/H/C/004583

Aerie Pharmaceuticals Ireland Ltd; indicated for the reduction of elevated intraocular pressure (IOP) in adults with open-angle glaucoma or ocular hypertension.

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 31.01.2019.

The CHMP agreed that no oral explanation is needed this time.

See 2.1

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

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

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

The summary of opinion was circulated for information.

3.1.6. Senstend - lidocaine / prilocaine - EMEA/H/C/005298

Plethora Pharma Solutions Limited; treatment of primary premature ejaculation

Scope: Opinion

Action: For adoption

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

List of Questions adopted on 25.07.2019.

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

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

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

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

The summary of opinion was circulated for information.

3.1.7. XOSPATA - gilteritinib - Orphan - EMEA/H/C/004752

Accelerated assessment

Astellas Pharma Europe B.V.; treatment of patients who have relapsed or refractory acute myeloid leukemia (AML) with a FLT3 mutation

Scope: Opinion

Action: For adoption

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

List of Questions adopted on 27.05.2019.

An oral explanation was held on Thursday 19 September 2019. The presentation by the applicant focused on clinical data supporting the indication wording with regard to prior treatment lines.

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 gilteritinib 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 17 September 2019.

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report for Xospata.

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

3.2.1. clopidogrel / acetylsalicylic acid - EMEA/H/C/004996

indicated for the secondary prevention of atherothrombotic events

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 31.01.2019.

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. deferasirox - EMEA/H/C/005156

treatment of chronic iron overload

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.03.2019.

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

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

3.2.3. dexmedetomidine - EMEA/H/C/005152

light to moderate sedation

Scope: List of outstanding issues

Letter from third party

Action: For adoption

List of Questions adopted on 26.04.2019.

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 noted the letter from the third party and the response letter.

3.2.4. recombinant vesicular stomatitis virus - zaire ebolavirus vaccine (live) - EMEA/H/C/004554

Accelerated assessment

Ebola Vaccine

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 25.06.2019.

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. fostamatinib - EMEA/H/C/005012

indicated for the treatment of thrombocytopenia

Scope: Possible oral explanation

Action: Possible oral explanation to be held on Thursday, 19 September 2019 at time 16:00

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 31.01.2019.

The CHMP agreed that no oral explanation is needed this time.

See 2.1

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.

3.2.6. enasidenib - Orphan - EMEA/H/C/004324

Celgene Europe BV; treatment of acute myeloid leukaemia (AML)

Scope: Possible oral explanation

Request by the applicant dated 12 September 2019 to postpone the oral explanation.

SAG Oncology report from meeting held on 18 June 2019

Action: Possible oral explanation to be held on Tuesday, 17 September 2019 at time 14:00

List of Outstanding Issues adopted on 26.04.2019. List of Questions adopted on 18.10.2018.

The CHMP noted the request by the applicant for a postponement of the oral explanation.

The CHMP agreed that no oral explanation is needed this time.

See 2.1

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

3.2.7. siponimod - EMEA/H/C/004712

treatment of secondary progressive multiple sclerosis (SPMS)

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday, 18 September 2019 at time 16:00

List of Outstanding Issues adopted on 29.05.2019. List of Questions adopted on 31.01.2019.

An oral explanation was held on Wednesday, 18 September 2019. The presentation by the applicant focused on efficacy data in different subgroups.

See 2.1

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

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

3.2.8. omadacycline - EMEA/H/C/004715

treatment of community-acquired bacterial pneumonia (CABP) and acute bacterial skin and

skin structure infections (ABSSSI) in adults

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday, 18 September 2019 at time 14:00

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 31.01.2019.

See 2.1

An oral explanation was held on Wednesday, 18 September 2019. The presentation by the applicant focused on efficacy and safety data in the two indications and the feasibility of a PAES.

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

3.2.9. alpelisib - EMEA/H/C/004804

treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor2 (HER2)-negative, advanced breast cancer with a PIK3CA mutation in combination with fulvestrant after disease progression following an endocrine-based regimen.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 29.05.2019.

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

The Committee adopted a list of outstanding issues.

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

3.2.10. polatuzumab vedotin - Orphan - EMEA/H/C/004870

Roche Registration GmbH; Treatment of mature B cell lymphomas

Scope: Oral explanation/opinion, Report from SAG Oncology meeting held on 13 September 2019

Action: Oral explanation to be held on Monday, 16 September 2019 at time 14:00

List of Outstanding Issues adopted on 25.07.2019, 25.06.2019. List of Questions adopted on 24.04.2019.

The members noted the report from the SAG.

An oral explanation was held on Monday, 16 September 2019. The presentation by the applicant focused on efficacy and safety data in different subgroups and possible post-approval studies.

See 2.1

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

3.2.11. delafloxacin - EMEA/H/C/004860

treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSI) in adults

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 29.05.2019. List of Questions adopted on 20.09.2018.

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.

3.2.12. upadacitinib - EMEA/H/C/004760

treatment of moderate to severe active rheumatoid arthritis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 29.05.2019.

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.

3.2.13. tigecycline - EMEA/H/C/005114

treatment of soft tissue and intra-abdominal infections, - complicated skin and soft tissue infections, excluding diabetic foot infections, - complicated intra-abdominal infections, should be used only in situations where it is known or suspected that other alternatives are not suitable

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 29.05.2019. List of Questions adopted on 13.12.2018.

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.

3.2.14. selinexor - Orphan - EMEA/H/C/005127

Karyopharm Europe GmbH; treatment of patients with relapsed refractory multiple myeloma (RRMM)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 24.04.2019.

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

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

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

3.3.1. indacaterol / mometasone furoate - EMEA/H/C/005067

treatment of asthma

Scope: 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. cabazitaxel - EMEA/H/C/005178

treatment of adult patients with metastatic castration resistant prostate cancer previously treated with a docetaxel-containing regimen

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

The CHMP agreed to consult the PKWP.

3.3.3. glasdegib - Orphan - EMEA/H/C/004878

Pfizer Europe MA EEIG; treatment of newly diagnosed de novo or secondary acute myeloid leukaemia

Scope: 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. doxorubicin - EMEA/H/C/005194

treatment of breast cancer, ovarian cancer, progressive multiple myeloma and AIDS-related Kaposi's sarcoma

Scope: 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. indacaterol / glycopyrronium / mometasone - EMEA/H/C/005061

treatment of asthma and to reduce asthma exacerbations

Scope: 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. fingolimod - EMEA/H/C/005191

treatment of multiple sclerosis

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.7. fingolimod - EMEA/H/C/005282

treatment of multiple sclerosis

Scope: 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. teriparatide - EMEA/H/C/005087

treatment of osteoporosis

Scope: 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. teriparatide - EMEA/H/C/005388

treatment of osteoporosis

Scope: 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.

3.3.10. luspatercept - Orphan - EMEA/H/C/004444

Celgene Europe BV; - treatment of adult patients with very low- to intermediate-risk myelodysplastic syndromes (MDS)-associated anaemia; - the treatment of adult patients with beta-thalassaemia (β-thalassaemia)-associated anaemia who require RBC transfusions.

Scope: 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. semaglutide - EMEA/H/C/004953

treatment of type 2 diabetes mellitus

Scope: 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. isatuximab - Orphan - EMEA/H/C/004977

sanofi-aventis groupe; For the treatment of patients with multiple myeloma (MM)

Scope: 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. trastuzumab - EMEA/H/C/005066

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

Scope: 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.

3.3.14. deferiprone - Orphan - EMEA/H/C/005004

Apotex B.V.; treatment of neurodegeneration with brain iron accumulation

Action: For adoption

The Committee discussed the issues identified in this application.

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

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

3.4.1. aripiprazole - EMEA/H/C/005062

treatment of schizophrenia, or of moderate to severe manic episodes in bipolar I disorder with sensor to measure medication adherence

Scope: Letter from the applicant dated 24 August 2019 requesting an extension of clock stop to respond to the list of questions adopted in July 2019

List of Questions adopted on 25.07.2019.

The CHMP agreed to the request for an extension of clock stop to respond to the list of questions adopted in July 2019.

3.4.2. diclofenamide - Orphan - EMEA/H/C/005141

Sun Pharmaceutical Industries Europe B.V.; treatment of periodic paralysis

Scope: Letter from the applicant dated 20 August 2019 requesting an extension of clock stop to respond to the list of questions adopted in May 2019

Action: For adoption

List of Questions adopted on 29.05.2019.

The CHMP agreed to the request for an extension of clock stop to respond to the list of questions adopted in May 2019

3.4.3. erlotinib - EMEA/H/C/005071

treatment of lung and pancreatic cancers

Scope: Letter from applicant dated 18 September 2019 requesting an extension of clock stop to respond to the list of outstanding issues adopted in May 2019.

Action: For adoption

List of Outstanding Issues adopted on 29.05.2019. List of Questions adopted on 13.12.2018.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the list of outstanding issues adopted in May 2019.

3.4.4. rituximab - EMEA/H/C/005387

treatment of Non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukaemia (CLL)

Scope: Letter from the applicant requesting an extension of clock stop to respond to the list of

outstanding issues adopted in June 2019

Action: For adoption

List of Outstanding Questions adopted on 27.06.2019.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the list of outstanding issues adopted in June 2019.

3.4.5. viable T-cells - Orphan - ATMP - EMEA/H/C/002397

Kiadis Pharma Netherlands B.V.; adjunctive treatment in haematopoietic stem cell transplantation (HSCT) for a malignant disease

Scope: Report from ad-hoc expert group meeting held on 3 September 2019

Action: For information

List of Outstanding Issues adopted on 27.06.2019, 14.09.2018, 25.05.2018. List of Questions adopted on 08.09.2017.

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

3.4.6. melphalan - EMEA/H/C/005173

used alone or in combination with other cytotoxic drugs and/or total body irradiation is indicated in the treatment of: multiple myeloma, malignant lymphoma (Hodgkin, non-Hodgkin lymphoma), acute lymphoblastic and myeloblastic leukemia, childhood neuroblastoma, ovarian adenocarcinoma, mammary adenocarcinoma.
in combination with other cytotoxic drugs and/or total body irradiation, in adult and paediatric population, is indicated as conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (HSCT) in haematological diseases.

Scope: Letter from the applicant requesting an extension of clock stop to respond to the List of Questions adopted in July 2019.

Action: For adoption

List of Questions adopted on 25.07.2019.

The CHMP agreed to the request by the applicant for an additional extension of clock stop to respond to the List of Questions adopted in July 2019.

3.4.7. rituximab - EMEA/H/C/004807

treatment of Non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukaemia (CLL) and rheumatoid arthritis

Scope: Letter from the applicant requesting an extension of clock stop to respond to the list of outstanding issues adopted in June 2019

Action: For adoption

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 18.10.2018.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the list of outstanding issues adopted in June 2019.

3.4.8. teriparatide - EMEA/H/C/005233

treatment of osteoporosis

Scope: Letter from the applicant requesting an extension of the clock stop to respond to the list of questions adopted in July 2019

Action: For adoption

List of Questions adopted on 25.07.2019.

The CHMP agreed to the request by the applicant for an extension of the clock stop to respond to the list of questions adopted in July 2019.

3.4.9. ivosidenib - Orphan - EMEA/H/C/005056

FGK Representative Service GmbH; treatment of adult patients (≥ 18 years old) with relapsed or refractory acute myeloid leukaemia (AML) with an isocitrate dehydrogenase-1 (IDH1) R132 mutation

Scope: Request by the applicant dated 25 August 2019 for an extension of clock stop to respond to the list of questions (adopted in May 2019) was adopted by written procedure

Action: For information

List of Questions adopted on 29.05.2019

The CHMP noted the request for an extension of clock stop to respond to the list of questions, which was adopted via written procedure.

3.4.10. onasemnogene abeparvovec - Orphan - ATMP - EMEA/H/C/004750

AveXis Netherlands B.V.; treatment of spinal muscular atrophy (SMA)

Scope: Letter from the applicant dated 23 August 2019 requesting an extension of clock stop to respond to the list of outstanding issues adopted in June 2019

SAG Neurology Report from the meeting held on 6 September 2019

Action: For adoption

List of outstanding issues adopted on 21.06.2019. List of Questions adopted on 22.02.2019.

The CHMP noted the report from the SAG meeting held on 6 September 2019.

The CHMP noted the extension of clock stop as adopted by CAT.

3.4.11. bupivacaine / meloxicam - EMEA/H/C/005205

for application into the surgical site to reduce postoperative pain

Scope: Letter from the applicant dated 17 August 2019 requesting an extension of the clock stop to respond to the list of questions adopted in July 2019

List of Questions adopted on 25.07.2019.

The CHMP agreed to the request by the applicant for an extension of the clock stop to respond to the list of questions adopted in July 2019.

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

3.5.1. Evenity - romosozumab - EMEA/H/C/004465

UCB Pharma S.A.; Treatment of osteoporosis

Scope: Draft list of questions and draft list of experts to the ad-hoc expert group meeting scheduled on 3 October 2019

Re-examination Timetable

Letter from third party

Action: For adoption

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

Opinion adopted on 27.06.2019, List of Outstanding Issues adopted on 29.05.2019, 28.02.2019, 15.11.2018, 20.09.2018. List of Questions adopted on 26.04.2018.

The CHMP agreed to consult an ad-hoc expert group and adopted the draft list of experts as well as a list of questions to this group.

The CHMP adopted the re-examination timetable.

The CHMP noted the letter from the third party.

3.6. Initial applications in the decision-making phase

3.6.1. Nuceiva - botulinum toxin type a - EMEA/H/C/004587

Evolus Pharma Limited; temporary improvement in the appearance of moderate to severe vertical lines between the eyebrows

Scope: Response from the European Commission to CHMP and response from EDQM on revision of Botulinum toxin A Ph. Eur. monograph

Action: For information

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

The CHMP noted the response letters from the European Commission and the EDQM.

3.7. Withdrawals of initial marketing authorisation application

4. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008

4.1. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Opinion

4.1.1. Remsima - infliximab - EMEA/H/C/002576/X/0062

Celltrion Healthcare Hungary Kft.

Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension application to introduce a new pharmaceutical form (solution for injection), a new strength (120 mg) and a new route of administration (subcutaneous use).
The RMP (version 9.1) is updated in accordance."

Action: For adoption

List of Outstanding Issues adopted on 25.07.2019. List of Questions adopted on 28.03.2019.

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

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

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

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

4.2.1. Akynzeo - fosnetupitant / palonosetron - EMEA/H/C/003728/X/0018

Helsinn Birex Pharmaceuticals Limited

Rapporteur: Peter Kiely, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: PRAC Rapporteur: Ilaria Baldelli

Scope: "Extension application to introduce the new pharmaceutical form 'powder for concentrate for solution for infusion' and a new strength for the fixed combination of fosnetupitant (pro-drug of netupitant) and palonosetron of 235 mg/0.25 mg, to be administered intravenously (new route of administration)."

Action: For adoption

List of Questions adopted on 28.03.2019.

The Committee discussed the issues identified in this application, mainly relating to quality, non-clinical, pharmacokinetics and RMP aspects.

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

4.2.2. Carbaglu - carglumic acid - Orphan - EMEA/H/C/000461/X/0038

Recordati Rare Diseases

Rapporteur: Fátima Ventura

Scope: "Extension application to introduce a new pharmaceutical form associated with 2 new strengths (200 mg and 800 mg soluble tablets)."

Action: For adoption

List of Questions adopted on 28.03.2019.

The Committee discussed the issues identified in this application, mainly in relation to the new formulation and the stability data as well as the use of an excipient taking into account the long-term administration of the product.

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

The CHMP did not agree to the request by the applicant for an extension to the clock stop.

4.2.3. Humalog - insulin lispro - EMEA/H/C/000088/X/0169

Eli Lilly Nederland B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: "Extension application to change process steps. The RMP is updated (version 9.3) accordingly and in line with revision 2 of GVP module V on 'Risk management systems."

Action: For adoption

List of Questions adopted on 26.04.2019.

The Committee discussed the issues identified in this application, mainly in relation to quality aspects.

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

4.2.4. Liprolog - insulin lispro - EMEA/H/C/000393/X/0130

Eli Lilly Nederland B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: "Extension application to change process steps. The RMP is updated (version 9.3) accordingly and in line with revision 2 of GVP module V on 'Risk management systems."

Action: For adoption

List of Questions adopted on 26.04.2019.

The Committee discussed the issues identified in this application, mainly in relation to quality aspects.

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

4.2.5. Pemetrexed Fresenius Kabi - pemetrexed - EMEA/H/C/003895/X/0009

Fresenius Kabi Deutschland GmbH

Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension application to introduce a new pharmaceutical form (concentrate for solution for infusion) associated with new strength 25 mg/ml."

Action: For adoption

List of Questions adopted on 31.01.2019.

The Committee discussed the issues identified in this application, mainly in relation to quality aspects.

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

4.2.6. Xeljanz - tofacitinib - EMEA/H/C/004214/X/0012

Pfizer Europe MA EEIG

Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Extension application to introduce a new pharmaceutical form (prolonged-release tablet) associated with a new strength (11 mg), and presented in pack sizes of 28, 30, 90 and 91 tablets. The extension application includes a change in pharmacokinetics. An updated RMP (version 4.0) has been provided."

Action: For adoption

List of Outstanding Issues adopted on 27.06.2019, 31.01.2019. List of Questions adopted on 26.07.2018.

See 2.3

The Committee discussed the issues identified in this application, mainly concerning the clinical efficacy data and the feasibility of a registry analyses.

The CHMP agreed that no oral explanation is needed this time.

The Committee adopted the CHMP recommendation and scientific discussion together with a 3rd 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. Kymriah - tisagenlecleucel - Orphan - ATMP - EMEA/H/C/004090/X/0010

Novartis Europharm Limited

Rapporteur: Rune Kjeken, Co-Rapporteur: Dariusz Sladowski, CHMP Coordinators: Ingrid Wang and Ewa Balkowiec Iskra

Scope: "Extension application to introduce a new manufacturing process."

Action: For adoption

The CHMP was updated on discussions at the CAT, mainly relating to some quality aspects.

The CHMP endorsed the list of questions as adopted by the CAT and a specific timetable.

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

4.4.1. Suboxone - buprenorphine / naloxone - EMEA/H/C/000697/X/0042

Indivior Europe Limited

Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber

Scope: “Extension application to introduce a new pharmaceutical form (sublingual film) associated with four new strengths (2/0.5, 4/1, 8/2, and 16/4 mg) and a new route of administration (either sublingual or buccal administration)”

Request by the applicant for an extension of clock stop to respond to the list of questions adopted in July 2019.

List of Questions adopted on 25.07.2019.

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the list of questions adopted in July 2019.

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. Alunbrig - brigatinib - EMEA/H/C/004248/II/0003

Takeda Pharma A/S

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: “Extension of indication to include first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously untreated with an ALK inhibitor for Alunbrig.
The addition of a new indication is supported by data from study 301 (AP26113-13-301; ALTA 1L), a phase 3, randomized, open label, comparative, multicenter, international phase 3 study. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package leaflet and labelling are updated in accordance. The RMP version 5.1 has also been submitted. Minor editorial corrections are also proposed.” 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, concerning the available clinical data. The Committee considered that longer exposure data was required for an appropriate assessment. In this context the request for 1 year of market protection was also discussed.

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

5.1.2. Bavencio - avelumab - Orphan - EMEA/H/C/004338/II/0009/G

Merck Europe B.V.

Rapporteur: Filip Josephson, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Hans Christian Siersted

Scope: "Extension of indication to include a new indication for Bavencio as the first-line combination treatment with avelumab and axitinib in adult patients with advanced renal cell carcinoma; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1. 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) takes the occasion to include change in posology section 4.2 of the SmPC to support the switch of the avelumab dosing regimen from 10 mg/kg every two weeks (weight-based) to a flat dose of 800 mg every two weeks applicable to the new proposed indication aRCC and the already existing one (MCC). The MAH took the occasion to also implement some editorial changes in the Product information. A proposed updated RMP has been submitted as well in version 1.7"

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019.

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.

5.1.3. Benlysta - belimumab - EMEA/H/C/002015/II/0062

GlaxoSmithKline (Ireland) Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: " Extension of indication to include patients aged 5 years and older in the current approved indication for Benlysta (belimumab powder for solution for infusion 120 mg/ml and 400 mg/ml) based on the results of the safety, efficacy and pharmacokinetics study in patients aged 5 years to 17 years (BEL114055). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated with safety and efficacy information. Update of sections 4.2, 4.4, 5.1, 5.2 and 6.4 of the SmPC for Benlysta (belimumab, solution for injection in pre-filled pen and pre-filled syringe, 200 mg) to reflect the paediatric data available for the intravenous formulation. The Annex IIIA and the Package Leaflet is updated accordingly. The RMP version 35.0 has been submitted to support this new indication. In addition, the MAH took the opportunity to make some editorial changes in the product information and bring it in line with the latest QRD template version 10.0"

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019, 28.02.2019.

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

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

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

The summary of opinion was circulated for information.

5.1.4. Dupixent - dupilumab - EMEA/H/C/004390/II/0017

sanofi-aventis groupe

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Kimmo Jaakkola

Scope: “Extension of indication in adult patients with CRSwNP. As a consequence of this new indication on patients with CRSwNP, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are being updated to include pharmacological, efficacy and safety data. The Package Leaflet (PL) is updated accordingly.
Additionally minor editorial QRD changes on excipients to the SmPC are introduced in section 6.6 in the 300mg and 200mg strengths accordingly. Consequently the Annex IIIA is updated. The variation leads to amendments to the Summary of Product Characteristics, annex IIIA and Package Leaflet and to the Risk Management Plan (RMP).”

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019.

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

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

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

The summary of opinion was circulated for information.

5.1.5. ECALTA - anidulafungin - EMEA/H/C/000788/II/0040

Pfizer Europe MA EEIG

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: “Extension of the approved indication "treatment of invasive candidiasis (ICC)" to include paediatric patients aged from 1 month to less than 18 years of age; consequently, sections 4.1, 4.2, 4.4, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated in order to add paediatric dosing instructions, warnings and precautions, clinical, and non-clinical information. The Package Leaflet is updated accordingly consequent to the revisions to the SmPC. In addition, the Marketing Authorisation Holder (MAH) has taken the opportunity to update the information in the SmPC and Package Leaflet in line with the current excipient’s guideline for fructose. The RMP Version number 13.0 dated 08 March 2019 which includes GVP module V rev 2 changes has also been submitted.”

Action: For adoption

The Committee discussed the issues identified in this application, relating to some

clarifications on the clinical data and the environmental risk assessment.

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

5.1.6. Erleada - apalutamide - EMEA/H/C/004452/II/0001

Janssen-Cilag International N.V.

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Natalja Karpova, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension of indication to include the treatment of metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT) for Erleada based on the results of study 56021927PCR3002 (TITAN study), a randomised, double-blind, placebo-controlled phase 3 study comparing apalutamide plus ADT versus ADT in patients with mHSPC. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add a warning on ischaemic cardiovascular events and to reflect new safety and efficacy information. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to make editorial update to the SmPC and Labelling. The RMP version 2.0 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, relating to some clinical aspects and the request for 1 year of market protection.

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

5.1.7. Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0045

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted

Scope: "Extension of indication to include the adjuvant treatment of adult patients with HER2-positive early breast cancer; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Applicant took the opportunity to introduce editorial changes." 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 29.05.2019.

The Committee discussed the issues identified in this application, mainly relating to the wording of the indication in relation to the studied population and the request for 1 year of market protection.

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

5.1.8. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0057

Merck Sharp & Dohme B.V.

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

Menno van der Elst

Scope: "Extension of indication to include 1st line treatment of locally advanced or metastatic non-small cell lung cancer tumours expressing PD-L1 with a ≥ 1% tumour proportion score (TPS), based on data from study KEYNOTE-042; an international, randomized, open-label Phase 3 study investigating Keytruda monotherapy compared to standard of care platinum-based chemotherapy in patients with locally advanced or metastatic PD-L1 positive (TPS ≥ 1%) NSCLC, and on supportive data from the final planned analysis of KEYNOTE-024; a Phase 3 randomized open-label study of Keytruda monotherapy compared to platinum-based chemotherapy in metastatic NSCLC with PD-L1 TPS ≥50%. As a result, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC have been updated. An updated RMP version 18.1 was provided as part of the application."

Action: For adoption

Request for Supplementary Information adopted on 28.03.2019, 18.10.2018.

The Committee discussed the issues identified in this application, mainly concerning the efficacy and safety data in a subgroup population and the proper selection of patients.

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

5.1.9. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0065

Merck Sharp & Dohme B.V.

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include, as monotherapy or in combination with platinum and 5-fluorouracil (5-FU) Chemotherapy, first-line treatment of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) in adults for Keytruda; based on the results from KEYNOTE-048, a randomized, multi-center, open-label phase 3 study investigating pembrolizumab, or pembrolizumab plus platinum plus 5-FU chemotherapy versus platinum plus 5-FU plus cetuximab in subjects with first-line recurrent or metastatic HNSCC.
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. An updated version of the RMP (Version 22.1) is also being submitted."

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019, 28.03.2019.

The Committee discussed the issues identified in this application, mainly concerning to the wording of the indication in relation to the appropriate patient population with regard to the combined positive score.

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

5.1.10. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0072

Merck Sharp & Dohme B.V.

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include a new indication for Keytruda as monotherapy for

the treatment of recurrent locally advanced or metastatic oesophageal cancer in adults whose tumours express PD L1 with a CPS ≥ 10 and who have received prior systemic therapy; as a consequence, sections 4.1, 4.2, and 5.1 of the SmPC, and section 1 of the PL are updated accordingly. The updated RMP version 25.1 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019.

The Committee discussed the issues identified in this application, mainly relating to the provided efficacy data.

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

5.1.11. Lucentis - ranibizumab - EMEA/H/C/000715/II/0076

Novartis Europharm Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include treatment of moderately severe to severe non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) in adults for Lucentis; as a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated with the safety information. The Package Leaflet is updated in accordance. RMP version 19.0 is also being submitted."

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019, 28.02.2019.

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.

5.1.12. MabThera - rituximab - EMEA/H/C/000165/II/0168

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Hans Christian Siersted

Scope: "Extension of indication to previously untreated, advanced stage paediatric B-cell Non-Hodgkin's Lymphoma (B-NHL)"

Action: For adoption

The Committee discussed the issues identified in this application, mainly in relation to the possible extrapolation of data to children below 3 years of age. In addition, some aspects concerning the study analyses and the wording of the indication in relation to the studied patient population were debated.

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

5.1.13. Revlimid - lenalidomide - Orphan - EMEA/H/C/000717/II/0107

Celgene Europe BV

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

Scope: "Extension of indication to include Revlimid in combination with rituximab (anti-CD20 antibody) for the treatment of adult patients with previously treated follicular lymphoma. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated; the PL is updated in accordance. An updated EU RMP (version 36.2) has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019.

The Committee discussed the issues identified in this application, mainly concerning the wording of the indication in relation to the studied patient population.

The CHMP noted the letter from the applicant dated 18 September 2019 informing of the withdrawal of the marginal zone lymphoma (MZL) population submitted as part of the type II variation.

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

5.1.14. SIRTURO - bedaquiline - Orphan - EMEA/H/C/002614/II/0033/G

Janssen-Cilag International NV

Rapporteur: Filip Josephson, Co-Rapporteur: Ingrid Wang, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Grouping of an extension of indication to include patients 12 years of age and older for Sirturo and a type II variation to change the safety information in section 4.9 of the SmPC. The extension of indication is supported by the Week 24 analysis of Cohort 1 (adolescent subjects aged ≥12 to <18 years) of study TMC207-C211. Based on these data, 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.
An updated version of the RMP (version 3.2) was included in the submission."

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019, 31.01.2019.

The Committee discussed the issues identified in this application, mainly concerning the appropriate dosage for children below 40 kg of weight.

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

5.1.15. Trulicity - dulaglutide - EMEA/H/C/002825/II/0040

Eli Lilly Nederland B.V.

Rapporteur: Martina Weise, PRAC Rapporteur: Ilaria Baldelli

Scope: "Update of sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC based on the data from Study H9X-MC-GBDJ (Researching Cardiovascular Events with a Weekly INcretin in Diabetes (REWIND)); a single pivotal Phase 3 long-term cardiovascular outcomes study, which

assessed the efficacy and safety of treatment with once-weekly injection of dulaglutide 1.5 mg when added to glucose-lowering regimen of patients with type 2 diabetes (T2D), compared to the addition of a once weekly placebo injection. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement a minor correction in section 5.1 of the SmPC, to implement editorial changes and to align the annexes with the latest QRD template."

Action: For adoption

Request for Supplementary Information adopted on 25.07.2019.

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.

5.1.16. WS1501
Anoro Ellipta - umeclidinium / vilanterol - EMEA/H/C/002751/WS1501/0024
Laventair Ellipta - umeclidinium / vilanterol - EMEA/H/C/003754/WS1501/0027

GlaxoSmithKline (Ireland) Limited

Lead Rapporteur: Peter Kiely, Lead Co-Rapporteur: Ewa Balkowiec Iskra

Scope: "Update of section 5.1 of the SmPC in order to add efficacy information based on the 52-week study CTT116855; a 52-week study designed to evaluate the efficacy of FF/UMEC/VI 100/62.5/25 compared with dual therapy of FF/VI 100/25 or UMEC/VI 62.5/25 in subjects with COPD. In addition, clarification on information related to the 24 week study submitted at time of initial authorisation is introduced in section 5.1. The worksharing procedure leads to amendments to the Summary of Product Characteristics."

Oral explanation

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019, 31.01.2019.

An oral explanation was held on Wednesday, 18 September 2019. The presentation by the applicant focused on the wording in section 5.1 of the SmPC with supporting clinical data.

See 2.3

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

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

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

The summary of opinion was circulated for information.

5.1.17. WS1505
Incruse Ellipta - umeclidinium bromide - EMEA/H/C/002809/WS1505/0023
Rolufta Ellipta - umeclidinium - EMEA/H/C/004654/WS1505/0008

GlaxoSmithKline (Ireland) Limited

Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead Co-Rapporteur: Peter Kiely

Scope: "Update of section 5.1 of the SmPC to add efficacy information based on the 52-week study CTT116855; a 52-week study designed to evaluate the efficacy of FF/UMEC/VI 100/62.5/25 compared with dual therapy of FF/VI 100/25 or UMEC/VI 62.5/25 in subjects with COPD. In addition, clarification on information related to the 24 week study submitted at time of initial authorisation is introduced in section 5.1. Update of section 4.8 of the SmPC to update the frequency of constipation from 'uncommon' to 'common'. The Package Leaflet is updated in accordance."

Oral explanation

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019, 31.01.2019.

An oral explanation was held on Wednesday, 18 September 2019. The presentation by the applicant focused on the wording in section 5.1 of the SmPC with supporting clinical data.

See 2.3

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.

5.1.18. WS1542
Bretaris Genuair - aclidinium - EMEA/H/C/002706/WS1542/0040
Eklira Genuair - aclidinium - EMEA/H/C/002211/WS1542/0040

AstraZeneca AB

Lead Rapporteur: Ewa Balkowiec Iskra, Lead Co-Rapporteur: Peter Kiely

Scope: "Extension of indication to include reduction of COPD exarcerbations for Eklira Genuair and Bretaris Genuair; as a consequence, sections 4.1, 4.4, 4.8 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet for Bretaris Genuair and to implement minor editorial changes in sections 4.4, 4.6, 5.3 of the SmPC and section 2 of the PL for both Eklira Genuair and Bretaris Genuair."

Action: For adoption

Request for Supplementary Information adopted on 26.04.2019.

The Committee discussed the issues identified in this application, mainly in relation to the

wording of the indication with regard to information to be included in section 4.1 versus 5.1.

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

5.1.19. WS1550
Docetaxel Zentiva - docetaxel - EMEA/H/C/000808/WS1550/0058
Taxotere - docetaxel - EMEA/H/C/000073/WS1550/0131

Aventis Pharma S.A.

Lead Rapporteur: Alexandre Moreau, Lead Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension of indication to include in combination with androgen-deprivation therapy (ADT), with or without prednisone or prednisolone, for the treatment of patients with metastatic hormone-sensitive prostate cancer for Taxotere and Docetaxel Zentiva; as a consequence, sections 4.1, 4.2, 4.4 and 4.8 of the SmPC are updated. The Package Leaflet is updated accordingly. The RMP version 1.0 has also been submitted. In addition, the Worksharing applicant took the opportunity to update information impacting the local representatives in the packages leaflets."

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019.

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

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

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

The summary of opinion was circulated for information.

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

5.2.1. Opsumit - macitentan - Orphan - EMEA/H/C/002697/II/0029

Janssen-Cilag International N.V.

Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia

Scope: "Extension of indication to include treatment of patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH), based on the pivotal study MERIT-1 (AC-055E201), together with 6 months of efficacy and safety data (cut-off date 17 October 2017) from its ongoing open-label extension study MERIT-2 (AC-055E202), as well as a drug-drug interaction (DDI) study (AC-055-122) of macitentan and rosuvastatine, a DDI study (AC-055-123) of macitentan and riociguat, and observational data from the OPUS Registry (OPsumit USers Registry; cut-off date of 17 April 2018).
As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 are being updated and the Package Leaflet is being updated accordingly. In addition, the MAH took the opportunity to implement

editorial changes and to align the annexes with the latest QRD template and to update the contact details of the local representatives in the Package Leaflet.
An updated RMP version 9.2 was provided as part of the application."

Request by the applicant for an extension to the clock stop to respond to the request for supplementary information adopted in March 2019.

Action: For adoption

Request for Supplementary Information adopted on 28.03.2019, 13.12.2018.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the request for supplementary information adopted in March 2019.

5.2.2. Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/II/0015

Pfizer Ireland Pharmaceuticals

Rapporteur: Bjorg Bolstad, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Rugile Pilviniene

Scope: "Extension of indication to include paediatric patients aged 3 months to less than 18 years for Zavicefta (for the treatment of cIAI and cUTI), based on data from paediatric studies D4280C00014, C3591004 and C3591005 and the population PK modelling/simulation analyses (CAZ-MS-PED-01 and CAZ-MS-PED-02).
As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2, 6.3 and 6.6 of the SmPC are updated in order to reflect this additional population, the paediatric posology, paediatric safety information, the description of the clinical trials and handling instructions for paediatric dosing. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct the sodium content in SmPC sections 2 and 4.4 and PL section 2 and the volumes of distribution of ceftazidime and avibactam in SmPC section 5.2. Furthermore, the MAH is also introducing a correction in the Czech SmPC to add missing values in the table in SmPC section 5.1. The RMP version 3.0 has also been submitted."

Letter from the applicant dated 20 August 2019 requesting an extension of clock stop to respond to the request for supplementary information adopted in July 2019.

Action: For adoption

Request for Supplementary Information adopted on 25.07.2019

The CHMP agreed to the request by the applicant for an extension of clock stop to respond to the request for supplementary information adopted in July 2019.

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

5.3.1. Translarna - ataluren - Orphan - EMEA/H/C/002720/II/0047

PTC Therapeutics International Limited

Re-examination rapporteur: Kristina Dunder, Re-examination co-rapporteur: Alexander Moreau

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: “Extension of indication to include non-ambulatory patients with duchenne muscular dystrophy; this variation additionally presents, as supportive data, the final results of the long term clinical study PTC-124-GD-019-DMD (an Open-Label Study for Previously Treated Ataluren (PTC124) Patients with Nonsense Mutation Dystrophinopathy), submitted in line with the requirements of the Article 46 of the Paediatric Regulation.
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. The RMP version 8.0 has also been submitted.”

List of question to the SAG, list of experts for the SAG meeting scheduled on 11 October 2019

The Re-examination timetable was adopted via written procedure on 30 August 2019

Action: For adoption

Opinion adopted on 27.06.2019. Oral explanation held on 25.06.2019. Request for Supplementary Information adopted on 28.02.2019, 13.12.2018.

5.3.2. Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0049

Novartis Europharm Limited

Re-examination Rapporteur: Milena Stain and re-examination Co-Rapporteur: Sinan B Sarac

Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia

Scope: “Extension of indication to include first line treatment of adult and paediatric patients aged 2 years and older with severe aplastic anaemia for Revolade in combination with standard immunosuppressive therapy; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 50 has also been updated.”

List of experts for the ad hoc expert group meeting scheduled on 7 October 2019, List of questions to the ad hoc expert group to be adopted after the plenary meeting via written procedure

Action: For information

Opinion adopted on 27.06.2019. Oral explanation held on 24.06.2019. Request for Supplementary Information adopted on 28.02.2019, 15.11.2018, 26.07.2018.

The list of experts for the ad hoc expert group meeting as well as the list of questions will be adopted after the plenary via written procedure.

Post meeting note:

The list of questions to the ad hoc expert group meeting was adopted via written procedure on 02.10.2019. The final list of experts for the ad hoc expert meeting was adopted via written procedure on 04.10.2019

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. monovalent, live, recombinant, replication-incompetent adenoviral serotype 26 (ad26)-vectored vaccine expressing the full length glycoprotein (gp) of the ebola virus (ebov) mayinga variant - H0005337

active immunisation for prevention of Ebola Viruses Disease caused by Zaire ebolavirus in adults => 18 years old

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

Action: For adoption

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

8.1.2. Bulevirtide - Orphan - H0004854

MYR GmbH; treatment of hepatitis delta in patients with compensated liver disease

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

Action: For adoption

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

8.1.3. multivalent, live, recombinant, non-replicating in human cells, modified vaccinia ankara (mva)-vectored vaccine, expressing the ebov mayinga glycoprotein (gp), the sudan virus (sudv) gulu gp, the marburg virus (marv) musoke gp, and the taï forest vir - H0005343

active immunisation for prevention of Ebola Viruses Disease caused by Zaire ebolavirus in adults => 18 years old

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

Action: For adoption

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

8.1.4. Pemigatinib - H0005266

Treatment of adult patients with previously treated, advanced/metastatic or surgically unresectable cholangiocarcinoma with FGFR2 fusions.

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

Action: For adoption

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

8.1.5. ivacaftor, tezacaftor, vx-445 - Orphan - H0005269

Vertex Pharmaceuticals (Ireland) Limited, indicated in a combination regimen with ivacaftor 150 mg tablet for the treatment of cystic fibrosis (CF) in patients aged 12 years and older who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

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

Action: For adoption

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

8.2. Priority Medicines (PRIME)

Disclosure of information related to priority medicines cannot be released at present time as these contain commercially confidential information

8.2.1. List of applications received

Action: For information

The CHMP noted the list of applications received.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 7 recommendations for eligibility to PRIME: 2 were granted and 5 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. Aerivio Spiromax - fluticasone propionate / salmeterol - EMEA/H/C/002752

Teva B.V.

Rapporteur: John Joseph Borg, Co-Rapporteur: Ewa Balkowiec Iskra

Scope: Withdrawal of marketing authorisation

Action: For information

The CHMP noted the withdrawal of the marketing authorisation.

9.1.2. Blincyto - blinatumomab - Orphan - EMEA/H/C/003731

Amgen Europe B.V.

Rapporteur: Alexandre Moreau, Co-Rapporteur: Daniela Melchiorri

Scope: DHPC and communication plan in order to prevent a risk of premedication errors with dexamethasone in paediatric patients treated with Blincyto adopted on 23 August 2019 by written procedure

Action: For information

The CHMP noted the DHPC and communication plan which were adopted via written procedure.

9.1.3. Increlex - mecasermin - EMEA/H/C/000704/II/0060

Applicant: Ipsen Pharma

Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.1, 4.2, 4.3, 4.4, 4.8 and 4.9 of the SmPC in order to update the safety information on benign or malignant neoplasia based on the EU registry study: the Ipsen global safety database and based on a literature review. The package leaflet and the RMP (version 11) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

DHPC and communication plan

Action: For adoption

The CHMP adopted the DHPC and communication plan.

9.1.4. Ocaliva - obeticholic acid - Orphan - EMEA/H/C/004093/R/0018

Intercept Pharma International Limited

Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst

Scope: Renewal of conditional marketing authorisation

Action: For discussion

The Committee discussed the issues identified in this application. The members were reminded of the conditional marketing authorisation and the adopted specific obligations. The members discussed the proposals for changing the specific obligations.

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

The CHMP agreed to consult the Gastroenterology Drafting Group and adopted a list of questions to this group.

9.1.5. Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0063

Biogen Netherlands B.V.

Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber

Scope: CHMP request for PRAC advice adopted via written procedure on 27 August 2019

Action: For information

The CHMP noted the request for PRAC advice adopted via written procedure.

9.1.6. Tresiba – insulin degludec – EMEA/H/C/002498

Novo Nordisk A/S

Rapporteur: Kristina Dunder, Co-Rapporteur: Sinan B. Sarac

Scope: Request for a LEG

Action: For adoption

The CHMP adopted the request for a LEG.

9.1.7. WS1587/G Abasaglar-EMEA/H/C/002835/WS1587/0028/G Humalog-EMEA/H/C/000088/WS1587/0178/G

Eli Lilly Nederland B.V.

Lead Rapporteur: Kristina Dunder

Scope: "Type II variation. B.IV.z. to introduce an additional prefilled pen presentation for Abasaglar, solution for injection (EU/1/14/944/007, EU/1/14/944/008, EU/1/14/944/012, EU/1/14/944/013), Humalog, solution for injection (EU/1/96/007/002, EU/1/96/007/004, EU/1/96/007/020, EU/1/96/007/021 EU/1/96/007/023), Humalog Kwikpen solution for injection (EU/1/96/007/031, EU/1/96/007/032, EU/1/96/007/039, EU/1/96/007/040, EU/1/96/007/041, EU/1/96/007/042) and Humalog Junior Kwikpen, solution for injection (EU/1/96/007/043, EU/1/96/007/044, EU/1/96/007/045). The pack contains 5 pre-filled pens. Type IAIN B. II.e.5.a.1 to request the 2x5 multipack.
As a consequence, the following sections were updated 1, 4.2, 4.4, 6.2, 6.4, 6.5, 6.6, 8 of the SmPC in order to add new pre-filled pen presentation; the Package Leaflet and Labelling are updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to make an editorial change (removing comma in SK address in the PL)

Action: For discussion

The Committee discussed the issues identified in this application, mainly relating to some quality aspects and changes to the SmPC.

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

10. Referral procedures

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

No items

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

10.2.1. Direct Oral Anticoagulants (DOAC) - EMEA/H/A-5(3)/1478

MAHs: various

Referral Rapporteur: Martina Weise, Referral Co-Rapporteurs: Kristina Dunder

Rapporteurs for involved CAPs:

Eliquis (APIXABAN):
Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bart van der Schueren;

Pradaxa (DABIGATRAN ETEXILATE):
Rapporteur: Mark Ainsworth, Co-Rapporteur: Jean-Michel Race;

Xarelto (RIVAROXABAN):
Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise

Scope: List of outstanding issues

To assess the results of a non-interventional study regarding the risks of major bleeding in patients with non-valvular atrial fibrillation.

Action: For adoption

The CHMP was reminded of the EMA initiated study on the real life use of DOACs. The members note the response from PRAC on the list of questions by CHMP.

The CHMP adopted a list of outstanding issues to the study authors with a specific timetable.

List of outstanding issues adopted: September 2019 CHMP

Authors' response: 30.11.2019

Rapporteur / co-rapporteur joint assessment report circulated to CHMP: 08.01.2020

CHMP comments: 15.01.2020

Updated rapporteur / co-rapporteur joint assessment report circulated to CHMP: 22.01.2020

CHMP opinion/LoOIs: January 2020 CHMP

10.2.2. Presence of nitrosamine impurities in human medicinal products containing chemically synthesised active pharmaceutical ingredients EMEA/H/A-5(3)/1490

MAHs: various

Referral Rapporteur: Martina Weise, Referral Co-Rapporteurs: Kristina Dunder

Scope: Building on the Article 31 referral on sartans with a tetrazole ring and the knowledge acquired on nitrosamines in medicinal products, EMA together with the EU Network has continued the review to identify if there are any consequences for medicinal products outside the class of sartans. EMA has been liaising with international partners to ensure concerted actions if relevant.

The evaluation that has been conducted so far has resulted in a common understanding that it would be appropriate as a means of precaution to ask all MAHs and manufacturers to review the potential risk for N-nitrosamines as part of their medicinal products containing chemically synthesised active pharmaceutical ingredients authorised in the EU and to ensure that their medicinal products are in line with the latest knowledge on the risk of formation of or contamination with nitrosamines.

Taking into account that nitrosamines have been found in sartans with a tetrazole ring and also in some batches of pioglitazone, it is foreseen that the CHMP's opinion is sought in accordance with Article 5(3) of Regulation (EC) No 726/2004 on the following to further investigate the issues at stake.

Action: For adoption

The CHMP appointed Martina Weise as Rapporteur and Kristina Dunder as Co-Rapporteur.

The CHMP, having considered the issue in a first phase of the procedure, is of the opinion that Marketing authorisation holders (MAHs) should review their manufacturing processes to identify and, if found, to mitigate risk of presence of nitrosamine impurities.

Regarding the matter identified in phase I of the notification, the CHMP has concluded that MAHs should ensure that their manufacturers of API and finished products review the API and finished product manufacturing processes with respect to the arrangements for preventing N-nitrosamine formation or contamination, taking into account their knowledge of the manufacturing processes as well as the potential sources of nitrosamine impurities.

The CHMP thus adopted a notice to the MAHs and a Questions & Answers document accompanying it.

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

No items

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

No items

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

No items

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

10.6.1. Fosfomycin containing medicinal products – EMEA/H/A-31/1476

MAH various

Rapporteur: Ondrej Slanar, Co-rapporteur: Janet Koenig

Scope: List of outstanding issues

Letter from third party

Action: For discussion

Need to re-evaluate the benefit-risk ratio of the approved indications considering the current scientific knowledge. Furthermore, the appropriate dose and duration of administration for both oral and intravenous formulations need to be discussed as well as the adequacy of safety relevant information and information about pharmacological properties.

The German National Competent Authority triggered a referral under Article 31 of Directive 2001/83 based on interest of the Union, requesting an opinion to CHMP on the benefit-risk of fosfomycin-containing products and on the need for regulatory measures to be taken.

The CHMP noted a letter from the third party.

The members discussed the responses received by marketing authorisation holders and noted the responses received by the infectious disease working party.

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

Submission of responses: 24.10.2019

Re-start of the procedure: 14.11.2019

Joint Assessment report circulated to CHMP: 22.11.2019

Comments: 29.11.2019

Updated joint assessment report circulated to CHMP: 05.12.2019

Oral explanation/CHMP opinion: December 2019 CHMP

10.6.2. Ranitidine - EMEA/H/A-31/1491

MAH various

Rapporteur: Johann Lodewijk Hillege, Co-rapporteur: Daniela Melchiorri

Scope: Tests performed in a random selection of ranitidine API batches and finished products available in the EU have shown levels of NDMA which raise concerns

Action: For information

According to preliminary results for NDMA levels in a random selection of ranitidine API batched and finished products available in the EU, the levels of NDMA detected range raise concerns. In addition, in vitro studies were performed with different pH solutions of ranitidine with and without nitrite to evaluate if similar pH conditions as in vivo conditions would lead to formation of NDMA. Although the nitrite levels used were far above those usually present in

human stomach, the results seem to indicate that NDMA could be formed from ranitidine at acidic pH in the presence of nitrite. In view of the analytical results presented so far, it appears that NDMA can also be formed from ranitidine during certain analytical procedures, especially those using high temperatures.

Overall, in view of preliminary results showing the presence of NDMA in some batches of drug substance and drug product and the preliminary findings that NDMA could be generated under certain conditions when dimethylamine (DMA) released from ranitidine is exposed to a source of nitrite (e.g. sodium nitrite), it is necessary to evaluate the relevance of these findings, the potential root causes and their impact on the benefit–risk balance of the medicinal products containing ranitidine.

In view of the above and the necessity to conduct an EU assessment for any potential action to be taken at EU level, the European Commission triggered on 12 September 2019 a referral procedure under Article 31 of Directive 2001/83/EC to evaluate the relevance of these findings, the potential root causes and their impact on the benefit-risk balance of medicinal products containing ranitidine.

The CHMP appointed rapporteurs, adopted list of questions to the MAHs of ranitidine containing medicinal products as well as the timetable for the procedure.

Additionally, EMA presented a proposal for a tender to perform a pharmacoepidemiological study to explore the potential association between ranitidine and the risk of cancer. While some CHMP members expressed concerns about the methodological challenges that such a study entails, the CHMP said the EMA is welcome to proceed with the tender but CHMP is currently not in a position to formally adopt a recommendation for it. EMA will further work on the tender to address some of the concerns whilst liaising with the CHMP rapporteurs' teams.

The CHMP appointed Johann Lodewijk Hillege as Rapporteur and Daniela Melchiorri as Co-Rapporteur.

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

September 2019 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

Action: For information

The CHMP noted the minutes from the task force

13.2. Innovation Task Force briefing meetings

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

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

No items

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 02-05 September 2019

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 September 2019

Action: For adoption

The CHMP adopted the EURD list.

CHMP-PRAC Strategic Review and Learning Meeting (SRLM) under the Finish presidency of the European Union (EU) Council – Helsinki, Finland, 21-23 October 2019

Action: For information

The CHMP noted the draft agenda of the CHMP-PRAC Strategic Review and Learning Meeting (SRLM) under the Finish presidency.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 11-13 September 2019

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 23-25 September 2019

Action: For information

The CHMP noted the report.

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at September 2019 PDCO

Action: For information

The CHMP noted the information.

Report from the PDCO meeting held on 17-20 September 2019

Action: For information

The CHMP noted the report.

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 10-12 September 2019

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 15-17 September 2019

Action: For information

The CHMP noted the report.

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

14.3.1. Scientific Advice Working Party (SAWP)

Chair: Anja Schiel

Report from the SAWP meeting held on 02-05 September 2019. Table of conclusions

Action: For information

The CHMP noted the report.

Scientific advice letters

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

14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 22-25 July 2019.

Action: For adoption

The CHMP adopted the table of decision.

Liposomal formulations - safety concerns linked to generic naming and applicability of recommendation issued in July to topical formulations

Questions from MAH

Action: For discussion

The CHMP was updated on liposomal formulations and whether a qualifier should be added for topical liposomal products where there is no existing safety concern linked to confusion with non-liposomal products. The CHMP agreed that in general, for any route of administration, a qualifier is only required in case of a risk of medication errors which would serious raise concerns in regards to the safe use of the medicinal product. Other elements such as medication error reporting or long established use should be taken into consideration when assessing the need for the qualifier.

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP September 2019 meeting to CHMP for adoption:

- 13 reports on products in scientific advice and protocol assistance
- 8 reports on products in pre-authorisation procedures
- 2 reports on products in post-authorisation procedures
- 1 report on products in plasma master file

Action: For adoption

The CHMP adopted the BWP reports.

14.3.4. Oncology Working Party (ONCWP)

Election of ONCWP Chair

Action: For election

The CHMP elected Sinan Sarac as new chair to the oncology working party.

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

14.8.1. Update of the Business Pipeline report for the human scientific committees

2019 initial marketing authorisation application submissions with eligibility request to centralised procedure

Action: For information

The CHMP noted the report.

14.9. Others

No items

15. Any other business

15.1. AOB topic

No items

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 September 2019 CHMP meeting

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Harald Enzmann	Chair	Germany	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	
Selma Arapovic Dzakula	Alternate	Croatia	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Emilia Mavrokordatou	Alternate	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Tomas Radimersky	Alternate	Czech Republic	No interests declared	
Sinan B. Sarac	Member	Denmark	No interests declared	
Mark Ainsworth	Alternate	Denmark	No interests declared	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Tuomo Lapveteläinen	Alternate	Finland	No interests declared	
Alexandre Moreau	Member	France	No interests declared	
Jean-Michel Race	Alternate	France	No interests declared	
Martina Weise	Member	Germany	No restrictions applicable to this meeting	
Janet Koenig	Alternate	Germany	No interests declared	
Konstantinos Markopoulos	Member	Greece	No interests declared	
Eleftheria Nikolaidi	Alternate	Greece	No interests declared	
Melinda Sobor	Member	Hungary	No part in discussions, final deliberations and voting as appropriate as regards the medicinal product	**Dupixent** EMEA/C/004390/II/0017
Agnes Gyurasics	Alternate	Hungary	No interests declared	
Hrefna Gudmundsdottir	Alternate	Iceland	No interests declared	
Jayne Crowe	Member	Ireland	No interests declared	
Peter Kiely	Alternate	Ireland	No interests declared	
Natalja Karpova	Member	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No interests declared	
Martine Trauffler	Member	Luxembourg	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Bjorg Bolstad	Member	Norway	No restrictions applicable to this meeting	
Ingrid Wang	Alternate	Norway	No interests declared	
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Bruno Sepodes	Member (Vice -Chair)	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	
Rajko Kenda	Member	Slovenia	No restrictions applicable to this meeting	
Maria Concepcion Prieto Yerro	Member	Spain	No interests declared	
Jorge Camarero Jiménez	Alternate	Spain	No participation in final deliberations and voting on	EMEA/H/C/004870 **Kadcyla** - EMEA/H/C/002389/II/0045 **MabThera** - EMEA/H/C/000165/II/0168
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Nithyanandan Nagercoil	Member	United Kingdom	No restrictions applicable to this meeting	
Christian Gartner	Co-opted member	Austria	No restrictions applicable to this meeting	
Koenraad Norga	Co-opted member	Belgium	No participation in final deliberations and voting on	**Benlysta** - EMEA/H/C/002015/II/006 **WS1501** **WS1505**
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Blanka Hirschlerova	Co-opted member	Czech Republic	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Nele Berthels	Expert - in person*	Belgium	No interests declared	
Susanne Høpner Rasmussen	Expert - in person*	Denmark	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Theis Moeslund Jensen	Expert - in person*	Denmark	No restrictions applicable to this meeting	
Astrid Doutreluingne	Expert - in person*	France	No part in discussions, final deliberations and voting as appropriate as regards	EMEA/H/C/004712 EMEA/H/C/004804 EMEA/H/C/005067 EMEA/H/C/005061 **Kymriah** - EMEA/H/C/004090/X/0010 **Lucentis** - EMEA/H/C/000715/II/0076 **Revolade** - EMEA/H/C/001110/II/0049
Billy Taouk	Expert - in person*	France	No restrictions applicable to this meeting	
Claire Christen	Expert - in person*	France	No part in discussions, final deliberations and voting as appropriate as regards	EMEA/H/C/004870 **Kadcyla** - EMEA/H/C/002389/II/0045 **MabThera** - EMEA/H/C/000165/II/0168
Isabel Araujo Fernandez	Expert - in person*	France	No restrictions applicable to this meeting	
Marie Peter	Expert - in person*	France	No interests declared	
Christine Greiner	Expert - in person*	Germany	No interests declared	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Maria Dimopoulou	Expert - in person*	Greece	No part in final deliberations and voting as appropriate as regards	EMEA/H/C/004444
Johanna de Groot	Expert - in person*	Netherlands	No interests declared	
Anja Schiel	Expert - in person*	Norway	No interests declared	
Lucia Lopez-Anglada Fernandez	Expert - in person*	Spain	No interests declared	
Milena Ezcurra	Expert - in person*	Spain	No interests declared	
Angelina Doriguzzi	Expert - via telephone*	Austria	No restrictions applicable to this meeting	
Christine Vaculik	Expert - via telephone*	Austria	No interests declared	
Stephan Lehr	Expert - via telephone*	Austria	No interests declared	
Aaron Sosa Mejia	Expert - via telephone*	Denmark	No restrictions applicable to this meeting	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Aldana Rosso	Expert - via telephone*	Denmark	No interests declared	
Anne-Marie Dalseg	Expert - via telephone*	Denmark	No restrictions applicable to this meeting	
Eskild Colding-Jorgensen	Expert - via telephone*	Denmark	No restrictions applicable to this meeting	
Susanne Høpner Rasmussen	Expert - in person*	Denmark	No restrictions applicable to this meeting	
Martina Schussler-Lenz	Expert - via telephone*	Germany	No interests declared	
Zane Neikena	Expert - via telephone*	Latvia	No interests declared	
Helga Haugom Olsen	Expert - via telephone*	Norway	No interests declared	
Hilde Roshol	Expert - via telephone*	Norway	No interests declared	
Mats Ökvist	Expert - via telephone*	Norway	No restrictions applicable to this meeting	
Maciej Kostrubiec	Expert - via telephone*	Poland	No interests declared	
Johanna Lähteenvuo	Expert - via Adobe*	Finland	No interests declared	
Carine Condy	Expert - via Adobe*	France	No interests declared	
Marika Doucet	Expert - via Adobe*	France	No interests declared	
Yvens Bien-Aime	Expert - via Adobe*	France	No interests declared	
Clemens Mittmann	Expert - via Adobe*	Germany	No interests declared	
Joerg Zinserling	Expert - via Adobe*	Germany	No interests declared	
Jutta Dedorath	Expert - via Adobe*	Germany	No interests declared	
Michal Zwiewka	Expert - via Adobe*	Germany	No interests declared	
Susanna Hausmann	Expert - via Adobe*	Germany	No interests declared	
Shirley Hopper	Expert - via Adobe*	UK	No interests declared	
Meeting run with the help of EMA staff				

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

17. Explanatory notes

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

Oral explanations *(section 2)*

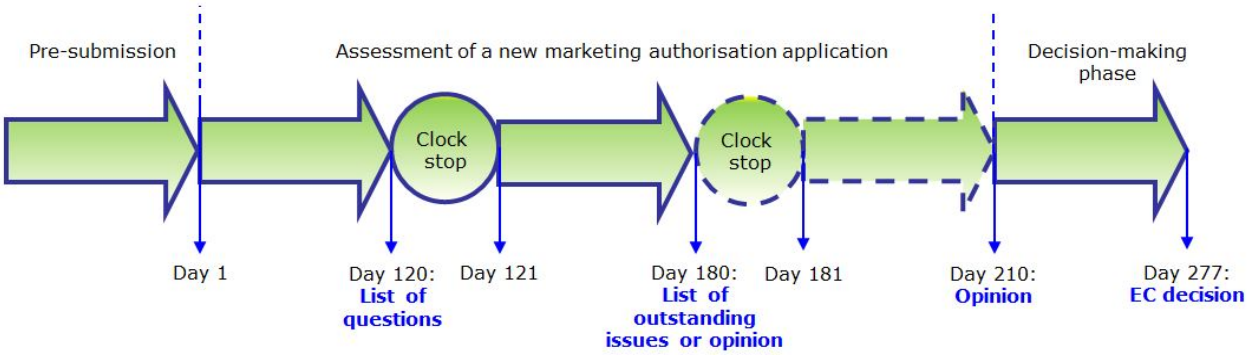
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

Initial applications *(section 3)*

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

Re-examination procedures *(section5.3)*

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

Withdrawal of application *(section 3.7)*

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

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

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

Pre-submission issues *(section 8)*

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

Post-authorisation issues *(section 9)*

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

Referral procedures *(section 10)*

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

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

Pharmacovigilance issues *(section 11)*

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

Inspections Issues *(section 12)*

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

Innovation task force *(section 13)*

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

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

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

Satellite groups / other committees *(section 14.2)*

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

Invented name issues *(section 14.3)*

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

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

19 November 2019
EMA/CHMP/599226/2019

Annex to 16-19 September 2019 CHMP Minutes

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A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for September 2019: **For adoption**	Adopted.

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

Final Outcome of Rapporteurship allocation for September 2019: **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

Kolbam - cholic acid - EMEA/H/C/002081/S/0029, Orphan Retrophin Europe Ltd, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Agni Kapou Request for Supplementary Information adopted on 27.06.2019, 26.04.2019.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The Marketing Authorisation remains under exceptional circumstances. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion.

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Clopidogrel ratiopharm - clopidogrel - EMEA/H/C/004006/R/0014 Teva B.V., Generic, Duplicate, Generic of Plavix, Duplicate of Clopidogrel Teva, Rapporteur: Rajko Kenda, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva	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.

Duavive - estrogens conjugated / bazedoxifene - EMEA/H/C/002314/R/0021 Pfizer Europe MA EEIG, Rapporteur: Martina Weise, Co-Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber Request for Supplementary Information adopted on 27.06.2019.	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.
IKERVIS - ciclosporin - EMEA/H/C/002066/R/0017 Santen Oy, Rapporteur: Peter Kiely, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Jan Neuhauser Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/R/0033 Orexigen Therapeutics Ireland Limited, Rapporteur: Mark Ainsworth, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Martin Huber Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
Orbactiv - oritavancin - EMEA/H/C/003785/R/0027 Menarini International Operations Luxembourg S.A., Rapporteur: Janet Koenig, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Adam Przybylkowski Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
Rixubis - nonacog gamma - EMEA/H/C/003771/R/0029 Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski Request for Supplementary Information adopted on 27.06.2019.	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.
SCENESSE - afamelanotide - EMEA/H/C/002548/R/0026, Orphan Clinuvel Europe Limited, Rapporteur: Janet Koenig, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Martin Huber	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information,

Request for Supplementary Information adopted on 25.07.2019.	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.
Sevelamer carbonate Winthrop - sevelamer carbonate - EMEA/H/C/003971/R/0022 Genzyme Europe BV, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Laurence de Fays Request for Supplementary Information adopted on 25.07.2019.	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.
Sivextro - tedizolid phosphate - EMEA/H/C/002846/R/0031 Merck Sharp & Dohme B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Maria del Pilar Rayon Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
Trevicta - paliperidone - EMEA/H/C/004066/R/0022 Janssen-Cilag International NV, Informed Consent of Xeplion, Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga Request for Supplementary Information adopted on 27.06.2019.	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.
Xydalba - dalbavancin - EMEA/H/C/002840/R/0028 Allergan Pharmaceuticals International Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Rugile Pilviniene Request for Supplementary Information adopted on 25.07.2019.	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

OCALIVA - obeticholic acid - EMEA/H/C/004093/R/0018, Orphan Intercept Pharma International Limited,	See agenda item 9.1 Request for supplementary information adopted

Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 19.09.2019.	with a specific timetable.

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection PRAC recommendations on signals adopted at the PRAC meeting held on 02-05 September 2019 PRAC:	
Signal of ischaemic stroke: Ibrutinib – IMBRUVICA **Action**: For adoption	Adopted.
New information on the known association between SGLT2 inhibitors and diabetic ketoacidosis (DKA) in surgical patients: Sodium-glucose co-transporter 2 (SGLT2) inhibitors: canagliflozin – INVOKANA; canagliflozin, metformin – VOKANAMET; dapagliflozin – EDISTRIDE; dapagliflozin – FORXIGA; dapagliflozin, metformin – EBYMECT; dapagliflozin, metformin – XIGDUO; empagliflozin – JARDIANCE; empagliflozin, metformin – SYNJARDY; empagliflozin, linagliptin – GLYXAMBI; ertugliflozin – STEGLATRO; ertugliflozin, metformin – SEGLUROMET; ertugliflozin, sitagliptin - STEGLUJAN; saxagliptin, dapagliflozin – QTERN **Action**: For adoption	Adopted.
Signal of psoriasis: Teriflunomide – AUBAGIO – **Action**: For adoption	Adopted.
PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its September 2019 meeting:	
EMEA/H/C/PSUSA/00000871/201902 (collagenase clostridium histolyticum (treatment of Dupuytren's contracture and treatment of Peyronie's disease)) CAPS: **Xiapex** (EMEA/H/C/002048) (collagenase clostridium histolyticum), Swedish Orphan Biovitrum AB (publ), Rapporteur: Janet Koenig,	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following changes:

PRAC Rapporteur: Martin Huber, “From: 27/02/2018 To: 27/02/2019”	Update of section 4.4 of the SmPC to add warnings on finger necrosis and on digital phalangeal fractures (both for Dupuytren’s contracture) and on the time span before resuming sexual activity and caution to be taken when resuming sexual activity (Peyronie’s disease). Update of section 4.8 of the SmPC to add the adverse reactions digital necrosis, digital fracture both with frequency not known (cannot be estimated from the available data) in Dupuytren’s contracture. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00001295/201902 (etanercept (except for biosimilars)) CAPS: **Enbrel** (EMEA/H/C/000262) (etanercept), Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, “From: 03/02/2018 To: 02/02/2019”	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 inflammatory bowel disease with a frequency ‘uncommon’. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00002162/201901 (nilotinib) CAPS: **Tasigna** (EMEA/H/C/000798) (nilotinib), Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, “From: 01/02/2018 To: 31/01/2019”	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 and 4.8 of the SmPC to add a warning and the adverse reaction ‘growth retardation in paediatric population’ with the frequency very common. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00002326/201901 (pegfilgrastim) CAPS:	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation

Fulphila (EMEA/H/C/004915) (pegfilgrastim), Mylan S.A.S, Rapporteur: Martina Weise **Neulasta** (EMEA/H/C/000420) (pegfilgrastim), Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege **Pelgraz** (EMEA/H/C/003961) (pegfilgrastim), Accord Healthcare S.L.U., Rapporteur: Sol Ruiz **Pelmeg** (EMEA/H/C/004700) (pegfilgrastim), Mundipharma Biologics S.L., Rapporteur: Koenraad Norga **UDENYCA** (EMEA/H/C/004413) (pegfilgrastim), ERA Consulting GmbH, Rapporteur: Martina Weise **Ziextenzo** (EMEA/H/C/004802) (pegfilgrastim), Sandoz GmbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Menno van der Elst, "From: 31/01/2016 To: 31/01/2019"	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 and 4.8 of the SmPC to add a warning on Stevens-Johnson syndrome and to add Stevens-Johnson syndrome as an adverse drug reaction (ADR) with a frequency rare. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00002435/201902 (pirfenidone) CAPS: **Esbriet** (EMEA/H/C/002154) (pirfenidone), Roche Registration GmbH, Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald, "27/02/2018 To: 27/02/2019"	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 and 4.8 of the SmPC to add anaphylaxis. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010022/201901 (axitinib) CAPS: **Inlyta** (EMEA/H/C/002406) (axitinib), Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: David Olsen, "From: 27/01/2018 To: 26/01/2019"	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 together with the detailed explanation of the scientific grounds for the differences with the PRAC recommendation, 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 cholecystitis with frequency 'common'. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

EMEA/H/C/PSUSA/00010035/201901 (ingenol mebutate) CAPS: **Picato** (EMEA/H/C/002275) (ingenol mebutate), LEO Laboratories Ltd, Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Adam Przybylkowski, "31/07/2018 To: 31/01/2019"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.4 of the SmPC to add a warning on cutaneous malignancies. The Package leaflet is updated accordingly. In addition, the MAH took the opportunity to correct the SmPC and Package Leaflet in order to indicate that Picato is under additional monitoring due to the obligation for submission of post-authorisation safety studies. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010123/201901 (paclitaxel albumin) CAPS: **Abraxane** (EMEA/H/C/000778) (paclitaxel), Celgene Europe BV, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "From: 05/01/2016 To: 05/01/2019"	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 scleroderma with a frequency not known. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010140/201901 (vismodegib) CAPS: **Erivedge** (EMEA/H/C/002602) (vismodegib), Roche Registration GmbH, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "From: 29/01/2018 To: 29/01/2019"	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 and 4.8 of the SmPC to add a warning on serious cutaneous adverse reactions and to add these adverse reactions with a frequency unknown. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

EMEA/H/C/PSUSA/00010340/201902 (ospemifene) CAPS: **Senshio** (EMEA/H/C/002780) (ospemifene), Shionogi B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Kirsti Villikka, "25/02/2018 To: 25/02/2019"	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 vaginal haemorrhage with the frequency 'common'. The package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010405/201901 (evolocumab) CAPS: **Repatha** (EMEA/H/C/003766) (evolocumab), Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola, "From: 17/07/2018 To: 17/01/2019"	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 hypersensitivity reaction with a common frequency. The Package Leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010448/201901 (carfilzomib) CAPS: **Kyprolis** (EMEA/H/C/003790) (carfilzomib), Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Nikica Mirošević Skvrce, "19/01/2018 To: 19/01/2019"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.4 of the SmPC in order to introduce new warnings of hepatitis virus B (HVB) reactivation and Progressive Multifocal Leukoencephalopathy (PML) and to amend the existing warnings on cardiac disorders and hypertension; and of section 4.8 of the SmPC in order to add HVB reactivation and PML in the list of adverse drug reactions with frequency uncommon and rare, respectively. The Package Leaflet is updated accordingly. The MAH also took the opportunity to introduce a minor editorial change to the SmPC and to update the Annex II in line with the QRD template.

	The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010452/201901 (etanercept (biosimilars)) CAPS: **Benepali** (EMEA/H/C/004007) (etanercept), Samsung Bioepis NL B.V., Rapporteur: Andrea Laslop **Erelzi** (EMEA/H/C/004192) (etanercept), Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia, "From: 14/01/2018 To: 14/01/2019"	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 products, concerning the following change(s): Update of section 4.8 of the SmPC to add the adverse reaction inflammatory bowel disease with a frequency uncommon. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010476/201902 (ferric maltol) CAPS: **Feraccru** (EMEA/H/C/002733) (ferric maltol), Norgine B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Adam Przybylkowski, "17/08/2018 To: 17/02/2019"	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 "discoloured faeces" with a frequency common. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010578/201902 (baricitinib) CAPS: **Olumiant** (EMEA/H/C/004085) (baricitinib), Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski, "From: 12/08/2018 To: 12/02/2019"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product, concerning the following change(s): Update of section 4.4 of the SmPC to add a warning on hypersensitivity and update of section 4.8 to add the adverse reactions "rash" with a frequency common and "swelling of the face, urticaria" with a frequency uncommon. The Package leaflet is updated accordingly. Update of section 4.4 of the SmPC to modify the wording on "Venous Thromboembolism" to indicate that if clinical features of DVT/PE occur

	baricitinib treatment should be discontinued and to update section 4.8 of the SmPC to add the adverse reaction pulmonary embolism and deep vein thrombosis with a frequency not known. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010639/201902 (telotristat) CAPS: **Xermelo** (EMEA/H/C/003937) (telotristat ethyl), Ipsen Pharma, Rapporteur: Martina Weise, PRAC Rapporteur: Adam Przybylkowski, "From: 28/08/2018 To: 27/02/2019"	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 include nausea, intestinal obstruction and depression with frequencies very common, uncommon and common, respectively; the Package leaflet is updated accordingly. In addition, the existing warning regarding depressive disorders in section 4.4 of the SmPC is updated in accordance. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

B.4. EPARs / WPARs

Xyndari - glutamine - EMEA/H/C/004734, Orphan Emmaus Medical Europe Ltd., treatment of sickle cell disease, Known active substance (Article 8(3) of Directive No 2001/83/EC) **WPAR**	For information only. Comments can be sent to the PL in case necessary.

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

Accofil - filgrastim - EMEA/H/C/003956/II/0034/G Accord Healthcare S.L.U., Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Advate - octocog alfa -	Positive Opinion adopted by consensus on

EMEA/H/C/000520/II/0100 Baxter AG, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 18.07.2019.	12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Afstyla - lonoctocog alfa - EMEA/H/C/004075/II/0023/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Alprolix - eftrenonacog alfa - EMEA/H/C/004142/II/0026, Orphan Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Apealea - paclitaxel - EMEA/H/C/004154/II/0003/G Oasmia Pharmaceutical AB, Rapporteur: Bart Van der Schueren Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 25.07.2019, 26.04.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Aripiprazole Mylan Pharma - aripiprazole - EMEA/H/C/003803/II/0012 Mylan S.A.S, Generic, Generic of Abilify, Rapporteur: Bjorg Bolstad Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Atazanavir Mylan - atazanavir - EMEA/H/C/004048/II/0012 Mylan S.A.S, Generic, Generic of Reyataz, Rapporteur: Bjorg Bolstad Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 11.07.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Atriance - nelarabine - EMEA/H/C/000752/II/0047/G Novartis Europharm Limited, Rapporteur: Sinan B. Sarac Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 25.07.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
BeneFIX - nonacog alfa - EMEA/H/C/000139/II/0160 Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 06.06.2019.	recommendation.
Benlysta - belimumab - EMEA/H/C/002015/II/0068 GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 27.06.2019, 26.04.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Betaferon - interferon beta-1b - EMEA/H/C/000081/II/0126/G Bayer AG, Rapporteur: Martina Weise Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Busulfan Fresenius Kabi - busulfan - EMEA/H/C/002806/II/0014 Fresenius Kabi Deutschland GmbH, Generic, Generic of Busilvex, Rapporteur: John Joseph Borg Opinion adopted on 19.09.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Buvidal - buprenorphine - EMEA/H/C/004651/II/0002 Camurus AB, Rapporteur: Peter Kiely Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cinryze - C1 esterase inhibitor (human) - EMEA/H/C/001207/II/0071/G Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
CRYSVITA - burosumab - EMEA/H/C/004275/II/0007/G, Orphan Kyowa Kirin Holdings B.V., Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Dupixent - dupilumab - EMEA/H/C/004390/II/0018/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 12.09.2019, 25.07.2019.	Request for supplementary information adopted with a specific timetable.
Elaprase - idursulfase - EMEA/H/C/000700/II/0082 Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 12.09.2019.	
Extavia - interferon beta-1b - EMEA/H/C/000933/II/0099/G Novartis Europharm Limited, Informed Consent of Betaferon, Rapporteur: Martina Weise Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Eylea - aflibercept - EMEA/H/C/002392/II/0053 Bayer AG, Rapporteur: Alexandre Moreau Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 04.07.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Hulio - adalimumab - EMEA/H/C/004429/II/0010/G Mylan S.A.S, Rapporteur: Bart Van der Schueren Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 06.06.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
HyQvia - human normal immunoglobulin - EMEA/H/C/002491/II/0051 Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 19.09.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Imfinzi - durvalumab - EMEA/H/C/004771/II/0009 AstraZeneca AB, Rapporteur: Sinan B. Sarac Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Lamzede - velmanase alfa - EMEA/H/C/003922/II/0007, Orphan Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Lonquex - lipegfilgrastim - EMEA/H/C/002556/II/0053/G Teva B.V., Rapporteur: Outi Mäki-Ikola Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
MVASI - bevacizumab - EMEA/H/C/004728/II/0008 Amgen Europe B.V., Duplicate, Duplicate of KYOMARC, Rapporteur: Bjorg Bolstad Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Nimenrix - meningococcal group a, c, w135 and y conjugate vaccine - EMEA/H/C/002226/II/0092/G	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad Opinion adopted on 12.09.2019.	recommendation.
Noxafil - posaconazole - EMEA/H/C/000610/II/0059 Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Nucala - mepolizumab - EMEA/H/C/003860/II/0025 GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely Opinion adopted on 19.09.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Nucala - mepolizumab - EMEA/H/C/003860/II/0026/G GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely Opinion adopted on 19.09.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
OCALIVA - obeticholic acid - EMEA/H/C/004093/II/0016/G, Orphan Intercept Pharma International Limited, Rapporteur: Jorge Camarero Jiménez Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0014/G Roche Registration GmbH, Rapporteur: Mark Ainsworth Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
OPDIVO - nivolumab - EMEA/H/C/003985/II/0067/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 25.07.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pelgraz - pegfilgrastim - EMEA/H/C/003961/II/0011/G Accord Healthcare S.L.U., Rapporteur: Sol Ruiz Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Pemetrexed Hospira - pemetrexed - EMEA/H/C/003970/II/0020/G Pfizer Europe MA EEIG, Generic, Generic of Alimta, Rapporteur: Alar Irs Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 12.09.2019.	
Prasugrel Mylan - prasugrel - EMEA/H/C/004644/II/0003/G Mylan S.A.S, Generic, Generic of Efient, Rapporteur: Alar Irs Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 11.07.2019, 16.05.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0180/G Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Repatha - evolocumab - EMEA/H/C/003766/II/0036 Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
RoActemra - tocilizumab - EMEA/H/C/000955/II/0084/G Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
RotaTeq - rotavirus vaccine (live, oral) - EMEA/H/C/000669/II/0079/G MSD Vaccins, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Skyrizi - risankizumab - EMEA/H/C/004759/II/0002/G AbbVie Deutschland GmbH & Co. KG, Rapporteur: Peter Kiely Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 18.07.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
SomaKit TOC - edotreotide - EMEA/H/C/004140/II/0011, Orphan Advanced Accelerator Applications, Rapporteur: Maria Concepcion Prieto Yerro Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Tepadina - thiotepa - EMEA/H/C/001046/II/0034, Orphan ADIENNE S.r.l., Rapporteur: Alexandre Moreau	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 19.09.2019.	
Tepadina - thiotepa - EMEA/H/C/001046/II/0035/G, Orphan ADIENNE S.r.l., Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
Tremfya - guselkumab - EMEA/H/C/004271/II/0015 Janssen-Cilag International N.V., Rapporteur: Melinda Sobor Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Verzenios - abemaciclib - EMEA/H/C/004302/II/0005 Eli Lilly Nederland B.V., Rapporteur: Filip Josephson Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vizarsin - sildenafil - EMEA/H/C/001076/II/0029 KRKA, d.d., Novo mesto, Generic, Generic of Viagra, Rapporteur: Alexandre Moreau Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 27.06.2019, 28.02.2019, 22.11.2018.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Voncento - human coagulation factor viii / human von willebrand factor - EMEA/H/C/002493/II/0041/G CSL Behring GmbH, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 18.07.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1524 **HyQvia-EMEA/H/C/002491/WS1524/0048** **Kiovig-EMEA/H/C/000628/WS1524/0090** Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 19.09.2019, 14.03.2019.	Request for supplementary information adopted with a specific timetable.
WS1587/G **Abasaglar-EMEA/H/C/002835/WS1587/0028/G** **Humalog-EMEA/H/C/000088/WS1587/0178/G** Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 19.09.2019.	
WS1612/G **Herceptin-EMEA/H/C/000278/WS1612/0155/G** **Kadcyla-EMEA/H/C/002389/WS1612/0047/G** Roche Registration GmbH, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
WS1630 **Bretaris Genuair-EMEA/H/C/002706/WS1630/0041** **Eklira Genuair-EMEA/H/C/002211/WS1630/0041** AstraZeneca AB, Lead Rapporteur: Ewa Balkowiec Iskra Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
WS1632/G **Brimica Genuair-EMEA/H/C/003969/WS1632/0027/G** **Duaklir Genuair-EMEA/H/C/003745/WS1632/0027/G** AstraZeneca AB, Lead Rapporteur: Ewa Balkowiec Iskra Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
WS1644/G **Insulatard-EMEA/H/C/000441/WS1644/0076/G** **Protaphane-EMEA/H/C/000442/WS1644/0075/G** Novo Nordisk A/S, Duplicate, Duplicate of Monotard (SRD), Ultratard (SRD), Lead Rapporteur: Sinan B. Sarac Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1662 **Nuwiq-EMEA/H/C/002813/WS1662/0031** **Vihuma-EMEA/H/C/004459/WS1662/0013** Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1674 **Actraphane-EMEA/H/C/000427/WS1674/0079**	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Actrapid-EMEA/H/C/000424/WS1674/0073 **Insulatard-EMEA/H/C/000441/WS1674/0077** **Mixtard-EMEA/H/C/000428/WS1674/0080** **Protaphane-EMEA/H/C/000442/WS1674/0076** Novo Nordisk A/S, Lead Rapporteur: Sinan B. Sarac Opinion adopted on 12.09.2019.	recommendation.
WS1678 **Rixathon-EMEA/H/C/003903/WS1678/0027** **Riximyo-EMEA/H/C/004729/WS1678/0028** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.

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

Advagraf - tacrolimus - EMEA/H/C/000712/II/0054 Astellas Pharma Europe B.V., Rapporteur: Jayne Crowe, “Update of section 4.2 of the SmPC to include a more clear statement for physicians regarding the potential risk of uncontrolled substitution between different tacrolimus formulations, even with those where BE has been proven, in order to minimise the risk of under or over exposure to tacrolimus.” Request for Supplementary Information adopted on 12.09.2019, 14.06.2019.	Request for supplementary information adopted with a specific timetable.
Brilique - ticagrelor - EMEA/H/C/001241/II/0045 AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, “Update of section 4.4 of the SmPC in order to add a new warning on interference with laboratories tests regarding platelet function tests to diagnose heparin induced thrombocytopenia (HIT) based on as safety review.” Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 29.05.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Brinavess - vernakalant -	Positive Opinion adopted by consensus on

EMEA/H/C/001215/II/0034 Correvio, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8 and 5.1 of the SmPC based on the final results from the non-interventional PASS SPECTRUM study, listed as a category 3 study in the RMP, in order to fulfil MEA 026.5; SPRECTRUM (6621-019) study is a prospective observational registry study to characterise normal conditions of use, dosing and safety following administration of vernakalant IV sterile concentrate." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 16.05.2019, 14.02.2019.	19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
CellCept - mycophenolate mofetil - EMEA/H/C/000082/II/0146 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC to update the safety information based on the reassessment of all available evidence from clinical trials, post-marketing experience and literature and to present ADRs in compliance with the SmPC guideline. Update of section 4.4 of the SmPC to include therapeutic dose monitoring for the addition or removal of an interacting medication based on an expert consensus. Update of section 4.7 of the SmPC to include a statement on the moderate influence on the ability to drive. Update of section 5.2 of the SmPC based on current literature on the pharmacokinetics in geriatric patients. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes throughout the PI and to bring the PI in line with the latest QRD template version 10.1." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 25.07.2019, 26.04.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cosentyx - secukinumab - EMEA/H/C/003729/II/0051 Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include additional dosing information for AS patients based on final results from study CAIN457F2314; this is a randomized, double-blind, double dummy, placebo controlled, parallel-group, Phase 3 multicentre study of secukinumab versus placebo	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

to demonstrate efficacy at 16 weeks and to assess long-term efficacy up to Week 156 in patients with active AS; the PL is updated accordingly." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 25.07.2019.	
Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0003/G Sanofi Pasteur, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Sonja Hrabcik, "C.I.13 grouping: Submission of the final report from studies CYD14 and CYD15 listed as category 3 studies in the RMP. These are the final results of the pivotal efficacy studies including amendments to long-term efficacy follow-up (to capture the full range of dengue disease in the study population prospectively i.e. return to active detection of all symptomatic dengue cases) and long-term safety monitoring. No changes to the PI or RMP identified are proposed at this stage. Minor updates of the RMP will follow." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 27.06.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Edurant - rilpivirine - EMEA/H/C/002264/II/0035 Janssen-Cilag International NV, Rapporteur: Paula Boudewina van Hennik, "Update of section 5.1 of the SmPC to reflect the week 240 results from the TMC278-TiDP38-C213(C213) study a phase II, open-label, single-arm trial to evaluate the pharmacokinetics, safety, tolerability, and antiviral activity of rilpivirine in antiretroviral-naïve HIV-1 infected adolescents and children aged ≥6 to <18 years, upon request by CHMP following the assessment of the paediatric study C213 submitted according to Art. 46 procedure (no. EMEA/H/C/2264/P46/028). In addition, the Marketing authorisation holder (MAH) took the opportunity to update Section 4.8 of the SmPC to indicate that no safety concerns were identified in the Week 240 analysis of the C213 trial in adolescents aged ≥12 to <18 years. Editorial changes have also been made to the product information." Opinion adopted on 19.09.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Edurant - rilpivirine - EMEA/H/C/002264/II/0036 Janssen-Cilag International NV, Rapporteur: Paula Boudewina van Hennik, "Update section 4.6 of the SmPC based on the most recent data described in the ARV Pregnancy Registry (APR). In addition, the Marketing authorisation holder (MAH) took the opportunity to update the Package Leaflet to include information on the sodium excipient, as per the revised Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' and the list of local representatives, as well as to make minor editorial changes in the SmPC and in the Package Leaflet." Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Eliquis - apixaban - EMEA/H/C/002148/II/0064 Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.4, 4.5 and 5.1 of the SmPC in order to update the safety information based on the final results from study CV185316 (AUGUSTUS), an open-label, randomised, controlled clinical trial to evaluate the safety of apixaban in patients with atrial fibrillation and acute coronary syndrome and/or percutaneous coronary intervention." Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0046 Merck Sharp & Dohme B.V., Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.3, 4.4 and 4.9 of the SmPC in order to revise the current text regarding Ovarian Hyperstimulation Syndrome (OHSS) to add clarity and remove clinical advice describing specific clinical interventions for reducing OHSS that have become outdated, based on post-marketing data and literature review. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder included some editorial changes in the Package Leaflet." Opinion adopted on 12.09.2019. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 14.06.2019.	
Eurartesim - piperaquine tetraphosphate / artenimol - EMEA/H/C/001199/II/0036 Alfasigma S.p.A., Rapporteur: Janet Koenig, "Changes to sections 4.2, 4.4 and 4.6 of the SmPC with reference to the posology and the recommendation during pregnancy; sections 2 and 3 of the leaflet (PL) are amended accordingly and refrence to the pregnancy register deleted from Annex II." Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
Eviplera - emtricitabine / rilpivirine / tenofovir disoproxil - EMEA/H/C/002312/II/0100 Gilead Sciences Ireland UC, Rapporteur: Johann Lodewijk Hillege, "Submission of the final study report for the drug utilisation study EDMS-ERI-139775027, an observational cohort study to assess rilpivirine utilisation according to the European SmPC, implemented using data from the EuroSIDA study cohort. The study is listed as a Category 3 study in the Eviplera RMP and submission of the final study report fulfils PAM MEA 011.5." Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Feraccru - ferric maltol - EMEA/H/C/002733/II/0022 Norgine B.V., Rapporteur: Maria Concepcion Prieto Yerro, "Update of sections 4.2, 4.4 and 5.2 of the SmPC to include information on patients with chronic kidney disease, following the submission of the final study report of study ST10-01-303." Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Fiasp - insulin aspart - EMEA/H/C/004046/II/0016 Novo Nordisk A/S, Rapporteur: Kristina Dunder, "Update of the SmPC section 4.8 with data from an updated safety pool, further to assessment of the last PSUR assessment for insulin aspart (EMEA/H/C/PSUSA/00001749/201809). This update is based on 3 efficacy and safety studies: NN1218-3852 (52 week) – a study of Fiasp compared to insulin aspart both in combination with insulin detemir in adults with Type 1 Diabetes; NN1218-3854 a study of	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Continuous Subcutaneous Insulin Infusion of Fiasp compared to NovoRapid in adults with Type 1 Diabetes; NN1218-4131 a study of Fiasp compared to NovoRapid both in combination with insulin degludec in adults with Type 1 Diabetes." Opinion adopted on 19.09.2019.	
IBRANCE - palbociclib - EMEA/H/C/003853/II/0024 Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, "Submission of the final report from a non-clinical study (PD-0332991) evaluating the correlation of palbociclib response to RB1 status." Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0027, Orphan CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.4 of the SmPC to update the warning with regards to inhibitor development. Section 4.8 of the SmPC and the PL have been updated accordingly." Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 14.06.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Imnovid - pomalidomide - EMEA/H/C/002682/II/0036/G, Orphan Celgene Europe BV, Rapporteur: Jorge Camarero Jiménez, "Group of two type II variations to update sections 4.2, 4.4 and 4.8 of the SmPC and section 4 of the PL with information on anaphylaxis and section 4.8 of SmPC with hypothyroidism ADR following a safety review. This group also includes a Type IB Variation to update section 6.6 of the SmPC in order to include recommendations to minimize the risk of unintended occupational exposures in healthcare professionals. The MAH has also proposed minor updates to section 4.4 of the SmPC and Annex IID regarding the educational materials, prescribing and dispensing restrictions in order to provide more clarity about the recommended maximum duration of treatment." Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Kisqali - ribociclib - EMEA/H/C/004213/II/0014 Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC based on the final results of study MONALEESA-7	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

(CLEE011E2301), a randomized, double-blind, placebo-controlled, multicenter Phase III study of ribociclib or placebo in combination with an NSAI and goserelin or tamoxifen and goserelin in pre- or perimenopausal women with HR-positive, HER2-negative, advanced breast cancer who had received no prior hormonal therapy for advanced disease." Opinion adopted on 19.09.2019.	
Kolbam - cholic acid - EMEA/H/C/002081/II/0028, Orphan Retrophin Europe Ltd, Rapporteur: Konstantinos Markopoulos, "Submission of the final report from study CAC-002-01, listed as a category 3 study in the RMP. This is a Phase 3, open-label, single arm, non-randomized study investigating cholic acid in the treatment of subjects with inborn errors of bile acid metabolism. The study was a continuation study that included eligible subjects who had previously received cholic acid in studies CAC-91-10-10 or CAC-001-01 as well as newly diagnosed subjects." Request for Supplementary Information adopted on 19.09.2019, 29.05.2019, 28.02.2019.	Request for supplementary information adopted with a specific timetable.
Kuvan - sapropterin - EMEA/H/C/000943/II/0068, Orphan BioMarin International Limited, Rapporteur: Peter Kiely, "Update of section 5.1 of the Summary Product Characteristics (SmPC) in order to reflect new paediatric information based on study PKU-015 evaluating the effect of Kuvan on neurocognitive function, maintenance of blood phenylalanine concentrations, safety, and population Pharmacokinetics in young Children with Phenylketonuria. The study is listed as MEA-C-Clinical, category 3 in the RMP for Kuvan and submitted in accordance to article 46 of the paediatric regulation." Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Kyprolis - carfilzomib - EMEA/H/C/003790/II/0038, Orphan Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of section 6.6 of the SmPC with information regarding the handling and preparation of Kyprolis. Labelling and PL are updated accordingly."	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 25.07.2019.	
Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0024 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Jean-Michel Race, "Update of section 5.1 of the SmPC to include data from the final clinical report from the Phase 3 study M16-126 (ENDURANCE-5,6, A Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Glecaprevir (GLE)/Pibrentasvir (PIB) in Adults with Chronic Hepatitis C Virus (HCV) Genotype 5 or 6 Infection)." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 27.06.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0007, Orphan Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, "Update of sections 4.8 and 5.1 of the SmPC based on safety and efficacy data for paediatric patients with relapsed or refractory AML from a systematic literature review, as requested by the gemtuzumab ozogamicin Paediatric Investigation Plan (PIP) EMEA-001733-PIP02-15-M01 (measure 4)." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 25.07.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0008, Orphan Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, "Update of sections 4.2 and 4.4 of the SmPC in relation to posology and administration and with information regarding traceability, respectively. Following the re-analysis of data from the paediatric study AAML0531 sections 4.8 and 5.1 of the SmPC are also updated with information on safety and efficacy of Mylotarg in previously untreated AML patients. In addition, the Marketing authorisation holder (MAH) took the opportunity to include minor editorial changes in sections 4.2, 4.4, 4.8 and 5.2 of the SmPC and to make minor updates to bring the PI in line with the latest QRD template version." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 25.07.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Noxafil - posaconazole - EMEA/H/C/000610/II/0058 Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau, “Update of section 4.8 of the SmPC in order to include 'pseudoaldosteronism' as an adverse event in post-marketing experience, following a review of six case reports in the scientific literature of concurrent hypertension and hypokalemia in patients treated with posaconazole. 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 version of the QRD template (version 10.1).” Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
OPDIVO - nivolumab - EMEA/H/C/003985/II/0069 Bristol-Myers Squibb Pharma EEIG, Co-Rapporteur: Paula Boudewina van Hennik, “Update of sections 4.2, 5.1 and 6.6 of the SmPC in order to replace the current weight-based dosing regimen for the adjuvant treatment of melanoma by the flat dose regimens of 240 mg every 2 weeks (Q2W) administered intravenously (IV) over 30 minutes or 480 mg every 4 weeks (Q4W) administered IV over 60 minutes based on population pharmacokinetic data and an exposure-response efficacy analysis. The Package leaflet has been updated accordingly.” Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 25.07.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0118/G Boehringer Ingelheim International GmbH, Rapporteur: Mark Ainsworth, “Update of section 4.5 of the SmPC in order to add a warning regarding the interaction between Pradaxa and the fixed-dose combination of the P-gp inhibitors glecaprevir and pibrentasvir based on the phase I drug-drug interaction study results. The Package Leaflet was updated accordingly. Update of section 4.8 of the SmPC with new safety information regarding adverse reaction alopecia following the confirmation of signal “alopecia associated with dabigatran” by the EMA and the cumulative review of cases of alopecia and related terms that was provided in PSUR submitted by 27 May 2019. In addition small	Request for supplementary information adopted with a specific timetable.

editorial corrections under "Adverse reaction" Table 2 were made additionally to highlight that information on some side effects was obtained from post-marketing data. The Package Leaflet was updated accordingly." Request for Supplementary Information adopted on 12.09.2019.	
Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0181 Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to update efficacy information based on results from a public health analysis and publication of data from the CAPiTA (Community-Acquired Pneumonia Immunization Trial in Adults), a double-blind, randomized, placebo-controlled efficacy trial of 13-valent pneumococcal conjugate vaccine (PCV13)." Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
Remicade - infliximab - EMEA/H/C/000240/II/0223 Janssen Biologics B.V., Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC and relevant section of the PL to include cerebrovascular accidents as rare underisable effect." Opinion adopted on 19.09.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Repatha - evolocumab - EMEA/H/C/003766/II/0033 Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, "Update of section 4.8 of the SmPC in order to update the safety information with regards to the adverse reaction "Influenza-like illness" with a frequency of Uncommon following the assessment of influenza-like illness with evolocumab in both the clinical database and postmarketing database. The Package Leaflet Section 4 was updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement changes to the package leaflet section 2 subsequent to the revised Annex to the EC guideline on excipients in the labelling (EMA/CHMP/302620/2017) to update the wording for sodium." Opinion adopted on 12.09.2019. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 29.05.2019.	
Revlimid - lenalidomide - EMEA/H/C/000717/II/0112/G, Orphan Celgene Europe BV, Rapporteur: Alexandre Moreau, “Group of variations including one type II to update sections 4.2, 4.4 and 4.8 of the SmPC and section 4 of the PL with anaphylaxis following a safety review a and a Type IB to update section 6.6 of the SmPC in order to include recommendations to minimize the risk of unintended occupational exposures in healthcare professionals. The MAH has also proposed minor updates to section 4.4 of the SmPC and Annex IID regarding the educational materials, prescribing and dispensing restrictions in order to provide more clarity about the recommended maximum duration of treatment. Finally the MAH took the opportunity to make editorial changes throughout the product information.” Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
RXULTI - brexpiprazole - EMEA/H/C/003841/II/0003 Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Daniela Melchiorri, “To update section 4.4 of the SmPC (paragraph “Impulse-control disorders”) based on the Company Core Data Sheet of brexpiprazole. In addition, the applicant has taken the opportunity to update the section 4.2 of the SmPC requested by EMA (see annex to cover letter) and to perform additional changes, i.e. editorial changes in the SmPC and Package Leaflet.” Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0016 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, “Update of section 4.5 of the SmPC in order to update the information related to coadministration based on the final results from studies ZOSTER-035 and ZOSTER-042; these are immunogenicity and safety studies in which Shingrix was co-administered either with Merck's 23-valent pneumococcal polysaccharide vaccine (Pneumovax 23; ZOSTER-035) or with GSK's reduced-antigen-content diphtheria and	Request for supplementary information adopted with a specific timetable.

tetanus toxoids and acellular pertussis (dTpa) vaccine (Boostrix; ZOSTER-042); the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 19.09.2019, 25.07.2019.	
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0017 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of sections 4.2 and 5.1 of the SmPC based on final results from study ZOSTER-048 (REC005); this is an immunogenicity and safety study of Shingrix in subjects previously vaccinated with Zostavax; the Package Leaflet is updated accordingly." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 25.07.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
SIMBRINZA - brinzolamide / brimonidine - EMEA/H/C/003698/II/0018/G Novartis Europharm Limited, Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 5.1 of the SmPC in order to update the safety information with adjunctive use of BID Simbrinza with a PGA therapy based on final results from study CQVJ499A2401; this is a phase 4, multicenter, randomized, double-masked, parallel-group study. Update of section 5.1 of the SmPC in order to update the safety information with adjunctive use of BID Simbrinza with a PGA/beta-blocker combination therapy based on final results from study CQVJ499A2402; this is a phase 4, multicenter, randomized, double-masked, parallel-group study." Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Symkevi - tezacaftor / ivacaftor - EMEA/H/C/004682/II/0012/G, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.5 and 5.2 of the SmPC in order to provide information on drug-drug interactions and pharmacogenetic data based on final results from two post-authorisation measures (PAMs) studies: VX18-661-011 (an open-label phase 1 study to examine the effects of combination of tezacaftor and ivacaftor on the pharmacokinetics and safety of pitavastatin in healthy subjects)	Request for supplementary information adopted with a specific timetable.

and pharmacokinetics study P088 (pharmacogenetic study of TEZ and IVA exposure with respect to CYP3A4*22 genotype)." Request for Supplementary Information adopted on 19.09.2019.	
TAGRISSO - osimertinib - EMEA/H/C/004124/II/0031 AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, "Update of section 4.8 of the SmPC to include onychalgia in the list of associated clustered terms for paronychia further to a MAH internal safety information review. The package leaflet has been updated accordingly." Opinion adopted on 19.09.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0061/G Biogen Netherlands B.V., Rapporteur: Martina Weise, "7xC.I.13: Submission of non-clinical studies: 1) Study Rsch-2013-023: A receptor binding study of Dimethyl Fumarate and Monomethyl Fumarate 2) Study P00012-14-04: Dimethyl Fumarate: A cardiovascular and respiratory assessment following oral administration to conscious, radiotelemetry-instrumented beagle dogs 3-4) Study P00012-05-03 and Study P00012-04-11: Amendments to two-year carcinogenicity study reports in mice and rats with DMF 5) Study P00012-12-02: A toxicity study of Dimethyl Fumarate when administered orally in juvenile male rats 6) Study P00012-13-07: Dimethyl Fumarate: Self-administration assessment in the male Sprague dawley rat 7) Study P00012-14-01: Dimethyl Fumarate: Drug discrimination assessment in the male Sprague dawley rat" Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Thalidomide Celgene - thalidomide - EMEA/H/C/000823/II/0061/G Celgene Europe BV, Rapporteur: Alexandre Moreau, "Group of variations including one type II to update sections 4.2, 4.4 and 4.8 of the SmPC and section 4 of the PL with anaphylaxis following a safety review and a Type IB to update section 6.6 of the SmPC in order to include recommendations to minimize the risk of	Request for supplementary information adopted with a specific timetable.

unintended occupational exposures in healthcare professionals. The MAH has also proposed minor updates to section 4.4 of the SmPC and Annex IID regarding the educational materials, prescribing and dispensing restrictions in order to provide more clarity." Request for Supplementary Information adopted on 12.09.2019.	
Tremfya - guselkumab - EMEA/H/C/004271/II/0010 Janssen-Cilag International N.V., Rapporteur: Melinda Sobor, "Update of sections 4.8 and 5.1 of the SmPC to add the long term 3-year clinical data from the two ongoing clinical studies CNTO1959PSO3001 (VOYAGE 1) and CNTO1959PSO3002 (VOYAGE 2) in subjects with plaque psoriasis. The requested variation proposed amendments to the Summary of Product Characteristics." Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 20.06.2019, 02.05.2019, 14.03.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tremfya - guselkumab - EMEA/H/C/004271/II/0014 Janssen-Cilag International N.V., Rapporteur: Melinda Sobor, "Update of section 5.1 of the SmPC in order to reflect the final results from the phase 3 Eclipse study CNTO1959PSO3009, comparing guselkumab (Tremfya) and secukinumab (Cosentyx) for the treatment of moderate to severe plaque psoriasis. CNTO1959PSO3009 is a Phase 3, randomized, double-blind, multicenter, active-comparator-controlled study in subjects with moderate to severe plaque psoriasis" Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 11.07.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Truvada - emtricitabine / tenofovir disoproxil - EMEA/H/C/000594/II/0161 Gilead Sciences Ireland UC, Rapporteur: Bruno Sepodes, "Submission of the final clinical study report for the non-interventional study GS-US-276-0103, 'A Prospective, Observational Study of Individuals Who Seroconvert While Taking Truvada for Pre-Exposure Prophylaxis (PrEP)', listed as a Category 3 study in the Truvada RMP." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 12.09.2019.	
Verzenios - abemaciclib - EMEA/H/C/004302/II/0003 Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC in order to add a criterion for discontinuing abemaciclib in the event of hepatic toxicity based on available safety data. Moreover, an unnecessary statement was removed from section 4.5 of the SmPC. In addition, the Marketing authorisation holder (MAH) took the opportunity to make editorial changes to section 5.1 of the SmPC and to the list of local representatives in the PL." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 25.07.2019, 29.05.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Verzenios - abemaciclib - EMEA/H/C/004302/II/0006 Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to add interstitial lung disease (ILD)-like events (including pneumonitis) as a new adverse drug reaction. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
Xaluprine - mercaptopurine - EMEA/H/C/002022/II/0022, Orphan Nova Laboratories Ireland Limited, Rapporteur: Filip Josephson, "Update of sections 4.4, 4.8 and 4.9 of the SmPC to add further information on hepatic toxicity. The MAH took the oportunity to implement minor editoral changes to the SmPC and PIL." Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0014, Orphan Ipsen Pharma, Rapporteur: Martina Weise, "To update sections 4.2 and 5.2 of the SmPC following final results from study LX1606-111; this is a Phase 1, open-label, parallel-group study to evaluate the single-dose pharmacokinetics of Telotristat Ethyl in Male and Female Subjects with Severe Hepatic Impairment and Matched	Request for supplementary information adopted with a specific timetable.

Subjects with Normal Function; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 19.09.2019, 11.07.2019.	
Yondelis - trabectedin - EMEA/H/C/000773/II/0058, Orphan Pharma Mar, S.A., Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, "Update of section 4.4 of the SmPC in order to add a warning based on results from study Cardiac Safety Report [Protocols ET743-SAR-3007, ET743-OVA-301, ET743-OVC-3006; Phase 3. JNJ-17027907; R270741 (trabectedin)] following the PSUSA procedure EMEA/H/C/PSUSA/00003001/201809; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
Zoely - nomegestrol acetate / estradiol - EMEA/H/C/001213/II/0050 Theramex Ireland Limited, Rapporteur: Jean-Michel Race, "Update of sections 4.3 and 4.4 of the SmPC in order to add a new contraindication and a new warning regarding meningioma, upon request by PRAC following the assessment of Post-authorisation measure "LEG 014". The Package Leaflet is being updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in the Netherlands and Portugal in the Package Leaflet." Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
WS1511/G **Advagraf-EMEA/H/C/000712/WS1511/0052/G** **Modigraf-EMEA/H/C/000954/WS1511/0031/G** Astellas Pharma Europe B.V., Lead Rapporteur: Jayne Crowe, "Update of sections 4.5 and 4.8 of the SmPC to add the drug-drug interaction with letermovir and to add the adverse reaction febrile neutropenia with frequency unknown, based on the cumulative review of the MAH safety database. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to implement the wording from the EC guideline on 'Excipients in the labelling	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

and package leaflet of medicinal products for human use' in the PI, to update the Maltese local representative in the PL and to implement minor editorial changes throughout the PI." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 14.06.2019, 14.03.2019.	
WS1605 **Lyrica-EMEA/H/C/000546/WS1605/0097** **Pregabalin Pfizer-EMEA/H/C/003880/WS1605/0027** Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, "Addition in the SmPC section 4.5 of the wording on the risk of death, including in patients who are substance abusers." Request for Supplementary Information adopted on 12.09.2019, 23.05.2019.	Request for supplementary information adopted with a specific timetable.
WS1647/G **Mirapexin-EMEA/H/C/000134/WS1647/0091/G** **Sifrol-EMEA/H/C/000133/WS1647/0082/G** Boehringer Ingelheim International GmbH, Lead Rapporteur: Mark Ainsworth Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1648 **Docetaxel Zentiva-EMEA/H/C/000808/WS1648/0060** **Taxotere-EMEA/H/C/000073/WS1648/0133** Aventis Pharma S.A., Lead Rapporteur: Alexandre Moreau, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning about cases of severe cutaneous reactions and to add acute generalized exanthematous pustulosis as an undesirable effect, respectively. The Package Leaflet is updated in accordance. In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet." Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1677 **Aluvia-EMEA/H/W/000764/WS1677/0110** **Kaletra-EMEA/H/C/000368/WS1677/0179** **Norvir-EMEA/H/C/000127/WS1677/0156** AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Jean-Michel Race, "Update of section 4.5 of the SmPC on the potential interaction with apalutamide, a moderate to strong CYP3A4	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

inducer, as well as with encorafenib, following an evaluation of the potential drug-drug interaction (DDI) between LPV/RTV (Kaletra and Aluvia) with apalutamide (Erleada) and encorafenib (Braftovi) through bibliographic and post-marketing data search. The Package Leaflet is also updated accordingly." Opinion adopted on 19.09.2019.	

B.5.3. CHMP-PRAC assessed procedures

Avastin - bevacizumab - EMEA/H/C/000582/II/0110 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, "Submission of the final report from study NEJ026 listed as an obligation in the Annex II of the Product Information. This is an open-label, randomized, Phase III study conducted in Japan to compare erlotinib + bevacizumab combination therapy versus erlotinib monotherapy as first-line therapies for patients with NSCLC with EGFR gene mutations (exon 19 deletion or exon 21 L858R substitution). The RMP version 30.0 has also been submitted. In addition, the Package leaflet is updated to reflect information on sodium content in compliance with the revised Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal products for human use"." Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
Avonex - interferon beta-1a - EMEA/H/C/000102/II/0182/G Biogen Netherlands B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, "To update sections 4.3 and 4.6 of the SmPC in order to remove the contraindication on the initiation of treatment in pregnancy and to update the recommendations on use in pregnancy and breastfeeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054). The MAH took the opportunity to add information about traceability in section 4.4 of the SmPC. The Package leaflet has been updated	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

accordingly. This submission fulfils MEA 87.2 and 84." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 29.05.2019, 28.02.2019.	
Betaferon - interferon beta-1b - EMEA/H/C/000081/II/0124/G Bayer AG, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "To update sections 4.3, 4.6 of the SmPC in order to remove the contraindication on the initiation of treatment in pregnancy and to update the recommendations on use in pregnancy and breastfeeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054). The MAH took the opportunity to add information about traceability in section 4.4 and to update the Product information to the QRD template version 10.1. The Package leaflet has been updated accordingly. This submission fulfils MEA 43.2 and 39. The RMP has been updated (ver 4.6) to include changes to the safety specification related to Pregnancy missing information status, in light of the new safety information received, as well as updates to other key sections of the RMP, adapting to the requirements of the GVP Module 5 revision 2 guidelines." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 29.05.2019, 28.02.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Brinavess - vernakalant - EMEA/H/C/001215/II/0035 Correvio, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information following updates to the Company Core Safety Datasheet (CCDS) based on the results of an integrated safety analysis performed on data of existing clinical studies with a stronger emphasis on treatment-related ADRs and an incidence rate above one percent. The Package Leaflet was updated accordingly. The RMP version 7.0 has also been submitted and incorporates the results from the new safety analysis. In addition the results from completed	Request for supplementary information adopted with a specific timetable.

observational Cohort SPECTRUM study (A Prospective Observational Registry Study to Characterise Normal Conditions of Use, Dosing and Safety Following Administration of Vernakalant IV Sterile Concentrate: PASS Protocol 6621-049) currently under assessment within Brinavess II/34 were included in the updated RMP. In addition, the Marketing authorisation holder (MAH) took the opportunity to update sections 4.2, 4.4, 4.6, 4.7, 4.8, 5.1, 5.2, 5.3, 6.4 of the SmPC, Annex II, Labelling sections 3 and 5, Package Leaflet sections 2, 4, 5 and 6 to include editorial changes, to correct typographical errors and to bring the PI in line with the latest QRD template version 10 as well as to update statements related to the excipients in the SmPC and Package Leaflet in line with the EC Guideline on "Excipients in the Labelling and Package Leaflet of medicinal products for human use" of March 2018 and the EMA Annex to the EC Guideline of October 2017 (SANTE-2017-11668)." Request for Supplementary Information adopted on 05.09.2019, 14.06.2019.	
Defitelio - defibrotide - EMEA/H/C/002393/II/0043, Orphan Gentium S.r.l., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the systematic literature analysis to fulfil a Specific Obligation (SOB) to provide comparative data on efficacy, including pooled outcomes of patients with veno-occlusive disease (VOD) treated with defibrotide; VOD incidence and outcomes in patients not treated with defibrotide. Consequently, the RMP v. 6.1 and Annex II of the Product Information have been revised. Additionally, the due date of the observational DefiFrance study (Category 3 Study in the RMP) has been revised; the RMP has been aligned with the template of EU RMP rev. 2 and minor editorial changes have been introduced." Opinion adopted on 19.09.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Extavia - interferon beta-1b - EMEA/H/C/000933/II/0096/G Novartis Europharm Limited, Informed Consent of Betaferon, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "To update sections 4.3, 4.6 of the SmPC in order to remove the	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

contraindication on the initiation of treatment in pregnancy and to update the recommendations on use in pregnancy and breastfeeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054). The MAH took the opportunity to add information about traceability in section 4.4 and to update the Product information to the QRD template version 10.1. The Package leaflet has been updated accordingly. This submission fulfils MEA 024.2 and 21. The RMP has been updated (ver 4.6) to include changes to the safety specification related to Pregnancy missing information status, in light of the new safety information received, as well as updates to other key sections of the RMP, adapting to the requirements of the GVP Module 5 revision 2 guidelines." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 29.05.2019, 28.02.2019.	
Iclusig - ponatinib - EMEA/H/C/002695/II/0051, Orphan Incyte Biosciences Distribution B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of the RMP to version 19.1, including deletion of previously agreed safety concerns; these deletions are proposed in line with the guideline on Good Pharmacovigilance Practices (GVP) Module V on RMP (revision 2 - dated on 31 March 2017). Other updates include: review of the categorisation of the posterior reversible encephalopathy syndrome (PRES) risk in the RMP in line with the request from PSUSA/00010128/201712; correction of the category (from Category 3 to 1) of the study AP24534-14-203, an imposed Annex II condition; revision of the due date for the submission of this study report to August 2021, as described in the Iclusig PI, and as agreed as part of procedure EMEA/H/C/002695/ANX/016. Additionally, The RMP and Annex II have been updated to remove the additional risk minimisation measures (Healthcare Professional Educational Brochure)." Opinion adopted on 05.09.2019. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 14.06.2019.	
Increlex - mecasermin - EMEA/H/C/000704/II/0060 Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.1, 4.2, 4.3, 4.4, 4.8 and 4.9 of the SmPC in order to update the safety information on benign or malignant neoplasia based on the EU Registry Study, the Ipsen global safety database and literature review. The Package Leaflet is updated accordingly. The MAH also submitted the updated RMP version 11. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet" Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0048/G Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, "C.1.4: Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information on the risk of Left ventricular dysfunction (LVD) based on the final results from study BO39807 listed as a category 3 study in the RMP. This is an observational study of cardiac events in patients with HER2-positive metastatic breast cancer who have a Left Ventricular Ejection Fraction (LVEF) between 40%-49% prior to initiating treatment with Kadcyla; The RMP version 10.0 has also been submitted. C.I.13: Submission of the final report from study BO28408 listed as a category 3 study in the RMP addressing cardiac safety, safety in elderly patients, and immunogenicity. This is a randomised, multicenter, open-label, two-arm, phase III neoadjuvant study evaluating the efficacy and safety of trastuzumab emtansine plus pertuzumab compared with chemotherapy plus trastuzumab and pertuzumab for patients with HER2-Positive Breast Cancer." Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
Lokelma - sodium zirconium cyclosilicate - EMEA/H/C/004029/II/0013 AstraZeneca AB, Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.2, 4.4 and 5.1 of the SmPC	Request for supplementary information adopted with a specific timetable.

in order to update the clinical information based final results from study DIALIZE. This was a Phase 3b, multicentre, prospective, randomised, double-blind, placebo-controlled study to reduce incidence of pre-dialysis hyperkalaemia with sodium zirconium cyclosilicate. The Package Leaflet and Labelling are updated accordingly. The RMP version 2.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement the new excipient statement for sodium in section 4.4 of the SmPC, section 2 of Labelling and section 2 of the Package Leaflet. Furthermore, minor editorial changes were introduced in section 2 of the Package leaflet." Request for Supplementary Information adopted on 19.09.2019.	
Lonsurf - trifluridine / tipiracil - EMEA/H/C/003897/II/0016 Les Laboratoires Servier, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Annika Folin, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update information on patients with severe renal impairment based on final results from study TO-TAS-102-107 (A Phase 1, Open-label Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of TAS-102 in Patients With Advanced Solid Tumors and Varying Degrees of Renal Impairment). The Package Leaflet is updated accordingly. The updated RMP version 6.3 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the RMP in line with the template revision 2 of the good Pharmacovigilance practice module V guideline." Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0029/G Orexigen Therapeutics Ireland Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber, "Group of variations consisting of the: 2) C.I.3.b: to update section 4.8 on the list of adverse drug reactions and their corresponding frequencies following the PRAC outcome on PSUR procedure (PSUSA/10366/201709). 2) C.I.4: to update sections 4.2, 4.4 and 5.2 of	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

the SmPC to add results from a phase I 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 hepatic function or varying degrees of impaired hepatic function and remove the recommendation to not use naltrexone/bupropion in patients with mild hepatic impairment. The existing warning has also been updated accordingly. The warning related to contraindications has also been aligned to section 4.3 to add end-stage renal failure patients. Consequentially an updated RMP (version 11) has also been submitted. In addition, the MAH takes the opportunity to update the warning on lactose to be in accordance with EC guideline on Guideline on "Excipients in the labelling and package leaflet of medicinal products for human use".” Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 25.07.2019, 29.05.2019, 28.02.2019, 15.11.2018.	
NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0030/G Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Submisison of the Guardian 4 (NN7008-3809) Clinical Trial in Previously Untretaed Patients (PUPs) and the Guardian 9 (NN7008-4239) PK Clinical Trial. In addition, the MAH has updated the SmPC to align with the 'EMA Core SmPC for human plasma derived and recombinant coagulation factor VIII products, revision 3' and Annex to the European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use'. Further, some administrative updates have also been applied.” Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0002 Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, “C.I.13: Submission of the Final Study Report for, ANNEXA-4 Study ("Prospective, Open-Label Study of Andexanet Alfa in Patients Receiving a Factor Xa Inhibitor Who Have Acute	Request for supplementary information adopted with a specific timetable.

Major Bleeding") listed as category 2 study in the RMP. This is an interventional non-randomized, multicentre, prospective, open-label, single-group study in patients with acute major bleeding. The results of ANNEXA-4 were requested to be submitted as Specific Obligation in the context of Conditional Marketing Authorisation. The RMP version 1.1 has also been submitted." Request for Supplementary Information adopted on 19.09.2019.	
Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0049 Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Rhea Fitzgerald, "Updated of section 4.8 of the SmPC with the safety data from the Phase 3, open-label, rollover study for Studies 109 and 011 Part B (Study 011B) designed to evaluate the long-term safety and tolerability of Orkambi treatment for 96 weeks in patients with cystic fibrosis, 6 years of age and older, homozygous for F508del." Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
Plegridy - peginterferon beta-1a - EMEA/H/C/002827/II/0052/G Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ulla Wändel Liminga, "To update sections 4.3 and 4.6 of the SmPC in order to remove the contraindication on the initiation of treatment in pregnancy and to update the recommendations on use in pregnancy and breastfeeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054). The MAH took the opportunity to add information about traceability in section 4.4 of the SmPC. The Package leaflet has been updated accordingly. This submission fulfils MEA 8.2 and 002. The RMP has been updated (ver 4.3) to include changes to the safety specification related to Pregnancy missing information status, in light of the new safety information received, as well as updates to other key sections of the RMP, adapting to the requirements of the GVP Module 5 revision 2 guidelines."	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 29.05.2019, 28.02.2019.	
Rapiscan - regadenoson - EMEA/H/C/001176/II/0034/G GE Healthcare AS, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "Grouping of variations: - Update of sections 4.4 and 4.8 of the SmPC regarding myocardial ischaemia (myocardial infarction, ventricular arrhythmias and cardiac arrest) based on a review of the safety database and CCDS update - Update of sections 4.4, 4.5, 4.8, 4.9 and 5.1 of the SmPC regarding co-administration with methylxanthines due to the risk of seizure and hypersensitivity including anaphylaxis based on a review of the safety database and CCDS update - Update of section 5.1 of the SmPC regarding the use of regadenoson in patients with inadequate stress test based on results from study 3606-CL-3004 and CCDS update. The RMP version (11.1) has also been submitted in order to fulfil LEG 016." Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
Rebif - interferon beta-1a - EMEA/H/C/000136/II/0137/G Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "To update sections 4.3, 4.6 and 5.3 of the SmPC in order to remove the contraindication on the initiation of treatment in pregnancy and to update the recommendations on use in pregnancy and breastfeeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054). The MAH took the opportunity to add information about traceability in section 4.4 and to update the Product information to the QRD template version 10.1. The Package leaflet has been updated accordingly. This submission fulfils MEA 43.2 and 39. The RMP has been updated (ver 10.2) to include changes to the safety specification related to Pregnancy missing information status, in light of the new safety information received, as well as	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

updates to other key sections of the RMP, adapting to the requirements of the GVP Module 5 revision 2 guidelines." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 29.05.2019, 28.02.2019.	
ReFacto AF - moroctocog alfa - EMEA/H/C/000232/II/0151 Pfizer Europe MA EEIG, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, "To update sections 4.8 Undesirable effects and 5.1 Pharmacodynamic effects of the SmPC based on the final results from study 3082B2-313 (B1831001 - "An Open-Label Study to Evaluate Prophylaxis Treatment, and to Characterize the Efficacy, Safety, and Pharmacokinetics of B-Domain Deleted Recombinant Factor VIII Albumin Free (Moroctocog Alfa [AF_CC]) in Children with Hemophilia A") listed as an additional pharmacovigilance activity in the Risk Management Plan (RMP; MEA 116). The RMP version 13.0 has also been submitted. In addition, the SmPC is being brought in line with the revised guidelines on core SmPC for human plasma derived and recombinant coagulation factor VIII products (Revision 3) in sections 4.2 Posology and Method of Administration, 4.4 Special warnings and special precautions for use, 4.8 Undesirable effects and 5.1 Pharmacodynamic effects." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 29.05.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Spinraza - nusinersen - EMEA/H/C/004312/II/0014, Orphan Biogen Netherlands B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from Phase 2 Study SM202 (EMBRACE or CS7) listed as a category 3 study in the RMP. This is a Phase 2, randomized, double-blind, sham-procedure-controlled study to assess the safety and tolerability and explore the efficacy of ISIS 396443 (BIIB058) administered intrathecally in subjects with spinal muscular atrophy who are not eligible to participate in the clinical studies ISIS 396443-CS3B or ISIS 396443-CS4 due to age at screening and/or SMN2 copy number. Version 10.2 of the RMP was approved."	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 14.06.2019.	
Stayveer - bosentan - EMEA/H/C/002644/II/0028 Janssen-Cilag International NV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, “Update of section 4.2 of the SmPC in order to include that patients should be given the Package Leaflet and the Patient Alert Card which are included in the pack and update of annex II.D to remove the Prescriber kit from the additional risk minimisation measures and also to remove the obligation to implement a formal "Controlled Distribution System" in EU countries following the assessment of LEG 10.2. The RMP version 11 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of the local representative in the UK, to bring the PI in line with the latest QRD template version 10, and with the guideline on Excipients in the labelling and package leaflet of medicinal products for human use (EMA/CHMP/302620/2017), and to implement some corrections to the Bulgarian translations.” Opinion adopted on 05.09.2019.	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
TAGRISSO - osimertinib - EMEA/H/C/004124/II/0029 AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst, “Update of sections 4.2 and 5.2 of the SmPC in order to reflect the outcome of study D5160C00035, an open-label, Phase I study to assess the pharmacokinetics, safety and tolerability of osimertinib following a single oral 80 mg dose to patients with advanced solid tumours and normal renal function or severe renal impairment. This study was a Category 3 study in the EU-RMP. The RMP version 13 has also been submitted.” Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 27.06.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0062 Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, “Update of sections 4.4 and 4.8 of the SmPC to add a	Request for supplementary information adopted with a specific timetable.

warning on the risk of herpes zoster based on cumulative review data submitted in the ongoing PSUSA/00010143/201903. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 19.09.2019.	
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0063 Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Update of sections 4.4 and 4.8 of the SmPC to reflect PML in the setting of mild lymphopenia based on data submitted in the ongoing PSUSA/00010143/201903. The Package Leaflet is updated accordingly. Additionally, the Product Information has been updated in line with QRD template (version 10.1)." Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
Tracleer - bosentan - EMEA/H/C/000401/II/0092 Janssen-Cilag International NV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, "Update of section 4.2 of the SmPC in order to include that patients should be given the Package Leaflet and the Patient Alert Card which are included in the pack and update of annex II.D to remove the Prescriber kit from the additional risk minimisation measures and also to remove the obligation to implement a formal "Controlled Distribution System" in EU countries following the assessment of LEG 086.2. The RMP version 11 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of the local representative in the UK, to bring the PI in line with the latest QRD template version 10, and with the guideline on Excipients in the labelling and package leaflet of medicinal products for human use (EMA/CHMP/302620/2017), and to implement some corrections to the Bulgarian translations." Opinion adopted on 05.09.2019.	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Truberzi - eluxadoline - EMEA/H/C/004098/II/0009/G Allergan Pharmaceuticals International Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Adam Przybylkowski, "Update of sections 4.2, 4.4	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

and 5.2 of the SmPC in order to update the safety information based on results from PK study ELX-PK-01 listed as a category 3 study in the RMP; this is a Single-dose, Open-label, Pharmacokinetic study of Eluxadoline in Healthy Subjects with normal Renal Function and Patients with Renal Impairment. Accordingly the RMP was updated to remove use in patients with renal impairment as missing information. Update of sections 4.4 and 4.8 of the SmPC following Company Core Data Sheet (CCDS) update based on review of clinical safety data and post- marketing safety data. Section 4.3 has been updated to add clarification in line with section 4.4. and section 5.1 has been updated to add Pharmacotherapeutic Group and ATC code. The RMP version 3.1 has also been submitted. The Package Leaflet is updated accordingly. In addition, the MAH also took the opportunity to change “eluxadoline” to “Truberzi” when referring to the medicinal product throughout the SmPC. Furthermore the MAH took the opportunity to update the list of local representatives in the PI.” Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 27.06.2019, 28.03.2019.	
UDENYCA - pegfilgrastim - EMEA/H/C/004413/II/0003 ERA Consulting GmbH, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, “To update section 4.6 of the SmPC to update the safety information based on feasability data regarding the pregnancy and lactation registry listed as a category 3 study in the RMP; this is a non-interventional registry. The Package Leaflet is updated accordingly. The updated RMP version 1.5 has also been submitted.” Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
Zelboraf - vemurafenib - EMEA/H/C/002409/II/0054 Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, “Update of sections 4.4 and 4.5 of the SmPC in order to add information and a precaution regarding concomitant strong CYP3A4 inhibitors based on final results from study GO29475 (MEA-011), a category 3 study in the RMP; the Package Leaflet is updated accordingly. The RMP version 12.0 has also been submitted. In	Request for supplementary information adopted with a specific timetable.

addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PL in line with the excipients guideline (EMA/CHMP/302620/2017) by adding information about the product's sodium content." Request for Supplementary Information adopted on 05.09.2019.	
Zydelig - idelalisib - EMEA/H/C/003843/II/0047 Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber, "submission of the final clinical study report for study 101-09, A Phase 2 Study to Assess the Efficacy and Safety of Idelalisib in Subjects with Indolent BCell Non-Hodgkin Lymphomas Refractory to Rituximab and Alkylating Agents. This submission is an Annex II postauthorisation measure (ANX 002) and a category I commitment in the Zydelig Risk Management Plan (RMP).This submission also includes an update to the PI" Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
WS1518 Epclusa-EMEA/H/C/004210/WS1518/0034 Harvoni-EMEA/H/C/003850/WS1518/0077 Sovaldi-EMEA/H/C/002798/WS1518/0055 Vosevi-EMEA/H/C/004350/WS1518/0025 Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC (Epclusa, Harvoni, Sovaldi) and 4.2, 4.4, 4.8 and 5.2 (Vosevi) in order to add new information regarding the use of the sofosbuvir-containing products in patients with renal impairment, based on final results from studies GS-US-342-4062, GS-US-337-4063 and GS-US-334-0154, listed as a category 3 study in the RMP and study GS-US-338-1125. Study GS-US-342-4062 was a phase 2, multi-centre, open-label study to evaluate the efficacy and safety of sofosbuvir/velpatasvir for 12 Weeks in subjects with chronic HCV infection who are on dialysis for end stage renal disease. Study GS-US-337-4063 was a phase 2, multi-centre, open-label study to evaluate the efficacy and safety of ledipasvir/sofosbuvir in subjects with genotype 1, 4, 5 and 6 chronic HCV	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

infection who are on dialysis for end stage renal disease. Study GS-US-334-0154 was a phase 2b, open label study of 200 mg or 400 mg sofosbuvir+ribavirin for 24 Weeks in Genotype 1 or 3 HCV infected subjects with renal insufficiency. Study GS-US-338-1125 was a phase 1, open-label, parallel-group, single-dose study to evaluate the pharmacokinetics of voxilaprevir in subjects with normal renal function and severe renal impairment. The Package Leaflet is updated accordingly. The RMPs have also been submitted for each of the products in this work-sharing procedure." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 14.06.2019, 11.04.2019.	
WS1599 **Rixathon-EMEA/H/C/003903/WS1599/0020** **Riximyo-EMEA/H/C/004729/WS1599/0020** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus, Lead PRAC Rapporteur: Hans Christian Siersted, "Submission of the final report from study (GP13-301) listed as a category 3 study in the RMP. This is a randomised, controlled double-blind Phase III trial to compare the efficacy, safety and pharmacokinetics of GP2013 plus cyclophosphamide, vincristine, prednisone vs MabThera plus cyclophosphamide, vincristine, prednisone, followed by GP2013 or MabThera maintenance therapy in patients with previously untreated advanced stage follicular lymphoma. The RMP version 4.1 has been agreed." Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 16.05.2019.	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.4. PRAC assessed procedures

PRAC Led **AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0025** sanofi-aventis groupe, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the patients and HCPs final survey reports to	Request for supplementary information adopted with a specific timetable.

assess the effectiveness of the education materials; the survey reports are part of the additional pharmacovigilance activities in the RMP (category 3 studies). Within this submission the MAH is proposing a revised patient card with the following revisions: the patient card was restructured (general guidance, possible side effects, pregnancy), details related to the Accelerated Elimination Procedure were deleted and symptoms related to liver and infections are described." Request for Supplementary Information adopted on 05.09.2019.	
PRAC Led **Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0081** UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from study (British Society for Rheumatology Biologics Register (BSRBR), RA0022) listed as a category 3 study in the RMP. This is a UK registry which aims to monitor the long term safety of TNF-α drugs and other targeted therapies in rheumatoid arthritis patients. Submission of the interim report from study (RABBIT registry, RA0020) listed as a category 3 study in the RMP. This is a Germany biologic registry, long-term observational cohort study of the safety and effectiveness of biologic agent in rheumatoid arthritis." Opinion adopted on 05.09.2019.	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Hemangiol - propranolol - EMEA/H/C/002621/II/0019** PIERRE FABRE DERMATOLOGIE, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Update of Package Leaflet in order to strengthen the warning on Hypoglycemia and Bronchospasm following completion of Drug Utilisation Study (DUS) performed in Germany and France to evaluate off-label use and effectiveness of RMM in a real-life clinical setting (MEA 002). In additions editorial changes have been introduced in section 4.4 of the SmPC as well as changes in the PL in accordance with QRD template 10.0. RMP version 3.1 has been submitted in order to update the additional RMMs	Request for supplementary information adopted with a specific timetable.

as a consequence of the results of the DUS." Request for Supplementary Information adopted on 05.09.2019, 16.05.2019, 14.02.2019.	
PRAC Led **Kiovig - human normal immunoglobulin - EMEA/H/C/000628/II/0091** Baxter AG, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 9.0 in order to include the new indication chronic inflammatory demyelinating polyradiculoneuropathy [CIDP] and update the list of safety concerns (implementation of new specifications from GCP Module V (Rev 2)." Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 14.06.2019.	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Kisplyx - lenvatinib - EMEA/H/C/004224/II/0024** Eisai GmbH, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Bjorg Bolstad, "Submission of an updated clinical study design of a PASS Study E7080-G000-218 (MEA 007) to change its design from phase 2 randomised, double-blind clinical trial to open label. The study assesses the Safety and efficacy of lenvatinib at two different starting doses (18mg vs. 14mg QD) in Combination to everolimus (5 mg QD) in Renal Cell carcinoma following one prior VEGF-Targeted treatment. This variation is consequence of the post authorisation measure MEA 06.1. and the change is at CHMP's request. Consequently the RMP v.11.1 has been revised also additional minor administrative changes have been implemented." Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 14.06.2019.	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Luveris - lutropin alfa - EMEA/H/C/000292/II/0082** Merck Europe B.V., Rapporteur: Mark Ainsworth, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP for Luveris 75 IU powder and solvent for injections version 3.1, 28 Nov 2018 in order to:	Request for supplementary information adopted with a specific timetable.

- adapt the RMP template to Good Pharmacovigilance Practice (GVP) Module V, rev 2. - delete reference to Luveris 450 IU solution for injection in pre-filled pen, following the withdrawal of this presentation (EU/1/00/155/007). - removal of important identified risks “Ovarian Hyperstimulation Syndrome (OHSS)” and “Mild to severe hypersensitivity reactions including anaphylactic reactions and shock” and important potential risks “Thromboembolic (TE) events”, “Reproductive system cancer”, “Ectopic pregnancy”, “Multiple pregnancies”, “Congenital anomaly” and “off label use”). For the missing information of “Hypogonadotropic hypogonadal women with severe LH and FSH deficiency of advanced maternal age (older than 40 years)”, the advanced maternal age has been changed from 40 to 42 years. - amendment and update of the epidemiology and non-clinical sections of the RMP, as per the most recent data. The clinical trial section and exclusion criteria in pivotal clinical studies section have been updated for recombinant human luteinizing hormone (rhLH). - update with the patient exposure data up to the data lock point (DLP) of 28 November 2018. - Other minor changes (e.g. reporting rates in RMP tables)” Request for Supplementary Information adopted on 05.09.2019.	
PRAC Led **Ozurdex - dexamethasone - EMEA/H/C/001140/II/0035** Allergan Pharmaceuticals Ireland, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, “C.I.13: Submission of the final report from study CMO-EPI-EYE-0522 listed as a category 3 study in the RMP. This is an observational, cross-sectional study conducted in France, Germany, Spain, and the UK having as primary objective the assessment of the effectiveness of the educational material provided to the treating physicians. In consequence, the SmPC sections 4.2, 6.6 and Annex II of Product information were updated to reflect the conclusions of the assessment. Package Leaflet is updated accordingly.	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

In addition, the Marketing authorisation holder took the opportunity to include updates to local representative in SK." Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 14.06.2019.	
PRAC Led **Selincro - nalmefene - EMEA/H/C/002583/II/0025** H. Lundbeck A/S, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "submission for the Final Study Reports for the PASS 15649A: Use of Nalmefene (Selincro) in European databases: Cohort design using longitudinal electronic medical records or claims databases and PASS 14910A a non-interventional multicountry prospective cohort study to investigate the pattern of use of Selincro and frequency of selected adverse reactions in routine clinical practice." Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **SIMBRINZA - brinzolamide / brimonidine - EMEA/H/C/003698/II/0019** Novartis Europharm Limited, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Submission of an updated RMP version 3.0 in order to remove metabolic acidosis/renal impairment as an important potential risk from the list of safety concerns and in addition update the Risk management plan to comply with the new GVP module V rev 2 RMP template." Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Slenyto - melatonin - EMEA/H/C/004425/II/0010** RAD Neurim Pharmaceuticals EEC SARL, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "The removal of "Delay of sexual maturation and development" as an "Important potential risk" from the EU-RMP." Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led	Positive Opinion adopted by consensus on

Tremfya - guselkumab - EMEA/H/C/004271/II/0013 Janssen-Cilag International N.V., Rapporteur: Melinda Sobor, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of RMP to remove exposure during lactation as missing information. In addition an update of the SmPC section 4.6 is introduced to amend information related to breastfeeding and reflect the current scientific knowledge." Opinion adopted on 19.09.2019. Request for Supplementary Information adopted on 27.06.2019.	19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Votrient - pazopanib - EMEA/H/C/001141/II/0054** Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 17.0 in order to postpone CSR submission for the COMPARZ study and its substudy, to reflect PRAC recommendations for additional assessments of some risks, to revise the list of safety concerns and to adapt the RMP to the template of the revised GVP module V guideline (rev 2)." Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 16.05.2019.	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Xadago - safinamide - EMEA/H/C/002396/II/0031** Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Submission of an updated RMP version 6.1 in order to implement RMP rev 2 template and introduce changes to pre-clinical, clinical and post-marketing exposure information and update the due date of DUS Z7219N02 from July 2019 to 28 February 2020." Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 14.06.2019.	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1581** **Rasilez-EMEA/H/C/000780/WS1581/0123** **Rasilez HCT-EMEA/H/C/000964/WS1581/**	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

0093 Noden Pharma DAC, Lead Rapporteur: Daniela Melchiorri, Lead PRAC Rapporteur: Ilaria Baldelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of an updated RMP version 14 in order to update the template in line with GVP Module V Rev2 required, add new important potential risk of non-melanoma skin cancer (related to Rasilez HCT only), and remove several important risks and missing information items as per PRAC endorsement of PSUR 12." Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 16.05.2019.	
PRAC Led **WS1655** **Aerius-EMEA/H/C/000313/WS1655/0091** **Azomyr-EMEA/H/C/000310/WS1655/0095** **Neoclarityn-EMEA/H/C/000314/WS1655/0089** Merck Sharp & Dohme B.V., Duplicate, Duplicate of Allex (SRD), Azomyr, Opulis (SRD), Lead Rapporteur: Koenraad Norga, Lead PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Bart Van der Schueren, "C.I.13: Submission of the final report from study (EUPAS15038) listed as a category 3 study in the RMP. This is a non-interventional non-imposed PASS study designed to assess the potential risk of desloratadine exposure on seizures, supraventricular tachycardia, and atrial fibrillation or flutter." Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.

B.5.5. CHMP-CAT assessed procedures

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0011, Orphan, ATMP Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang Opinion adopted on 19.09.2019, 13.09.2019. Request for Supplementary Information adopted on 19.07.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Spherox - spheroids of human autologous matrix-associated chondrocytes -	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP

EMEA/H/C/002736/II/0005/G, ATMP CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder, "Update of the product information to reflect the study results of the 36-month follow up data for trial cod 16 HS 13 and the final study report with 60-month follow-up data for trial cod 16 HS 14. Study cod 16 HS 13, is a Prospective, randomised, open label, multicentre Phase-III clinical trial to compare the efficacy and safety of the treatment with the autologous chondrocyte transplantation product co.don chondrosphere (ACT3D-CS) with microfracture in subjects with cartilage defects of the knee with a defect size between 1 and 4 cm2. Study cod 16 HS 14, is a Prospective, randomised, open label, multicentre Phase-II clinical trial to investigate the efficacy and safety of the treatment of large defects (4-10 cm2) with three different doses of the autologous chondrocyte transplantation product co.don chondrosphere (ACT3D-CS) in subjects with cartilage defects of the knee." Opinion adopted on 19.09.2019, 13.09.2019. Request for Supplementary Information adopted on 21.06.2019, 24.05.2019.	Members were in agreement with the CHMP recommendation.
Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0008, ATMP CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder Opinion adopted on 19.09.2019, 13.09.2019. Request for Supplementary Information adopted on 21.06.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0008, Orphan, ATMP Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus Opinion adopted on 19.09.2019, 13.09.2019. Request for Supplementary Information adopted on 21.06.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0011, Orphan, ATMP Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 13.09.2019.	
YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0012, Orphan, ATMP Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus Opinion adopted on 19.09.2019, 13.09.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zynteglo - autologous cd34+ cell enriched population that contains hematopoietic stem cells transduced with lentiglobin bb305 lentiviral vector encoding the beta-a-t87q-globin gene - EMEA/H/C/003691/II/0001/G, Orphan, ATMP bluebird bio (Netherlands) B.V, Rapporteur: Carla Herberts, CHMP Coordinator: Paula Boudewina van Hennik Request for Supplementary Information adopted on 13.09.2019.	Request for supplementary information adopted with a specific timetable.

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

PRAC Led **Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0034, ATMP** Amgen Europe B.V., Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, “To update the RMP for Imlygic to version 7.0 in order to add 2 category 3 studies (Studies 20180062 and 20180099), as well as an internal evaluation of managed distribution process metrics, to evaluate the effectiveness of additional risk minimization measures (aRMM).” Opinion adopted on 19.09.2019, 13.09.2019. Request for Supplementary Information adopted on 19.07.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

WS1634 **Advate-EMEA/H/C/000520/WS1634/0102** **ADYNOVI-EMEA/H/C/004195/WS1634/**	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

0007 Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 12.09.2019.	recommendation.
WS1643/G **Halimatoz-EMEA/H/C/004866/WS1643/0012/G** **Hefiya-EMEA/H/C/004865/WS1643/0012/G** **Hyrimoz-EMEA/H/C/004320/WS1643/0012/G** Sandoz GmbH, Lead Rapporteur: Milena Stain Opinion adopted on 19.09.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1650 **Olanzapine Glenmark-EMEA/H/C/001085/WS1650/0031** **Olanzapine Glenmark Europe-EMEA/H/C/001086/WS1650/0028** **Olazax-EMEA/H/C/001087/WS1650/0024** **Olazax Disperzi-EMEA/H/C/001088/WS1650/0025** Glenmark Arzneimittel GmbH, Generic, Generic of Olansek (SRD), Zyprexa, Zyprexa Velotab, Lead Rapporteur: Alexandre Moreau, “To updated section 4.8 of the SmPC to add "stuttering", section 5.2 of the SmPC to include new section with a sub heading 'Hepatic Impairment' and text related to smoking in line with PI text of the reference product. The PL has been updated accordingly. In addition the MAH has taken the opportunity to align the annexes with minor linguistic changes in line with the reference product.” Opinion adopted on 12.09.2019. Request for Supplementary Information adopted on 11.07.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1656/G **Copalia-EMEA/H/C/000774/WS1656/0108/G** **Copalia HCT-EMEA/H/C/001159/WS1656/0079/G** **Dafiro-EMEA/H/C/000776/WS1656/0111/G** **Dafiro HCT-EMEA/H/C/001160/WS1656/0081/G** **Exforge HCT-EMEA/H/C/001068/WS1656/0078/G** Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 19.09.2019.	
WS1658/G **Eucreas-EMEA/H/C/000807/WS1658/0075/G** **Galvus-EMEA/H/C/000771/WS1658/0063/G** **Icandra-EMEA/H/C/001050/WS1658/0078/G** **Jalra-EMEA/H/C/001048/WS1658/0065/G** **Xiliarx-EMEA/H/C/001051/WS1658/0062/G** **Zomarist-EMEA/H/C/001049/WS1658/0077/G** Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1659/G **Silodosin Recordati-EMEA/H/C/004964/WS1659/0001/G** **Silodyx-EMEA/H/C/001209/WS1659/0036/G** **Urorec-EMEA/H/C/001092/WS1659/0039/G** Recordati Ireland Ltd, Lead Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 19.09.2019.	Request for supplementary information adopted with a specific timetable.
WS1665 **Clopidogrel Zentiva-EMEA/H/C/000975/WS1665/0065** **Clopidogrel/Acetylsalicylic acid Zentiva-EMEA/H/C/001144/WS1665/0053** **DuoPlavin-EMEA/H/C/001143/WS1665/0052** **Iscover-EMEA/H/C/000175/WS1665/0135** **Plavix-EMEA/H/C/000174/WS1665/0132** Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, “To update SmPC section 4.5 “Interaction with other medicinal products and other forms of interaction” of the SmPC and the corresponding section of the PL for the interaction between clopidogrel and morphine and other opioids. Furthermore a slight mistake about the number of patients for the TROPICAL-ACS study that was included in the SmPC section 5.1 in a different	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

procedure is being corrected. The MAH has also taken the opportunity to update the Danish and Dutch local representatives in the PL of Plavix, Iscover, DuoPlavin and Clopidogrel/Acetylsalicylic acid Zentiva" Opinion adopted on 19.09.2019.	
WS1669 **Ryzodeg-EMEA/H/C/002499/WS1669/0035** **Tresiba-EMEA/H/C/002498/WS1669/0042** **Xultophy-EMEA/H/C/002647/WS1669/0032** Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
WS1672 **Mirapexin-EMEA/H/C/000134/WS1672/0092** **Sifrol-EMEA/H/C/000133/WS1672/0083** Boehringer Ingelheim International GmbH, Lead Rapporteur: Mark Ainsworth, "To delete the dosage strength of 1.1mg for Pramipexole tablets." Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1675 **Abseamed-EMEA/H/C/000727/WS1675/0085** **Binocrit-EMEA/H/C/000725/WS1675/0084** **Epoetin alfa Hexal-EMEA/H/C/000726/WS1675/0084** Sandoz GmbH, Lead Rapporteur: Alexandre Moreau, "To update sections 4.2, 4.4, 4.8 and 5.1 of the SmPC to align the PI with the NAP originator Eprex. The PL was updated accordingly. In addition, Annex II was updated following procedure EMEA/H/C/IG0970/G." Opinion adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1682 **Filgrastim Hexal-EMEA/H/C/000918/WS1682/0051** **Zarzio-EMEA/H/C/000917/WS1682/0052** Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "To update section 2 of the Package Leaflet in order to align the PI with its NAP originator Neupogen. Editorial changes are also proposed to the HU, IS, LT, PL and SV	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

annexes." Opinion adopted on 12.09.2019.	
WS1688 **Abseamed-EMEA/H/C/000727/WS1688/0086** **Binocrit-EMEA/H/C/000725/WS1688/0085** **Epoetin alfa Hexal-EMEA/H/C/000726/WS1688/0085** Sandoz GmbH, Lead Rapporteur: Alexandre Moreau Opinion adopted on 19.09.2019.	Positive Opinion adopted by consensus on 19.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Vimpat - lacosamide - EMEA/H/C/000863/II/0082 UCB Pharma S.A., Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC in order to warn that Vimpat tablets must not be divided based on the results of safety Evaluation Report on 'chopped tablets'. The Package Leaflet is updated accordingly. "Withdrawal request submitted on 18.09.2019.	The MAH withdrew the procedure on 18.09.2019
Keppra - levetiracetam - EMEA/H/C/000277/II/0178/G UCB Pharma S.A., Rapporteur: Koenraad Norga Request for Supplementary Information adopted on 14.06.2019. Withdrawal request submitted on 09.09.2019.	The MAH withdrew the procedure on 09.09.2019.

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

OPDIVO - nivolumab - EMEA/H/C/003985/II/0065 Bristol-Myers Squibb Pharma EEIG, Co-Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update posology and clinical related information based on interim results from Phase 3b/4 Study CA209384 (A Dose Frequency Optimization, Phase IIIB/IV Trial of Nivolumab 240 mg Every 2 Weeks vs Nivolumab 480 mg Every 4 weeks in Subjects with Advanced or Metastatic Non-small Cell Lung Cancer who Received Up to 12 Months of Nivolumab at 3 mg/kg or 240 mg Every 2 Weeks.) and further supported by pharmacometric analyses in	The CHMP agreed to the request for an extension to the clock stop to respond to the request for supplementary infomration adopted on 27.06.2019

subjects with 2L+ NSCLC."
Request for Supplementary Information adopted on 27.06.2019.

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

satralizumab - EMEA/H/C/004788, Orphan **Accelerated review**
Roche Registration GmbH, treatment of adult and adolescent patients from 12 years of age with neuromyelitis optica spectrum disorders (NMOSD)

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

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

cefiderocol - EMEA/H/C/004829
treatment of infections due to aerobic Gram-negative bacteria
List of Questions adopted on 25.06.2019.

insulin lispro - EMEA/H/C/005037
Treatment of diabetes mellitus in adults
List of Questions adopted on 25.07.2019.

bempedoic acid - EMEA/H/C/004958
treatment of primary hypercholesterolaemia or mixed dyslipidaemia
List of Questions adopted on 27.06.2019.

bempedoic acid / ezetimibe - EMEA/H/C/004959
treatment of primary hypercholesterolaemia or mixed dyslipidaemia
List of Questions adopted on 27.06.2019.

darolutamide - EMEA/H/C/004790
treatment of non-metastatic castration resistant prostate cancer (nmCRPC)
List of Questions adopted on 25.07.2019.

Pemetrexed Fresenius Kabi - pemetrexed - EMEA/H/C/003895/X/0009
Fresenius Kabi Deutschland GmbH, Generic, Generic of Alimta, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ghania Chamouni, "Extension application to introduce a new pharmaceutical form (concentrate for solution for infusion) associated with new strength 25 mg/ml."

List of Questions adopted on 31.01.2019.

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

Strensiq - asfotase alfa -
EMEA/H/C/003794/S/0041, Orphan
Alexion Europe SAS, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Rhea Fitzgerald

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

Aripiprazole Mylan Pharma - aripiprazole -
EMEA/H/C/003803/R/0013
Mylan S.A.S, Generic, Generic of Abilify, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ana Sofia Diniz Martins

Cometriq - cabozantinib -
EMEA/H/C/002640/R/0032, Orphan
Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Menno van der Elst

Duloxetine Mylan - duloxetine -
EMEA/H/C/003981/R/0021
Mylan S.A.S, Generic, Generic of Cymbalta, Rapporteur: John Joseph Borg, PRAC Rapporteur: Maria del Pilar Rayon

EVOTAZ - atazanavir / cobicistat -
EMEA/H/C/003904/R/0031
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Adrien Inoubli

Keytruda - pembrolizumab -
EMEA/H/C/003820/R/0081
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Lenvima - lenvatinib -
EMEA/H/C/003727/R/0031
Eisai GmbH, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Lixiana - edoxaban -
EMEA/H/C/002629/R/0023

Daiichi Sankyo Europe GmbH, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Adrien Inoubli

Lumark - lutetium (177lu) chloride - EMEA/H/C/002749/R/0014
I.D.B. Holland B.V., Rapporteur: Jean-Michel Race, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Ronan Grimes

OPDIVO - nivolumab - EMEA/H/C/003985/R/0074
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski

Pregabalin Mylan - pregabalin - EMEA/H/C/004078/R/0014
Mylan S.A.S, Generic, Duplicate, Generic of Lyrica, Duplicate of Pregabalin Mylan Pharma, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Liana Gross-Martirosyan

Pregabalin Mylan Pharma - pregabalin - EMEA/H/C/003962/R/0012
Mylan S.A.S, Generic, Generic of Lyrica, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Liana Gross-Martirosyan

SIRTURO - bedaquiline - EMEA/H/C/002614/R/0035, Orphan
Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Voriconazole Hikma - voriconazole - EMEA/H/C/003737/R/0010
Hikma Farmaceutica (Portugal), S.A., Generic, Generic of Vfend, Rapporteur: Natalja Karpova, PRAC Rapporteur: Liana Gross-Martirosyan

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

Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0039/G
Biofrontera Bioscience GmbH, Rapporteur: Janet Koenig, Co-Rapporteur: Peter Kiely, “C.I.6.a - To modify the approved therapeutic indication to

include the treatment of mild to severe actinic keratosis on extremities, trunk and neck. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC and sections 1 and 4 of the PL are updated accordingly.
C.I.4 - To update section 5.1 of the SmPC based on follow-up data from study ALA-AK-CT009; this is a randomized, observer-blind, intra-individual phase III study to evaluate the safety and efficacy of Ameluz in combination with daylight PDT (photodynamic therapy) in comparison with Metvix for the treatment of mild to moderate actinic keratosis."

Cosentyx - secukinumab - EMEA/H/C/003729/II/0053/G

Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, PRAC Rapporteur: Eva A. Segovia, "Grouping of two variations:
One type II variation II C.I.6.a: Extension of indication to include the treatment of Non-radiographic axial spondyloarthritis (nr-axSpA) / axial spondyloarthritis (axSpA) without radiographic evidence for Cosentyx. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 of the SmPC are amended. The package leaflet is amended in accordance. The updated RMP version 5.0 has also been submitted.
One type IB C.I.11.z to change the due date of the Psoriasis Registry (category 3 study) within the RMP."

Fycompa - perampanel - EMEA/H/C/002434/II/0047

Eisai GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Extension of indication to include adjunctive treatment in paediatric patients from 2 to 11 years of age in Partial-Onset (focal) Seizures with or without secondary generalisation and Primary Generalised Tonic-Clonic Seizures with idiopathic generalised epilepsy for Fycompa;
As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 4.3 has also been submitted."

OFEV - nintedanib - EMEA/H/C/003821/II/0027, Orphan

Boehringer Ingelheim International GmbH, Rapporteur: Peter Kiely, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica

Mirošević Skvrce, “Extension of indication to include new indication for OFEV for the treatment of other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype based on the results of pharmacology studies and the double-blind, randomised, placebo-controlled phase III trial (INBUILD). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to reflect the use of Ofev in the new indication. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to introduce minor formatting changes in the PI. Furthermore, the PI is brought in line with the latest QRD template version 10.1. The RMP version 9.0 has also been submitted.” Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)	
Taltz - ixekizumab - EMEA/H/C/003943/II/0030 Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Extension of indication to include treatment of adult patients with active axial spondyloarthritis; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC and relevant section of the PL are updated. The PI was also brought in line with the latest QRD template version 10.1. In addition, an updated RMP version 6.1 has also been submitted.” Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)	
Votubia - everolimus - EMEA/H/C/002311/II/0061, Orphan Novartis Europharm Limited, Rapporteur: Janet Koenig, “To modify the approved therapeutic indication (adjunctive treatment of patients aged 2 years and older whose refractory partial-onset seizures, with or without secondary generalisation, are associated with tuberous sclerosis complex, TSC) to include the new population of patients from 6 months to less than 2 years of age. As a consequence, sections 4.1, 4.2, 5.1, 5.2 of the SmPC and sections 1 and 2 of the PL are updated accordingly. Furthermore, the PI is brought in line with the	

latest QRD template version 10.1."

Zinforo - ceftaroline fosamil -
EMEA/H/C/002252/II/0048
Pfizer Ireland Pharmaceuticals, Rapporteur: Alar Irs, "Extension of the indication for the treatment of community acquired pneumonia (CAP) to include concurrent bacteraemia due to Streptococcus pneumoniae (SP) for all age groups, based on the results of previously submitted studies: FOCUS 1 (study P903-08) and FOCUS 2 (study P903-09), paediatric CAP study (study P903-31) and relevant post-marketing safety experience with ceftaroline for bacteraemic Streptococcus pneumoniae CAP. As a consequence sections 4.1 and 5.1 of the SmPC are updated accordingly. No RMP has been provided within this application."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

CellCept - mycophenolate mofetil -
EMEA/H/C/000082/II/0149/G
Roche Registration GmbH, Rapporteur: Sinan B. Sarac

Eylea - aflibercept -
EMEA/H/C/002392/II/0055/G
Bayer AG, Rapporteur: Alexandre Moreau

Eylea - aflibercept -
EMEA/H/C/002392/II/0058
Bayer AG, Rapporteur: Alexandre Moreau

Kalydeco - ivacaftor -
EMEA/H/C/002494/II/0080, Orphan
Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Maria Concepcion Prieto Yerro

LIBTAYO - cemiplimab -
EMEA/H/C/004844/II/0003
Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Sinan B. Sarac

Mozobil - plerixafor -
EMEA/H/C/001030/II/0040/G, Orphan
Genzyme Europe BV, Rapporteur: Paula Boudewina van Hennik

Natpar - parathyroid hormone -
EMEA/H/C/003861/II/0020/G, Orphan
Shire Pharmaceuticals Ireland Limited,

Rapporteur: Bart Van der Schueren

Natpar - parathyroid hormone -
EMEA/H/C/003861/II/0021, Orphan
Shire Pharmaceuticals Ireland Limited,
Rapporteur: Bart Van der Schueren

NeuroBloc - botulinum toxin type b -
EMEA/H/C/000301/II/0104/G
Sloan Pharma S.a.r.l, Rapporteur: Bruno
Sepodes
Request for Supplementary Information adopted
on 26.09.2019.

Palynziq - pegvaliase -
EMEA/H/C/004744/II/0002, Orphan
BioMarin International Limited, Rapporteur:
Johann Lodewijk Hillege

Pelgraz - pegfilgrastim -
EMEA/H/C/003961/II/0013/G
Accord Healthcare S.L.U., Rapporteur: Sol Ruiz

Praluent - alirocumab -
EMEA/H/C/003882/II/0049/G
sanofi-aventis groupe, Rapporteur: Johann
Lodewijk Hillege

Synflorix - pneumococcal polysaccharide
conjugate vaccine (adsorbed) -
EMEA/H/C/000973/II/0141
GlaxoSmithkline Biologicals SA, Rapporteur:
Kristina Dunder

Xofigo - radium-223 -
EMEA/H/C/002653/II/0037
Bayer AG, Rapporteur: Janet Koenig

Zessly - infliximab -
EMEA/H/C/004647/II/0009/G
Sandoz GmbH, Rapporteur: Bjorg Bolstad

WS1700/G
Humalog-EMEA/H/C/000088/WS1700/
0180/G
Liprolog-EMEA/H/C/000393/WS1700/
0141/G
Eli Lilly Nederland B.V., Informed Consent of
Humalog, Lead Rapporteur: Kristina Dunder

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

Abraxane - paclitaxel -
EMEA/H/C/000778/II/0097

Celgene Europe BV, Rapporteur: Paula Boudewina van Hennik, “Update of sections 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC based on the results of study ABI-007-PST-001. This was a phase 1/2, multicenter, open-label, dose-finding study to assess the safety, tolerability and efficacy of weekly abraxane in paediatric patients with recurrent or refractory solid tumours, listed in the PIP, submitted in order to fulfil Article 46.”

Cufence - trientine dihydrochloride - EMEA/H/C/004111/II/0002/G
Univar BV, Rapporteur: Milena Stain

Dovato - dolutegravir / lamivudine - EMEA/H/C/004909/II/0001
ViiV Healthcare B.V., Rapporteur: Filip Josephson, “Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegavir. The SmPC is updated accordingly. The RMP is not submitted.”

Faslodex - fulvestrant - EMEA/H/C/000540/II/0067
AstraZeneca AB, Rapporteur: Filip Josephson, “To update a warning in section 4.6 of the SmPC following an overview of non-clinical data, clinical pharmacology simulation/modelling data, supporting documentation and safety data. The Package Leaflet is updated accordingly. In addition, the applicant has taken the opportunity to correct a minor mistake in the address of one of the manufacturers responsible for batch release in Annex II and PL.”

Herceptin - trastuzumab - EMEA/H/C/000278/II/0157
Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus

IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0034, Orphan
CSL Behring GmbH, Rapporteur: Jan

Mueller-Berghaus, “Submission of a variation to update the dosing regimen as follows: -21-day prophylaxis regimen with rIX-FP at a dose of 100 IU/kg body weight for patients ≥ 12 years who are well controlled on a 14-day prophylaxis regimen. -10- or 14-day prophylaxis regimen with rIX-FP at a dose of 75 IU/kg body weight for patients < 12 years who are well controlled on a 7-day prophylaxis regimen. This submission also updates the existing population PK model with additional intravenous and subcutaneous (SC) data from the PTPs in the PTP arm of study CSL654_3003 and re-evaluates the covariates that are possible determinants of PK variability.”	
Juluca - dolutegravir / rilpivirine - EMEA/H/C/004427/II/0016 ViiV Healthcare B.V., Rapporteur: Janet Koenig, “Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegavir. The SmPC is updated accordingly. The RMP is not submitted.”	
Kisqali - ribociclib - EMEA/H/C/004213/II/0018 Novartis Europharm Limited, Rapporteur: Filip Josephson, “Update of section 5.2 of the SmPC to include updated information about the use of Kisqali in patients with mild or moderate renal impairment based on the results of Study CLEE011A2116 Part II and additional data from breast cancer patients with mild or moderate renal impairment.”	
Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0027 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Jean-Michel Race, “Submission of the final clinical study report from study M16-133, this is a phase 3b, single Arm, open label,	

multicenter study aimed to evaluate the efficacy and safety of glecaprevir (GLE)/pibrentasvir (PIB) in treatment of naïve adults with chronic Hepatitis C Virus (HCV) Genotypes 1 – 6 infection and aspartate aminotransferase to platelet ratio index (APRI) ≤ 1."

Mimpara - cinacalcet - EMEA/H/C/000570/II/0065

Amgen Europe B.V., Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to the new ADR 'chondrocalcinosis pyrophosphate' with a frequency of unknown. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1 and to implement a minor correction to the List of Excipients in section 6.1 of the SmPC."

Ongentys - opicapone - EMEA/H/C/002790/II/0020

Bial - Portela & Cª, S.A., Rapporteur: Martina Weise, "Update of sections 4.5 and 5.2 of the SmPC to add information on drug interaction and pharmacokinetic properties of opicapone based on final results from drug interaction studies NBI-OPC-1708 and NBI-OPC-1707. Study NBI-OPC-1708 is a phase 1, open-label, one-sequence crossover, drug-interaction study to evaluate and compare the pharmacokinetics of repaglinide when administered alone and concomitantly with opicapone. Study NBI-OPC-1707 is a Phase 1, randomized, open-label, 2-period crossover drug interaction study of the effect of administration of single dose of quinidine on the pharmacokinetics of opicapone.
In addition, the marketing authorisation holder took the opportunity to delete the local representative for UK from the PL, according to the guidance provided on UK's withdrawal from the EU regarding medicinal products for human and veterinary use within the framework of the Centralised Procedure"

OPDIVO - nivolumab - EMEA/H/C/003985/II/0073

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, "To update sections 4.8 and 5.1 of the SmPC based on the final results from two studies: CA209017 Open-label Randomized Phase III Trial comparing Nivolumab

Versus Docetaxel in Previously Treated Advanced or Metastatic Squamous Cell Non-small Cell Lung Cancer and CA209057 Open-label Randomized Phase III Trial comparing Nivolumab Versus Docetaxel in Previously Treated Metastatic Non-Squamous Non-small Cell Lung Cancer."

Repatha - evolocumab - EMEA/H/C/003766/II/0038

Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update the safety information based on final results from study 20140213. This is a phase 1 open-label interventional study to evaluate the safety, pharmacokinetics, and pharmacodynamics of evolocumab after a single 140 mg subcutaneous dose in subjects with normal renal function or severe renal insufficiency or end stage renal disease receiving haemodialysis. The Package Leaflet are updated accordingly."

Resolor - prucalopride - EMEA/H/C/001012/II/0049/G

Shire Pharmaceuticals Ireland Limited, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to update the safety information following the final results from study SHP555-802 (a cohort Study of the Relative Incidence of Major Cardiovascular Events) and based on an analysis of all potential major adverse cardiovascular events (MACE) from completed Phase 2/4 clinical studies in adult subjects. In addition, the Marketing authorisation holder (MAH) took the opportunity to update typographical errors in sections 4.4 and 5.1"

Rezolsta - darunavir / cobicistat - EMEA/H/C/002819/II/0035

Janssen-Cilag International NV, Rapporteur: Johann Lodewijk Hillege, "C.I.4 Update of sections 4.8 and 5.1 of the SmPC to update the efficacy and safety information of Rezolsta following results from study TMC114FD2HTX3001 (AMBER); this is an ongoing Phase 3, randomized, active-controlled, double-blind study to evaluate efficacy and safety of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) once daily fixed dose combination (FDC) regimen versus a regimen consisting of darunavir/cobicistat (DRV/COBI)

FDC co-administered with emtricitabine/tenofovir disoproxil fumarate FDC in antiretroviral treatment-naïve human immunodeficiency virus type 1 infected subjects. The applicant takes the opportunity to update section 4.5 to remove the interaction with simeprevir, following the withdrawal of Olysio Marketing Authorization. In addition, the MAH has implemented some minor administrative updates throughout the Product Information. The Package Leaflet is updated accordingly."	
Rizmoic - naldemedine - EMEA/H/C/004256/II/0004 Shionogi B.V., Rapporteur: Mark Ainsworth, "Submission of the final report from non-clinical study S-297995-PF-360-N as agreed in letter of recommendation to CHMP: In-vitro data determining whether naldemedine inhibits in a time dependent manner the OATP1B1, OATP1B3, OAT1 and OAT3 transporters."	
RoActemra - tocilizumab - EMEA/H/C/000955/II/0089 Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, "Submission of the final report from study WA28119. This is a Phase III, multicenter,randomized, double-blind, placebo-controlled study to assess the efficacy and safety of tocilizumab in subjects with giant cell arteritis.)."	
Sivextro - tedizolid phosphate - EMEA/H/C/002846/II/0032 Merck Sharp & Dohme B.V., Rapporteur: Bruno Sepodes, "To update the Marketing Authorization for Sivextro with the final report from Phase 3 study for the treatment of Hospital-Acquired Bacterial Pneumonia and Ventilator-Associated Bacterial Pneumonia (HABP/VABP) MK-1986-002; protocol TR701-132."	
Tivicay - dolutegravir - EMEA/H/C/002753/II/0052 ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral	

regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegavir. The SmPC is updated accordingly. The RMP is not submitted."

Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/II/0069

ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegavir. The SmPC is updated accordingly. The RMP is not submitted."

XALKORI - crizotinib - EMEA/H/C/002489/II/0064

Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, "Update of section 5.1 of the SmPC in order to reflect updated efficacy data from Study A8081001 in patients with ROS1-positive NSCLC. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1."

WS1701

Epclusa-EMEA/H/C/004210/WS1701/0040

Vosevi-EMEA/H/C/004350/WS1701/0032

Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to add new safety information on rash and angioedema following a cumulative review of hypersensitivity with Epclusa and Vosevi, prompted by routine pharmacovigilance and signal detection activities. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes throughout the Product Information."

WS1705

Aluvia-EMEA/H/W/000764/WS1705/0111

Kaletra-EMEA/H/C/000368/WS1705/0180
AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Jean-Michel Race, “Change of section 4.8 of the SmPC to update the safety information of Kaltera and Aluvia following a cumulative safety review of the incidence rate of Stevens-Johnson syndrome, erythema multiforme and jaundice during clinical trials according to LEG 110 (from EMEA/H/C/000368/R/107). The Package Leaflet is updated accordingly.”

B.6.10. CHMP-PRAC assessed procedures

Odomzo - sonidegib - EMEA/H/C/002839/II/0024
Sun Pharmaceutical Industries Europe B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Željana Margan Koletić, “To submit the final report of study CLDE225X2116, listed as a category 3 study in the RMP. This is an interventional Phase Ib/II, open-label, multi-center, dose-finding study to assess the safety and efficacy of the oral combination of LDE225 and INC424 (Ruxolitinib) in subjects with myelofibrosis. The RMP version 7.1 has also been submitted.”

Raxone - idebenone - EMEA/H/C/003834/II/0018, Orphan
Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli, “C.I.11z for SOB studies: Submission of the final report from study SNT-EAP-001 listed as a Specific Obligation (SOB11, former SOB4) in the Annex II of the Product Information. This is a follow-up study of patients in the Expanded Access Program (SNT-EPA-001) for Raxone in the treatment of patients with Leber's Hereditary Optic Neuropathy (LHON). The goal is to collect further long-term real-world efficacy and safety data. Annex II is modified accordingly. Submission of an updated RMP version 1.9 accordingly.”

WS1690
Clopidogrel Zentiva-EMEA/H/C/000975/WS1690/0066
DuoPlavin-EMEA/H/C/001143/WS1690/0053

Iscover-EMEA/H/C/000175/WS1690/0136
Plavix-EMEA/H/C/000174/WS1690/0133
Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "To modify the Product Information (PI) in section 4.5 "Interaction with other medicinal products and other forms of interaction" of the SmPC and the corresponding section of the PL to add the signal of interaction of clopidogrel with boosted antiviral HIV therapy leading to insufficient inhibition of platelet aggregation in line with EPITT 19325. The MAH has made minor adjustments to the wording."

B.6.11. PRAC assessed procedures

PRAC Led
Adempas - riociguat - EMEA/H/C/002737/II/0030, Orphan
Bayer AG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Tuomo Lapveteläinen, "Submission of the final report from risk management plan (RMP) category 3 study 16657, EXPERT (EXPosurE Registry RiociguaT in patients with pulmonary hypertension) to collect information about the long term use of Adempas in real clinical practice.The RMP version 7.1 has also been submitted."

PRAC Led
Colobreathe - colistimethate sodium - EMEA/H/C/001225/II/0044/G
Teva B.V., Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Adam Przybylkowski, PRAC-CHMP liaison: Ewa Balkowiec Iskra, "Submission of the final Post-authorisation safety study report for CLB-MD-05: An observational safety study of Colobreathe (colistimethate sodium dry powder for inhalation) compared with other inhaled anti-pseudomonal antibiotics in cystic fibrosis patients using cystic fibrosis registries. The MAH is also providing an updated RMP, reflecting results from CLB-MD-05 but also the results form CLB-MD-08 that had been provided previously."

PRAC Led

Cubicin - daptomycin -
EMEA/H/C/000637/II/0074
Merck Sharp & Dohme B.V., PRAC Rapporteur: Pernille Harg, PRAC-CHMP liaison: Bjorg Bolstad, "Submission of an updated RMP version 11.1 in order to delete all risks and additional risk minimisation measures in line with GVP module V revision 2. Annex II of the Product Information is updated accordingly. In addition, the MAH took the opportunity to align the Product Information with the QRD template version 10.1 and update the list of local representatives."

PRAC Led

Invokana - canagliflozin -
EMEA/H/C/002649/II/0045/G
Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the final report from 3 non-interventional studies (listed as category 3 studies in the RMP):
- Study RRA-21410, an Epidemiology Study to characterize the risk of LLA in subjects in the overall T2DM population and in a subpopulation with established CVD.
- NAP4001, a Meta-Analysis from CANVAS, CANVAS-R and CREDENCE Studies to characterize the risk of LLA in subjects at high risk for CV events and/or progression of kidney disease.
- Meta-Analysis from CANVAS, CANVAS-R and CREDENCE to evaluate the incidence of bladder cancer in the canagliflozin group compared to the placebo group."

PRAC Led

Praluent - alirocumab -
EMEA/H/C/003882/II/0050/G
sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 5.0 in order to amend the list of safety concerns (removing 'cataract (in the context of very low LDL-C)' as important potential risk; 'long-term use (>5years)' and 'clinical impact of very low LDL-C for extended period of time' as missing information; and consequentially to remove the following additional Pharmacovigilance activities (category 3 studies in the RMP) from the RMP: study R727-CL-1609 (MEA 016), study OBS14697

(MEA 019) and study ALIROC07997 (MEA 017) based on a review of data since the MA was granted including the 1st interim report for study OBS14697, a drug utilisation study (DUS) of alirocumab in Europe to assess the effectiveness of the dosing recommendation to avoid very low LDL-C levels, in order to fulfil MEA 019.4."

PRAC Led

VELCADE - bortezomib - EMEA/H/C/000539/II/0093

Janssen-Cilag International NV, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of an updated RMP version 30.1 in order to revise the list of safety concerns. This revision has been triggered by the PRAC recommendation received in outcome of the EU-PSUR covering the period from 26 April 2017 to 25 April 2018. As a consequence, the Annex II of the PI has been updated to reflect the removal of the additional risk minimisation activities. In addition, the applicant took the opportunity to update the list of local representatives in the PL. Furthermore, the PI is being brought in line with the latest QRD template (version 10.1)."

PRAC Led

Vokanamet - canagliflozin / metformin - EMEA/H/C/002656/II/0050/G

Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report from 3 non-interventional studies (listed as category 3 studies in the RMP):
- Study RRA-21410, an Epidemiology Study to characterize the risk of LLA in subjects in the overall T2DM population and in a subpopulation with established CVD.
- NAP4001, a Meta-Analysis from CANVAS, CANVAS-R and CREDENCE Studies to characterize the risk of LLA in subjects at high risk for CV events and/or progression of kidney disease.
- Meta-Analysis from CANVAS, CANVAS-R and CREDENCE to evaluate the incidence of bladder cancer in the canagliflozin group compared to the placebo group."

PRAC Led

WS1654

Enbrel-EMEA/H/C/000262/WS1654/0228
LIFMIOR-EMEA/H/C/004167/WS1654/0022

Pfizer Europe MA EEIG, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "C.I.13: Submission of the final report from study (B1801311 - BADDIR) listed as a category 3 study in the RMP. This is a prospective cohort study that compared patients treated with biologic interventions (etanercept, adalimumab, and ustekinumab) and patients with similar disease characteristics but exposed only to conventional non-biologic systemic therapies."

B.6.12. CHMP-CAT assessed procedures

Alofisel - darvadstrocel - EMEA/H/C/004258/II/0009, Orphan, ATMP

Takeda Pharma A/S, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0014, Orphan, ATMP

Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

B.6.13. CHMP-PRAC-CAT assessed procedures

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0013/G, Orphan, ATMP

Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Group of variations consisting of:
1) C.I.4: a type II to update sections 4.4, 4.8, 5.1 and 5.2 of the SmPC with the long-term efficacy and safety of Kymriah in relapsed/refractory DLBCL based on the 24 months follow-up results from study CCTL019C2201.
2) C.I.4: a type II to update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC based on interim results from study CCTL019B2202.
3) C.I.4: a type II to update section 5.2 of the SmPC based on interim results from study

CCTL019B2205J. The Annex II and the Package Leaflet are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to clarify the wording of the indication in order to reflect that patients of 25 years of age are being included and to introduce some minor editorial corrections throughout the SmPC and the Package Leaflet. The RMP version 2.0 has also been submitted.”

B.6.14. PRAC assessed ATMP procedures

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

WS1661/G **Entresto-EMEA/H/C/004062/WS1661/0026/G** **Neparvis-EMEA/H/C/004343/WS1661/0025/G** Novartis Europharm Limited, Lead Rapporteur: Johann Lodewijk Hillege
WS1673 **Infanrix hexa-EMEA/H/C/000296/WS1673/0263** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren
WS1685 **Juluca-EMEA/H/C/004427/WS1685/0017** **Tivicay-EMEA/H/C/002753/WS1685/0053** **Triumeq-EMEA/H/C/002754/WS1685/0072** ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson
WS1697 **Ebymect-EMEA/H/C/004162/WS1697/0040** **Xigduo-EMEA/H/C/002672/WS1697/0051** AstraZeneca AB, Lead Rapporteur: Kristina Dunder
WS1706 **Enurev Breezhaler-EMEA/H/C/002691/WS1706/ 0030** **Seebri Breezhaler-EMEA/H/C/002430/WS1706/0030** **Tovanor Breezhaler-EMEA/H/C/002690/WS1706/0034** Novartis Europharm Limited, Duplicate, Duplicate

of Seebri Breezhaler, Lead Rapporteur: Mark Ainsworth, “To introduce a modification of the Instructions for Use (IFU) for the Breezhaler devices affecting the labeling (SmPC and PL) through simplification of its content and layout - condensing textual instructions, optimizing illustrations, and clustering of content to aid comprehension of the procedure of use. In addition both the packaging and IFU in the SmPC and PL have included device-specific information in precise locations in order to meet the MDR requirements. This is because the device does not have its own packaging or leaflet.”	
WS1707 **Ultibro Breezhaler-EMEA/H/C/002679/WS1707/0031** **Ulunar Breezhaler-EMEA/H/C/003875/WS1707/0032** **Xoterna Breezhaler-EMEA/H/C/003755/WS1707/0035** Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth, “To add onto the packaging and IFU in the SmPC and PL device-specific information in precise locations in order to meet the MDR requirements. This is because the device does not have its own packaging or leaflet.”	
WS1708 **Hirobriz Breezhaler-EMEA/H/C/001211/WS1708/0055** **Onbrez Breezhaler-EMEA/H/C/001114/WS1708/0053** **Oslif Breezhaler-EMEA/H/C/001210/WS1708/0053** Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth, “To introduce a modification of the Instructions for Use (IFU) for the Breezhaler devices affecting the labeling (SmPC and PL) through simplification of its content and layout - condensing textual instructions, optimizing illustrations, and clustering of content to aid comprehension of the procedure of use. In addition both the packaging and IFU in the SmPC and PL have included device-specific information in precise locations in order to meet the MDR requirements. This is because the device does not have its own packaging or leaflet. Finally, as notified to the Agency, the MAH took this opportunity to remove unnecessary details from the quality module 3.2.P.7 currently	

registered for Onbrez/ Hirobriz/ Oslif Breezhaler."

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.

G.2. Post-Scientific Advice Issues

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 16-19 September 2019 CHMP plenary:

Oncology		
1.	(SME);ATMP;Treatment of patients with recurrent, metastatic, or persistent cervical cancer with disease progression during or after chemotherapy	The CHMP denied eligibility to PRIME and adopted the critical summary report.
2.	**Fully human anti-BCMA autologous CAR T Cell (CT053);**(SME); ATMPTreatment of patients with relapsed and/or refractory multiple myeloma (MM) whose prior regimens included a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody	The CHMP granted eligibility to PRIME and adopted the critical summary report.
3.	Treatment, in combination with carboplatin and paclitaxel, of patients with stage III or IV epithelial ovarian, or primary peritoneal cancer following optimally debulked initial surgical resection	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Psychiatry		
4.	Treatment of schizophrenia	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Neurology		
5.	(SME); Treatment of multiple system atrophy	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Cardiovascular diseases		
6.	(SME);ATMP; Treatment of no-option patients with peripheral arterial disease (PAD) and critical limb ischemia (CLI)	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Infectious Diseases		
7.	**Chikungunya virus virus-like particle vaccine (PXVX0317)** Active immunisation to prevent disease caused by chikungunya virus infection	The CHMP granted eligibility to PRIME and adopted the critical summary report.

G.3.2. List of procedures starting in September 2019 for October 2019 CHMP adoption of outcomes

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