27 May 2020
EMA/CHMP/225128/2020
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Final Minutes for the meeting on 24-27 February 2020

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) February 2020 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 24-27 February 2020 (to be published post March 2020 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 24-27 February 2020.

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 27-30 January 2020.

The CHMP adopted the minutes.

CHMP ORGAM minutes for 17 February 2020.

The Minutes of the February 2020 CHMP ORGAM meeting held on 17 February 2020, together with all decisions taken at that meeting, were adopted.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. rituximab - EMEA/H/C/005387

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

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday, 26 February 2020 at 09:00

List of Outstanding Issues adopted on 12.12.2019, 27.06.2019.

An oral explanation was held on Wednesday, 26 February 2020. The presentation by the applicant focused on biosimilarity as well as the clinical and commercial drug product.

2.1.2. 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: Oral explanation

Action: Oral explanation to be held on Wednesday, 26 February 2020 at 15:30

List of Outstanding Issues adopted on 19.09.2019. List of Questions adopted on 29.05.2019.

An oral explanation was held on Wednesday, 26 February 2020. The presentation from the company focused on the clinical data to support the sought indication.

See 3.2

2.1.3. rituximab - EMEA/H/C/004807

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

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday, 26 February 2020 at 09:00

List of Outstanding Issues adopted on 12.12.2019, 27.06.2019. List of Questions adopted on 18.10.2018.

An oral explanation was held on Wednesday, 26 February 2020. The presentation by the applicant focused on biosimilarity as well as the clinical and commercial drug product.

2.2. Re-examination procedure oral explanations

2.2.1. Hopveus - sodium oxybate - EMEA/H/C/004962

D&A PHARMA; for the treatment of alcohol dependence

Scope: Oral explanation,
Report from ad-hoc expert group meeting held on 11 February 2020

Action: Oral explanation to be held on Tuesday, 25 February 2020 at 14:00

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

Opinion adopted on 17.10.2019. List of Outstanding Issues adopted on 26.04.2019. List of Questions adopted on 15.11.2018.

The CHMP agreed to postpone the oral explanation.

See 3.5

2.3. Post-authorisation procedure oral explanations

2.3.1. WS1683, Elebrato Ellipta-EMEA/H/C/004781/WS1683/0012, Temybric Ellipta-EMEA/H/C/005254/WS1683/0001, Trelegy Ellipta-EMEA/H/C/004363/WS1683/0010

GlaxoSmithKline Trading Services Limited

Lead Rapporteur: Peter Kiely

Scope: "Update of SmPC in order to add information in section 5.1 on survival data from the IMPACT study"

Oral explanation

Action: Oral explanation to be held on Tuesday, 25 February 2020 at 16:00

Request for Supplementary Information adopted on 12.12.2019, 17.10.2019.

An oral explanation was held on Tuesday, 25 February 2020. The presentation from the MAH concentrated on the wording of section 5.1 of the SmPC and its related clinical data.

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

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

The refusal question and answers document was circulated for information.

2.4. Referral procedure oral explanations

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

MAH various

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

Scope: Oral explanations

Action: Oral explanations to be held on Tuesday, 25 February 2020 at 09:00, 10:00 and 11:00

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.

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.

Four oral explanations were held face-to-face and remotely on 25 and 26 February 2020.

The presentations by the MAHs concerned the NDMA root cause investigation, NDMA exposure calculations for different formulations, risk mitigation as well as possible conditions for lifting the suspension of the marketing authorisation.

See 10.6

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Fetcroja - cefiderocol - EMEA/H/C/004829

Shionogi B.V.; treatment of infections due to aerobic Gram-negative bacteria

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 14.11.2019. List of Questions adopted on 25.06.2019.

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.

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

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

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

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report.

3.1.2. Tigecycline Accord - tigecycline - EMEA/H/C/005114

Accord Healthcare S.L.U.; 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: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 12.12.2019, 19.09.2019, 29.05.2019. List of Questions adopted on 13.12.2018.

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 26.02.2020.

The summary of opinion was circulated for information.

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

3.2.1. 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 outstanding issues

Action: For adoption

List of Questions adopted on 19.09.2019.

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.

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

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 19.09.2019.

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. doxorubicin - EMEA/H/C/005194

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

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 12.12.2019. List of Questions adopted on 19.09.2019.

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.

3.2.4. fingolimod - EMEA/H/C/005191

treatment of multiple sclerosis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 19.09.2019.

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. fingolimod - EMEA/H/C/005282

treatment of multiple sclerosis

Scope: List of outstanding issues

Letter from the applicant dated 21 February 2020 requesting an extension of clock-stop to respond to the list of questions adopted in September 2019.

Action: For adoption

List of Questions adopted on 19.09.2019.

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 did not agree to the request by the applicant for an extension of clock-stop but

agreed to a shorter clock stop.

3.2.6. influenza vaccine (surface antigen, inactivated) - Article 28 - EMEA/H/C/004993

Active immunisation against influenza in the elderly (65 years of age and older).

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 12.12.2019. List of Questions adopted on 25.07.2019.

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.

3.2.7. imlifidase - Orphan - EMEA/H/C/004849

Hansa Biopharma AB; indicated for desensitization treatment of highly sensitized adult kidney transplant patients with positive crossmatch against an available deceased donor.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 27.06.2019.

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.

The CHMP agreed to consult an ad-hoc expert group and adopted a list of questions to this group.

3.2.8. insulin aspart - EMEA/H/C/005033

treatment of diabetes mellitus

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 17.10.2019.

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.

3.2.9. teriparatide - EMEA/H/C/005087

treatment of osteoporosis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 19.09.2019.

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.

3.2.10. 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 Outstanding Issues adopted on 19.09.2019. List of Questions adopted on 29.05.2019.

See 2.1

An oral explanation was held on Wednesday, 26 February 2020. The presentation from the company focused on the clinical data to support the sought indication.

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

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

3.2.11. teriparatide - EMEA/H/C/005388

treatment of osteoporosis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 19.09.2019.

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.

3.2.12. 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 outstanding issues

Action: For adoption

List of Questions adopted on 19.09.2019.

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

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

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 12.12.2019. List of Questions adopted on 19.09.2019.

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.

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

Agios Netherlands B.V.; Treatment of adult patients (≥ 18 years old) with relapsed or refractory acute myeloid leukaemia (AML) with an isocitrate dehydrogenase-1 (IDH1) R132 mutation

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.

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

for application into the surgical site to reduce postoperative pain

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 25.07.2019.

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. salmeterol xinafoate / fluticasone propionate - EMEA/H/C/005591

for 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. acalabrutinib - Orphan - EMEA/H/C/005299

AstraZeneca AB; Treatment of adult patients with chronic lymphocytic leukaemia (CLL)/small lymphocytic lymphoma (SLL)

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.

3.3.3. insulin aspart - EMEA/H/C/004965

treatment of 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.

3.3.4. Meningococcal group A, C, W135 and Y conjugate vaccine - Article 28 - EMEA/H/C/005084

immunization against Neisseria meningitidis serogroups A, C, W-135 and Y

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. Ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005343

Accelerated assessment

is indicated for active immunization for prevention of disease caused by Ebola virus

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. caffeine citrate - EMEA/H/C/005435

treatment of primary apnoea

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. salmeterol xinafoate / fluticasone propionate - EMEA/H/C/004881

for 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.

3.3.8. sunitinib - EMEA/H/C/005419

treatment of gastrointestinal stromal tumour (GIST) and metastatic renal cell carcinoma (MRCC) and pancreatic neuroendocrine tumours (pNET)

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. influenza quadrivalent vaccine (rDNA) - EMEA/H/C/005159

prevention of influenza disease

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. Ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005337

Accelerated assessment

is indicated for active immunization for prevention of disease caused by Ebola virus (Zaire ebolavirus species)

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.

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

3.4.1. tagraxofusp - Orphan - EMEA/H/C/005031

TMC Pharma (EU) Limited; treatment of adult patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN)

Scope: List of questions for the SAG meeting scheduled on 05 March 2020

Action: For adoption

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

The CHMP discussed the list of questions for the SAG meeting and agreed to keep it as adopted in June 2019.

3.4.2. elexacaftor / tezacaftor / ivacaftor - Orphan - EMEA/H/C/005269

Vertex Pharmaceuticals (Ireland) Limited; treatment of cystic fibrosis

Scope: Letter from third party, draft response letter

Action: For information

List of Questions adopted on 30.01.2020.

The CHMP noted the letter from a third party and agreed to the response letter.

3.4.3. arachis hypogaea allergens - EMEA/H/C/004917

immunotherapy (OIT) for patients aged 4 to 17 years with a confirmed diagnosis of peanut allergy

Scope: Letter from the applicant dated 17 February 2020 requesting an extension of clock-stop to respond to the list of questions adopted in November 2019.

Action: For adoption

List of Questions adopted on 14.11.2019

The CHMP agreed to the request by the applicant for an extension of clock-stop to respond

to the list of questions adopted in November 2019.

3.4.4. pexidartinib - Orphan - EMEA/H/C/004832

Daiichi Sankyo Europe GmbH; treatment of adult patients with symptomatic tenosynovial giant cell tumour (TGCT), also referred to as giant cell tumour of the tendon sheath (GCT-TS) or pigmented villonodular synovitis (PVNS)

Scope: Draft list of experts for SAG Oncology meeting scheduled on 04 March 2020

Action: For adoption

List of Outstanding Issues adopted on 12.12.2019. List of Questions adopted on 25.07.2019.

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

3.4.5. trastuzumab - EMEA/H/C/005066

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

Scope: Letter from the applicant dated 04 February 2020 requesting an extension of clock-stop to respond to the list of questions adopted in September 2019.

Action: For adoption

List of Questions adopted on 19.09.2019.

The CHMP discussed the request by the applicant and agreed an extension of clock-stop to respond to the list of questions adopted in September 2019.

3.4.6. ozanimod - EMEA/H/C/004835

Treatment of multiple sclerosis

Scope: List of experts for the SAG Neurology meeting to be held on 16 March 2020.

Action: For adoption

List of Outstanding Issues adopted on 12.12.2019. List of Questions adopted on 25.07.2019.

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

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

3.5.1. Hopveus - sodium oxybate - EMEA/H/C/004962

D&A PHARMA; for the treatment of alcohol dependence

Scope: Oral explanation,
Report from ad-hoc expert group meeting held on 11 February 2020

Action: For adoption

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

Opinion adopted on 17.10.2019. List of Outstanding Issues adopted on 26.04.2019. List of Questions adopted on 15.11.2018.

See 2.2

The CHMP agreed to postpone the oral explanation.

The CHMP noted the letter from the applicant.

The CHMP agreed to reconvene an ad-hoc expert group meeting.

The CHMP adopted the specific timetable.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

4.1.1. Emgality - galcanezumab - EMEA/H/C/004648/X/0004

Eli Lilly Nederland B.V.

Rapporteur: Daniela Melchiorri (IT) (MNAT with ES for Quality), Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Kirsti Villikka

Scope: "Extension application to add a new strength of 100 mg/ml solution for injection in pre-filled syringe for Emgality, associated with a new indication (episodic cluster headache)."

Action: For adoption

List of Outstanding Issues adopted on 17.10.2019. List of Questions adopted on 27.06.2019.

The Committee discussed the issues identified in this application, relating to the clinical efficacy data on the prevention of attacks in patients with episodic cluster headache. The view was expressed that efficacy has not been sufficiently shown.

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

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

The refusal question-and-answer was circulated for information.

4.1.2. Entyvio - vedolizumab - EMEA/H/C/002782/X/0040

Takeda Pharma A/S

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension application to introduce a new pharmaceutical form (solution for injection), associated with a new strength (108 mg) and a new route of administration (subcutaneous use)."

Action: For adoption

List of Outstanding Issues adopted on 12.12.2019. 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 by consensus together with the CHMP Assessment Report and translation timetable.

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

The CHMP noted the letter of recommendations dated 18.02.2020.

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. Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/X/0081/G

Gilead Sciences Ireland UC

Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "Extension application to introduce a new strength (45/200 mg film-coated tablets) and a new pharmaceutical form (oral granules) associated with new strengths (33.75/150 and 45/200 mg). The new presentations are indicated in combination with other medicinal products for the treatment of chronic hepatitis C (CHC) in patients aged 3 to < 12 years. The extension application is grouped with a type II variation (C.I.6.a) to include paediatric use in patients aged 3 to < 12 years who weigh greater than or equal to 35 kg to the existing presentations of 90/400 mg film-coated tablets. The RMP (version 8.3) is updated in accordance. In addition, the MAH took the opportunity to implement minor linguistic corrections throughout the Product Information."

Action: For adoption

List of Questions adopted on 17.10.2019.

The Committee discussed the issues identified in this application, relating to some quality aspects, the environmental risk assessment as well as some SmPC wording.

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

4.2.2. Sovaldi - sofosbuvir - EMEA/H/C/002798/X/0059/G

Gilead Sciences Ireland UC

Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "Extension application to introduce a new strength (200 mg film-coated tablets) and a new pharmaceutical form (oral granules) associated with new strengths (150 and 200 mg). The new presentations are indicated in combination with other medicinal products for the treatment of chronic hepatitis C (CHC) in patients aged 3 to < 12 years. The extension application is grouped with a type II variation (C.I.6.a) to include paediatric use in patients aged 3 to < 12 years who weigh greater than or equal to 35 kg to the existing presentations of 400 mg film-coated tablets. The RMP (version 8.3) is updated in accordance. In addition, the MAH took the opportunity to implement minor linguistic corrections throughout the Product Information."

Action: For adoption

List of Questions adopted on 17.10.2019.

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

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

4.2.3. 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)"

Action: For adoption

List of Questions adopted on 25.07.2019.

The Committee discussed the issues identified in this application, relating to some quality and non-clinical aspects, as well as the environmental risk assessment and the RMP.

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

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

4.3.1. Epclusa - sofosbuvir / velpatasvir - EMEA/H/C/004210/X/0043/G

Gilead Sciences Ireland UC

Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "Extension application to introduce a new strength (200/50 mg film-coated tablets). The new formulation is indicated for the treatment of chronic hepatitis C (CHC) in patients aged 6 years and older.
The extension application is grouped with a type II variation (C.I.6.a) to include paediatric use in patients aged 6 to < 18 years who weigh greater than or equal to 35 kg to the existing presentation (400/100 mg film-coated tablets).
Sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC and the Package Leaflet are updated to support the extended indication. The RMP (version 5.1) is updated in accordance."

Action: For adoption

The Committee discussed the issues identified in this application, mainly concerning some quality aspects like the nitrosamine risk assessment, some clinical issues including the posology for patients below 17 kg and the RMP.

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

4.3.2. Pemetrexed Hospira - pemetrexed - EMEA/H/C/003970/X/0021

Pfizer Europe MA EEIG

Rapporteur: Alar Irs

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

Action: For adoption

The Committee discussed the issues identified in this application, relating to some quality issues, the environmental risk assessment and the RMP.

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

4.3.3. Pradaxa - dabigatran etexilate - EMEA/H/C/000829/X/0122/G

Boehringer Ingelheim International GmbH

Rapporteur: Mark Ainsworth, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Anette Kirstine Stark

Scope: "Extension application to add two new pharmaceutical forms for Pradaxa (coated granules (20 mg, 30 mg, 40 mg, 50 mg, 110 mg, 150 mg) and powder and solvent for oral solution (6.25 mg/ml)), grouped with:

-A type II variation (C.I.6.a) - Extension of indication to include new indication for Pradaxa 75 mg, 110 mg, 150 mg capsules based on the paediatric trials 1160.106 and 1160.108. As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 37.0 has also been submitted.
-Type IB (B.I.b.1.c)
-Type IA (B.I.b.1.b)
-Type IB (B.I.b.1.d)
-Type IA (B.I.b.2.a)
-Type IA (B.I.b.1.d)
-Type IA (B.I.d.1.a.1)
-Type IA (B.II.d.1.a)
-Type IB (B.II.d.1.d)
-Type IA (B.II.d.2.a)
-Type IA (B.II.c.1.c).”

Action: For adoption

The Committee discussed the issues identified in this application, mainly relating to the quality (including the reconstitution and related possibility of dosing errors, the clinical part (the dosing algorism in relation to the bioavailability as well as limited data in the young patient population below 1 year of age) as well as the RMP.

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

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

No items

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

No items

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

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

5.1.1. Alunbrig - brigatinib / 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

Request for Supplementary Information adopted on 19.09.2019.

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.

5.1.2. Carmustine Obvius - carmustine - EMEA/H/C/004326/II/0002

Obvius Investment B.V

Rapporteur: Natalja Karpova, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Jan Neuhauser

Scope: "carmustine with or without total body irradiation (TBI), as conditioning treatment prior to allogeneic or autologous haematopoietic progenitor cell transplantation (HPCT) in haematological diseases"

Action: For adoption

Request for Supplementary Information adopted on 17.10.2019.

The Committee discussed the issues identified in this application, mainly concerning the indication wording in relation to available clinical data.

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

5.1.3. Cosentyx - secukinumab - EMEA/H/C/003729/II/0057

Novartis Europharm Limited

Rapporteur: Tuomo Lapveteläinen, PRAC Rapporteur: Eva A. Segovia

Scope: "Extension of indication to include the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years who are candidates for systemic therapy for Cosentyx; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. Section 6.6 of the SmPC for the solution for injection is also updated. The Package Leaflet is updated in accordance. In addition, the Marketing

authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 6.0 has also been submitted.
Furthermore, the Annex II is brought in line with the latest QRD template version 11.0."

Action: For adoption

The Committee discussed the issues identified in this application, mainly relating to the clinical data in children below the age of 12, patients weighing less than 25 kg, and patients with different stages of disease severity.

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

5.1.4. Deltyba - delamanid - Orphan - EMEA/H/C/002552/II/0040

Otsuka Novel Products GmbH

Rapporteur: Koenraad Norga, PRAC Rapporteur: Laurence de Fays

Scope: "Extension of indication to include adolescents and children above 6 years with a body weight of at least 30 kg. As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC and corresponding, relevant sections of the PL are updated accordingly. The updated RMP version 3.2 has also been submitted. Furthermore, the PI is being brought in line with the latest QRD template."

Action: For adoption

The Committee discussed the issues identified in this application, concerning the inclusion of non-clinical data in the EPAR and SmPC and some pharmacology and modelling aspects.

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

5.1.5. Imfinzi - durvalumab - EMEA/H/C/004771/II/0014/G

AstraZeneca AB

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: David Olsen

Scope: "Extension of indication to include the use of Imfinzi in combination with etoposide and either carboplatin or cisplatin for the first-line treatment of adults with extensive-stage small cell lung cancer (ES-SCLC). The proposed indication is supported by study D419QC00001 (CASPIAN), an ongoing Phase III randomised, multicentre, open-label, comparative study designed to determine the efficacy and safety of durvalumab, or durvalumab and tremelimumab, in combination with etoposide and platinum-based chemotherapy (EP) for the first-line treatment of patients with ES-SCLC.
In addition, the MAH proposes to update sections 4.4 and 4.8 of the SmPC to update the safety information based on the Durvalumab Pan-Tumour Pool, a safety dataset comprising of 9 clinical studies building on the existing safety database and summarising the safety information for durvalumab monotherapy characterised across tumour types in the durvalumab clinical program to date.
The Package Leaflet is updated in accordance. The RMP version 2S1 has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application, mainly concerning the

wording of the indication and the appropriate patient population.

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

5.1.6. Invokana - canagliflozin - EMEA/H/C/002649/II/0046

Janssen-Cilag International NV

Rapporteur: Martina Weise, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Martin Huber

Scope: "Update of sections 4.1, 4.2, 4.8 and 5.1 of the Summary of Product Characteristics to add a new therapeutic indication for Invokana (canagliflozin) for the treatment of stage 2 or 3 chronic kidney disease and albuminuria, as an adjunct to standard of care, in adults with type 2 diabetes mellitus. The proposed new indication is based upon new clinical efficacy and safety data from the Phase 3 study: Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation Trial (CREDENCE) (DNE3001).
The Package Leaflet is updated in accordance. The RMP version 8.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 14.11.2019.

The Committee discussed the issues identified in this application, mainly concerning the new indication in relation to the already approved indication and in this context the request for one additional year of market protection.

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

5.1.7. 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 19.09.2019, 28.03.2019, 18.10.2018.

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

wording of the indication with specific regard to the appropriate patient population.

The Committee adopted a 4th request for supplementary information with a specific timetable.

5.1.8. OFEV - nintedanib - Orphan - EMEA/H/C/003821/II/0026

Boehringer Ingelheim International GmbH

Rapporteur: Peter Kiely, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication to include new indication for OFEV for the treatment of Systemic Sclerosis associated Interstitial Lung Disease (SSc-ILD).
As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The MAH takes this opportunity to also introduce minor linguistic corrections to the Annexes for France and Sweden. The RMP version 7.0 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

Request for Supplementary Information adopted on 14.11.2019, 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 CHMP noted the letter of recommendations dated 26.02.2020.

The summary of opinion was circulated for information.

5.1.9. Otezla - apremilast - EMEA/H/C/003746/II/0029

Amgen Europe B.V.

Rapporteur: Peter Kiely, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Eva A. Segovia

Scope: "Extension of indication to include treatment of adult patients with oral ulcers associated with Behçet's disease (BD) who are candidates for systemic therapy. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the applicant took the opportunity to update the list of local representatives in the PL. Furthermore, the PI is brought in line with the latest QRD template v10.1. The updated RMP version 13.0 has also been submitted.
The variation leads to amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP).", 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 17.10.2019.

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.

5.1.10. Sivextro - tedizolid phosphate - EMEA/H/C/002846/II/0035

Merck Sharp & Dohme B.V.

Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maria del Pilar Rayon

Scope: "Extension of indication (treatment of ABSSSI in adults) to include adolescent population from 12 years old and older for Sivextro; as a consequence, sections 4.1, 4.2, 4.8 and 5.2 of the SmPC are updated. Sections 1 and 2 of the Package Leaflet are updated in accordance. The updated RMP version 5.1 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1."

Action: For adoption

The Committee discussed the issues identified in this application, concerning some non-clinical and clinical aspects.

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

5.1.11. Vokanamet - canagliflozin / metformin - EMEA/H/C/002656/II/0051

Janssen-Cilag International NV

Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst

Scope: "Update of sections 4.2, 4.8 and 5.1 of the Summary of Product Characteristics based upon new clinical efficacy and safety data from the Phase 3 study: Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation Trial (CREDENCE) (DNE3001). The Package Leaflet is updated in accordance. The RMP version 8.1 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 14.11.2019.

The Committee discussed the issues identified in this application. The Committee noted that the applicant withdrew the request for a new indication as well as the request for one year market protection. The members discussed some RMP aspects and PI updates.

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

5.1.12. Xolair - omalizumab - EMEA/H/C/000606/II/0101

Novartis Europharm Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: "Extension of indication to include treatment of nasal polyps in adult patients with inadequate response to intranasal corticosteroids for Xolair; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in section 4.2 of the SmPC and in the PL and to update the phone number of the NL local representative. The RMP version 16.0 has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.1."

Action: For adoption

The Committee discussed the issues identified in this application, mainly concerning the clinical data from the pivotal studies and the wording of the indication with regard to the appropriate patient population.

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

5.1.13. Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/II/0019

Pfizer Ireland Pharmaceuticals

Rapporteur: Bjorg Bolstad, Co-Rapporteur: Simona Stankeviciute

Scope: "Extension of indication to include bacteraemia (in association with, or suspected to be associated with, the currently approved indications for complicated intra-abdominal infection (cIAI), complicated urinary tract infection (cUTI) and hospital-acquired pneumonia, including ventilator-associated pneumonia (HAP/VAP)) for Zavicefta; as a consequence, sections 4.1 and 4.2 of the SmPC are updated in order to add this indication and the posology. The Package Leaflet is updated in accordance."

Action: For adoption

The Committee discussed the issues identified in this application, relating to some clinical aspects and the environmental risk assessment.

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

5.1.14. WS1737
Edistride - dapagliflozin - EMEA/H/C/004161/WS1737/0034
Forxiga - dapagliflozin - EMEA/H/C/002322/WS1737/0053

AstraZeneca AB

Lead Rapporteur: Kristina Dunder, Lead Co-Rapporteur: Martina Weise, PRAC Rapporteur: Annika Folin

Scope: "Update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC for Edistride and Forxiga to add a new indication for the treatment of symptomatic heart failure with reduced ejection fraction in adults. The Package Leaflet and Labelling are updated in accordance.
The RMP version 18 has also been submitted.

Furthermore, the PI is brought in line with the latest QRD template version 10.1, as well as editorial change (addition of SI unit for blood glucose).” 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, mainly concerning the wording of the indication and in particular the appropriate target population in relation to the studied population and in this context the request for one year additional market protection.

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

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

5.2.1. BLINCYTO - blinatumomab - Orphan - EMEA/H/C/003731/II/0030

Amgen Europe B.V.

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

Scope: “To modify the approved therapeutic indication to include the treatment of Philadelphia chromosome positive CD19 positive B-cell precursor acute lymphoblastic leukaemia (ALL) in adult and paediatric patients with relapsed or refractory ALL and adult patients in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and the PL are updated accordingly. The updated RMP version 10.0 has also been submitted.”

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

Action: For adoption

Request for Supplementary Information adopted on 14.11.2019.

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 November 2019.

5.2.2. Xyrem - sodium oxybate - EMEA/H/C/000593/II/0076

UCB Pharma S.A.

Rapporteur: Bruno Sepodes, Co-Rapporteur: Mark Ainsworth, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: “Extension of indication to include adolescents and children older then 7 years for Xyrem; As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. The updated version (9.0) of the RMP was submitted.”

Request by the applicant for an extension to the clock stop to respond to the request for

supplementary information adopted in December 2019.

Action: For adoption

Request for Supplementary Information adopted on 12.12.2019, 29.05.2019, 15.11.2018.

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

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

No items

6. Ancillary medicinal substances in medical devices

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

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. lonafarnib - H0005271

E34.8 Hutchinson-Gilford Progeria Syndrome and Progeroid Laminopathies

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. berotralstat - H0005138

Indicated for routine prophylaxis to prevent hereditary angioedema (HAE) attacks in adults and adolescents 12 years of age and older.

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.

8.1.3. lumasiran - Orphan - H0005040

Alnylam Netherlands B.V.; Treatment of Primary Hyperoxaluria Type 1

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 information.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 5 recommendations for eligibility to PRIME: 1 was granted and 4 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. Bavencio - avelumab - EMEA/H/C/004338/II/0013

Merck Europe B.V.

Rapporteur: Filip Josephson, PRAC Rapporteur: Hans Christian Siersted

Scope: "Update of section 5.1 of the SmPC in order to update efficacy information following results from study EMR100070-003 Part B listed as a specific obligation in the Annex II; this is a Phase II, open-label, multicenter trial to investigate the clinical activity and safety of avelumab (MSB0010718C) in subjects with Merkel cell carcinoma. With this submission the company is also taking the opportunity to update annex-II proposing deletion of the specific obligation and proposing the switch from conditional to full marketing authorisation. The package leaflet and the RMP (version 2.1) are updated accordingly."

Action: For adoption

The Committee discussed the issues identified in this application, relating to the proposed switch from conditional to full marketing authorisation.

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

9.1.2. Cablivi - caplacizumab - EMEA/H/C/004426/II/0021, Orphan

Ablynx NV

Rapporteur: Filip Josephson

Scope: "Submission of the results of the study ALX-0681-MS-01, a Modelling/Simulation study performed for the paediatric population as part of the approved Paediatric Investigation Plan (EMEA-001157-PIP-01-11-M02) for Cablivi"

Action: For discussion

The Committee discussed the issues identified in this application, concerning the data for the paediatric population.

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

9.1.3. Juluca - dolutegravir / rilpivirine - EMEA/H/C/004427/II/0016
Dovato - dolutegravir / lamivudine - EMEA/H/C/004909/II/0001
Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/II/0069
Tivicay - dolutegravir - EMEA/H/C/002753/II/0052

ViiV Healthcare B.V.

Lead Rapporteur: Filip Josephson

Scope: 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 dolutegravir. The SmPC is updated accordingly. The RMP is not submitted.

List of experts for the SAG-HIV/viral diseases meeting adopted via written procedure on 05 February 2020, Report from SAG-HIV/viral diseases meeting held on 06 February 2020

CHMP request for PRAC advice

Action: For adoption

The CHMP noted the report from the SAG and adopted the request for PRAC advice.

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

Action: For discussion

Request for Supplementary Information adopted on 17.10.2019, 19.09.2019.

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

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

The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.

The Marketing Authorisation remains conditional.

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

9.1.5. Qutenza - capsaicin - EMEA/H/C/000909/II/0048

Grunenthal GmbH

Rapporteur: Bruno Sepodes

Scope: "Update of sections 4.2 and 5.1 of the SmPC in order to amend the posology based on PACE and STRIDE studies. The Package Leaflet is updated accordingly."

Action: For discussion

Request for Supplementary Information adopted on 12.12.2019.

The Committee discussed the issues identified in this application, concerning clarification on the safety profile with the proposed amended posology.

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

9.1.6. 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/R/0005, Orphan, ATMP

bluebird bio (Netherlands) B.V

Rapporteur: Carla Herberts, Co-Rapporteur: Violaine Closson Carella, CHMP Coordinator Rapporteur: Paula Boudewina van Hennik, CHMP Coordinator Co-Rapporteur: Alexander Moreau

Scope: Opinion

Action: For adoption

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

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

The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.

The Marketing Authorisation remains conditional.

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

9.1.7. Lifmior – etanercept - EMEA/H/C/004167

Pfizer Europe MA EEIG

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

Scope: The marketing authorisation of Lifmior expired on 16 February 2020 due to end of the sunset clause

Action: For information

The CHMP noted the expiry of marketing authorisation.

10. Referral procedures

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

10.1.1. Yondelis - EMEA/H/C/0773/A-20/0060

MAH: Pharma Mar S.A.

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jorge Camarero Jiménez

Scope: Start of procedure, List of Questions, Timetable, Appointment of Rapporteurs

Action: For adoption

European Commission triggered a referral procedure under Article 20 of Regulation (EC) No 726/2004 to request CHMP to assess study OVC-3006, which failed to meet its endpoints in the indication of ovarian cancer, and its impact on the benefit risk balance for the centrally authorised medicinal product(s) Yondelis (trabectedin).

The CHMP appointed Sinan B Sarac as Referral Rapporteur and Jorge Camarero Jiménez as referral Co-Rapporteur.

The CHMP adopted a list of questions to the MAH with a specific timetable.

Notification: 21.02.2020

Start of the procedure (CHMP): February 2020 CHMP

List of questions: 27.02.2020

Submission of responses: 02.04.2020

Re-start of the procedure: 30.04.2020

Rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 05.05.2020

Comments: 12.05.2020

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 18.05.2020

CHMP LoOI, or CHMP opinion: May 2020 CHMP

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: Opinion

Action: For adoption

The CHMP agreed to postpone the opinion.

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: Preparation for the ad-hoc expert group meeting scheduled on 27-28 February 2020

Action: For adoption

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

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

MAH various

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

Scope: Oral explanations

Action: Oral explanations to be held on Tuesday, 25 February 2020 at 09:00, 10:00 and 11:00

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.

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.

See 2.4

Four oral explanations were held face-to-face and remotely on 25 and 26 February 2020.

The presentations by the MAHs concerned the NDMA root cause investigation, NDMA exposure calculations for different formulations, risk mitigation as well as possible conditions for lifting the suspension of the marketing authorisation.

Following the oral explanations the CHMP agreed to seek further clarifications.

The CHMP adopted a 2nd list of outstanding issues.

The CHMP adopted the specific timetable.

CHMP list of outstanding issues: February 2020 CHMP

Submission of responses: 09.03.2020

Re-start of the procedure: 16.03.2020

Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 20.03.2020

Comments: 15.04.2020

Updated Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 23.04.2020

CHMP list of outstanding issues/opinion: April 2020 CHMP

10.6.2. Panexcell Clinical Laboratories Priv. Ltd - Multiple NAPs (EMEA/H/A-31/1494)

MAH: various

Referral Rapporteur: Janet Koenig, Referral Co-Rapporteur: Jayne Crowe

Scope: Start of procedure, List of Questions, Timetable, Appointment of Rapporteurs

Action: For adoption

Article 31 procedure triggered by the German Federal Institute of Drugs and Medical Devices (BfArM) concerning the contract research organisation (CRO) Panexcell Clinical Laboratories Priv. Ltd. located in Navi Mumbai 400 701, India.

The CHMP appointed Janet Koenig as referral Rapporteur and Jayne Crowe as referral Co-Rapporteur.

The CHMP adopted a list of questions with a specific timetable.

Notification: 19.02.2020

Start of the procedure (CHMP): February, 2020 CHMP

List of questions: 27.02.2020

Submission of responses: 09.04.2020

Re-start of the procedure: 30.04.2020

Rapporteur / co-rapporteur assessment reports circulated to CHMP: 08.05.2020

CHMP comments: 15.05.2020

Updated rapporteur/co-rapporteur assessment reports circulated to CHMP: 20.05.2020

CHMP list of outstanding issues / CHMP opinion: May 2020 CHMP

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

February 2020 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

13.2. Innovation Task Force briefing meetings

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 10-13 February 2020

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 February 2020

Action: For adoption

The CHMP adopted the EURD list.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 19-21 February 2020

Action: For information

The CHMP noted the draft minutes.

14.2.3. Paediatric Committee (PDCO)

PIPs reaching D30 at February 2020 PDCO

Action: For information

The CHMP noted the information.

Report from the PDCO meeting held on 25-28 February 2020

Action: For information

The CHMP noted the report.

14.2.4. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 18-20 February 2020

Action: For information

The CHMP noted the report.

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

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 25-27 February 2020

Action: For information

The CHMP noted the report.

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

14.3.1. Ad-hoc Influenza Working Group

Scope EU Strain selection for the Influenza Vaccines for the Season 2020/2021: Report from the Ad Hoc Influenza working group to the BWP

Action: For adoption

Postponed to March 2020 CHMP.

Scope: EU Recommendation for the Seasonal Influenza Vaccine Composition for the Season 2020/2021

Action: For adoption

Postponed to March 2020 CHMP.

14.3.2. Biologics Working Party (BWP)

Chair: Sol Ruiz

Reports from BWP February 2020 meeting to CHMP:

- 11 reports on products in scientific advice and protocol assistance
- 14 reports on products in pre-authorisation procedures
- 5 reports on products in post-authorisation procedures
- 3 reports on products in plasma master file

Action: For adoption

The CHMP adopted the reports.

Election of the BWP chair

Action: For adoption

Nomination(s) received

The CHMP re-elected Sol Ruiz as BWP chairperson.

14.3.3. Central Nervous System Working Party (CNSWP)

Chair: Karl Broich/André Elferink

CNSWP response to CMDh question on bioequivalence requirements for Cmax for carbamazepine as NTI drug

Action: For adoption

The CHMP adopted the CNSWP response to CMDh.

14.3.4. Scientific Advice Working Party (SAWP)

Chair: Anja Schiel

Report from the SAWP meeting held on 10-13 February 2020. 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.

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

14.5.1. International Council on Harmonisation (ICH)

ICH M13 – Bioequivalence for immediate-release dosage forms: nomination of expert

Action: For adoption

The CHMP appointed Paulo Paixao as an expert for ICH M13.

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

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Oncology Training

Action: For information

The Oncology training was held.

15.1.2. UK withdrawal from the EU – update

Action: For discussion

The CHMP noted the update.

15.1.3. Update on Corona Viruses

Action: For information

The CHMP noted the update on the coronavirus situation.

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 February 2020 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	
Loizos Panayi	Member	Cyprus	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	
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Tuomo Lapveteläinen	Alternate	Finland	No interests declared	
Alexandre Moreau	Member	France	No interests declared	
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	
Melinda Sobor	Member	Hungary	No restrictions applicable to this meeting	
Agnes Gyurasics	Alternate	Hungary	No interests declared	
Kolbeinn Gudmundsson	Member	Iceland	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Jayne Crowe	Member	Ireland	No interests declared	
Peter Kiely	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No restrictions applicable to this meeting	
Giuseppa Pistritto	Alternate	Italy	No interests declared	
Natalja Karpova	Member	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No interests declared	
Martine Trauffler	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	
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	
Marcin Kolakowski	Alternate	Poland	No interests declared	
Bruno Sepodes	Member (Vice-Chair)	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meeting	
Dana Gabriela Marin	Alternate	Romania	No interests declared	
Francisek Drafi	Member	Slovakia	No interests declared	
Rajko Kenda	Member	Slovenia	No restrictions applicable to this meeting	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Maria Concepcion Prieto Yerro	Member	Spain	No interests declared	
Jorge Camarero Jiménez	Alternate	Spain	No restrictions applicable to this meeting	
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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:	WS1683 (Elebrato Ellipta, Temybric Ellipta, Trelegy Ellipta)
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	
Valerie Lescrainier	Expert - in person*	Belgium	No interests declared	
Kristina Bech Jensen	Expert - in person*	Denmark	No interests declared	
Mette Linnert Jensen	Expert - in person*	Denmark	No interests declared	
Trine Jensen	Expert - in person*	Denmark	No restrictions applicable to this meeting	
Celine Chu	Expert - in person*	France	No interests declared	
Nicolas Glasser	Expert - in person*	France	No interests declared	
Sylvain Gueho	Expert - in person*	France	No interests declared	
Daniela Karra	Expert - in person*	Germany	No interests declared	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Angela de Kleynen	Expert - in person*	Netherlands	No interests declared	
Eleonora Wijnans	Expert - in person*	Netherlands	No interests declared	
Leon van Aerts	Expert - in person*	Netherlands	No interests declared	
Wouter Iwema Bakker	Expert - in person*	Netherlands	No interests declared	
Anja Schiel	Expert - in person*	Norway	No interests declared	
Maria Victoria Tudanca Pacios	Expert - in person*	Spain	No participation in final deliberations on:	(EMEA/H/C/005299) Imfinzi (EMEA/H/C/004771/II/0014/G)
Dulce Aldana Sanchez	Expert - in person*	Spain	No restrictions applicable to this meeting	
Brigitte Mueller	Expert - via telephone*	Austria	No interests declared	
Martin Walter	Expert - via telephone*	Austria	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Susanne Wolf	Expert - via telephone*	Austria	No interests declared	
Laurence de Fays	Expert - via telephone*	Belgium	No interests declared	
Violette Dirix	Expert - via telephone*	Belgium	No interests declared	
Aaron Sosa	Expert - via telephone*	Denmark	No restrictions applicable to this meeting	
Bettina Bryne Nielsen	Expert - via telephone*	Denmark	No interests declared	
Claus Stage	Expert - via telephone*	Denmark	No interests declared	
Mogens Westergaard	Expert - via telephone*	Denmark	No restrictions applicable to this meeting	
Nanna Borup Johansen	Expert - via telephone*	Denmark	No interests declared	
Joos Romme	Expert - via telephone*	Netherlands	No interests declared	
Menno van der Elst	Expert - via telephone*	Netherlands	No interests declared	
Ingrid Lund	Expert - via telephone*	Norway	No interests declared	
Jonas Bergh	Expert - via telephone*	Sweden	No interests declared	
Diederica Claeys	Expert - via Adobe*	Belgium	No interests declared	
Celine Chartier	Expert - via Adobe*	France	No interests declared	
Frederique D Herbe	Expert - via Adobe*	France	No interests declared	
Isabelle Parent du Chatelet	Expert - via Adobe*	France	No interests declared	
Sandrine Chiappini	Expert - via Adobe*	France	No interests declared	
Anne Isabel Roth	Expert - via Adobe*	Germany	No interests declared	
Annette Lommel	Expert - via Adobe*	Germany	No interests declared	
Clemens Mittmann	Expert - via Adobe*	Germany	No interests declared	
Ralf Wagner	Expert - via Adobe*	Germany	No interests declared	
Steffen Haffner	Expert - via Adobe*	Germany	No interests declared	
Yuansheng Sun	Expert - via Adobe*	Germany	No interests declared	
Clare Foley	Expert - via Adobe*	Ireland	No interests declared	
Donal O`Connor	Expert - via Adobe*	Ireland	No interests declared	
Finbarr Leacy	Expert - via Adobe*	Ireland	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Johann Castaneda	Expert - via Adobe*	Ireland	No interests declared	
Kate Brown	Expert - via Adobe*	Ireland	No interests declared	
Olive Smyth	Expert - via Adobe*	Ireland	No interests declared	
Erik Hergarden	Expert - via Adobe*	Netherlands	No interests declared	
Ineke Havinga	Expert - via Adobe*	Netherlands	No interests declared	
Johannes Span	Expert - via Adobe*	Netherlands	No interests declared	
Nienke Rodenhuis	Expert - via Adobe*	Netherlands	No interests declared	
Susanne Breedijk-von den Ende	Expert - via Adobe*	Netherlands	No restrictions applicable to this meeting	
Agustin Portela	Expert - via Adobe*	Spain	No interests declared	
Alicia Perez Gonzalez	Expert - via Adobe*	Spain	No interests declared	
Marcos Timon	Expert - via Adobe*	Spain	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)*

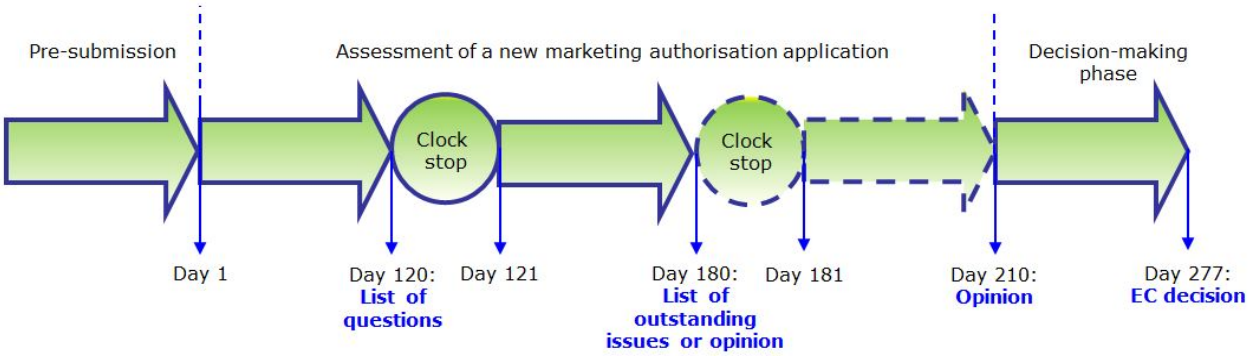
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

27 May 2020
EMA/CHMP/228166/2020

Annex to 24-27 February 2020 CHMP Minutes

Pre-submission and post-authorisations issues

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A. PRE-SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for February 2020: **For adoption**	Adopted.

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

Final Outcome of Rapporteurship allocation for February 2020: **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

Defitelio - defibrotide - EMEA/H/C/002393/S/0045, Orphan Gentium S.r.l., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga	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.
Naglazyme - galsulfase - EMEA/H/C/000640/S/0078 BioMarin International Limited, Rapporteur: Fátima Ventura, PRAC Rapporteur: Ana Sofia Diniz Martins Request for Supplementary Information adopted on 14.11.2019.	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.
Obizur - susoctocog alfa - EMEA/H/C/002792/S/0028 Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 27.02.2020.	
Orphacol - cholic acid - EMEA/H/C/001250/S/0033, Orphan Laboratoires CTRS, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Sofia Trantza Request for Supplementary Information adopted on 27.02.2020.	Request for supplementary information adopted with a specific timetable.
Raxone - idebenone - EMEA/H/C/003834/S/0019, Orphan Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli Request for Supplementary Information adopted on 30.01.2020.	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.
Vedrop - tocofersolan - EMEA/H/C/000920/S/0035 Recordati Rare Diseases, Rapporteur: Melinda Sobor, PRAC Rapporteur: Melinda Palfi	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

Bortezomib Accord - bortezomib - EMEA/H/C/003984/R/0022 Accord Healthcare S.L.U., Generic, Generic of VELCADE, Rapporteur: Milena Stain, PRAC Rapporteur: Amelia Cupelli Request for Supplementary Information adopted on 30.01.2020.	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.
Farydak - panobinostat - EMEA/H/C/003725/R/0020, Orphan Secura Bio Limited, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Sofia Trantza	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.	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.
Kanuma - sebelipase alfa - EMEA/H/C/004004/R/0025, Orphan Alexion Europe SAS, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Fátima Ventura, PRAC Rapporteur: Ulla Wändel Liminga	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.
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 Request for Supplementary Information adopted on 12.12.2019.	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.
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 Request for Supplementary Information adopted on 12.12.2019.	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.
Pregabalin Sandoz - pregabalin - EMEA/H/C/004010/R/0012 Sandoz GmbH, Generic, Generic of Lyrica, Rapporteur: Tomas Radimersky, PRAC	Request for an extension to the clock stop to respond to the RSI adopted on 30.01.2020. The CHMP agreed to the request for an extension to the clock stop.

Rapporteur: Liana Gross-Martirosyan Request for Supplementary Information adopted on 30.01.2020.	
Pregabalin Sandoz GmbH - pregabalin - EMEA/H/C/004070/R/0013 Sandoz GmbH, Generic, Duplicate, Generic of Lyrica, Duplicate of Pregabalin Sandoz, Rapporteur: Tomas Radimersky, PRAC Rapporteur: Liana Gross-Martirosyan Request for Supplementary Information adopted on 30.01.2020.	Request for an extension to the clock stop to respond to the RSI adopted on 30.01.2020. The CHMP agreed to the request for an extension to the clock stop.
Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/R/0036 CSL Behring GmbH, Rapporteur: Kristina Dunder, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Maria del Pilar Rayon	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.
Strensiq - asfotase alfa - EMEA/H/C/003794/R/0044, Orphan Alexion Europe SAS, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald Request for Supplementary Information adopted on 30.01.2020.	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.
Zerbaxa - ceftolozane / tazobactam - EMEA/H/C/003772/R/0026 Merck Sharp & Dohme B.V., Rapporteur: Bjorg Bolstad, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Adam Przybylkowski	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

Deltyba - delamanid - EMEA/H/C/002552/R/0041, Orphan Otsuka Novel Products GmbH, Rapporteur: Koenraad Norga, PRAC Rapporteur: Jean-Michel	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The CHMP was of the opinion that the renewal

Dogné Request for Supplementary Information adopted on 30.01.2020.	for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Natpar - parathyroid hormone - EMEA/H/C/003861/R/0022, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Rhea Fitzgerald Request for Supplementary Information adopted on 12.12.2019.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
OCALIVA - obeticholic acid - EMEA/H/C/004093/R/0018, Orphan Intercept Pharma International Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Liana Gross-Martirosyan Request for Supplementary Information adopted on 19.09.2019.	See agenda 9.1 Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Rubraca - rucaparib - EMEA/H/C/004272/R/0016 Clovis Oncology Ireland Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Annika Folin Request for Supplementary Information adopted on 30.01.2020.	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
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/R/0005, Orphan,	See agenda 9.1 Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The CHMP was of the opinion that the renewal

ATMP bluebird bio (Netherlands) B.V, Rapporteur: Carla Herberts, Co-Rapporteur: Violaine Closson Carella, CHMP Coordinators: Paula Boudewina van Hennik and Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski Request for Supplementary Information adopted on 24.01.2020.	for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection **PRAC recommendations on signals adopted at the PRAC meeting held on 10-13 February 2020 PRAC:**	
Signal of haemophagocytic lumphohistiocytosis: OPDIVO - nivolumab – EMEA/H/C/003985 Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Paula Boudewina van Hennik PRAC recommendation on a variation **Action**: For adoption	Adopted.
Post-authorisation safety studies **PRAC recommendations on PASS results adopted at the PRAC meeting held on 10-13 February 2020 PRAC:**	
Bronchitol (CAP) EMEA/H/C/PSR/S/0020 (mannitol) PRAC Rapp: Adrien Inoubli Scope: An Observational Safety 5 Year Safety Study of Bronchitol (inhaled mannitol) to assess the identified and potential risks of Bronchitol in CF through a comparison between Bronchitol-exposed patients and an unexposed patient group matched for key characteristics. PRAC recommendation to CHMP **Action**: For adoption	Adopted.

Periodic safety update reports **PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its February 2020 meeting:**	
EMEA/H/C/PSUSA/00002127/201908 (natalizumab) CAPS: **Tysabri** (EMEA/H/C/000603) (natalizumab), Biogen Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Period Covered From: 06/08/2018 To: 06/08/2019"	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 and 5.2 of the SmPC to add a warning on lack of significant effect of plasma exchange/plasmapheresis (PLEX) on natalizumab-associated 2-year survival and post-progressive multifocal leukoencephalopathy (PML) outcome in a retrospective analysis of natalizumab-treated patients since its approval. Update of section 4.8 of the SmPC to change the adverse drug reaction (ADR) frequencies of some adverse events (from "common" to "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/00009255/201907 (perampanel) CAPS: **Fycompa** (EMEA/H/C/002434) (perampanel), Eisai GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Period Covered From: 21/07/2018 To: 21/07/2019"	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 EU SmPC to add a warning on hepatotoxicity. The Package leaflet is updated accordingly. Update of sections 4.4, 4.5, and 4.6 of the EU SmPC to modify the label regarding the use of contraceptives from oral contraceptive to hormonal contraceptive. The Package leaflet is updated accordingly. Update of sections 4.4 and 4.8 of the EU SmPC to add Stevens – Johnson Syndrom (SJS) to the severe cutaneous adverse reactions warning. The Icelandic and the Norwegian CHMP members agree with the above-mentioned

	recommendation of the CHMP.
EMEA/H/C/PSUSA/00010457/201907 (pegaspargase (centrally authorised product)) CAPS: **Oncaspar** (EMEA/H/C/003789) (pegaspargase), Les Laboratoires Servier, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Annika Folin, "From: 14/07/2018 To: 14/07/2019"	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 the ADR 'anaphylactic shock' with frequency not known. The Package leaflet is updated accordingly. In addition, the ADR 'Toxic epidermal necrolysis' in section 4.8 of the SmPC is reclassified under the SOC Skin and subcutaneous system disorders. In addition, the product information has been updated in accordance to the latest QRD template (version 10.1). The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010609/201907 (sarilumab) CAPS: **Kevzara** (EMEA/H/C/004254) (sarilumab), sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Eva A. Segovia, "From: 12/07/2018 To: 12/07/2019"	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(s): Update of section 4.8 of the SmPC to add the adverse reactions pneumonia and cellulitis with a frequency 'uncommon'. The Package leaflet is updated accordingly. In addition there's a minor change in Section 4.8 to the title of the tabulated list of ADRs. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

B.4. EPARs / WPARs

Arsenic trioxide Mylan - arsenic trioxide - EMEA/H/C/005235 Mylan Ireland Limited, treatment of relapsed acute promyelocytic leukaemia (APL), Generic, Generic of TRISENOX, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Azacitidine betapharm - azacitidine -	For information only. Comments can be sent to

EMEA/H/C/005075 betapharm Arzneimittel GmbH, Treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML) and acute myeloid leukemia (AML), Generic, Generic of Vidaza, Generic application (Article 10(1) of Directive No 2001/83/EC)	the PL in case necessary.
Azacitidine Mylan - azacitidine - EMEA/H/C/004984 Mylan Ireland Limited, treatment of adult patients who are not eligible for haematopoietic stem cell transplantation (HSCT), Generic, Generic of Vidaza, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Budesonide/Formoterol Teva Pharma B.V. - budesonide / formoterol fumarate dihydrate - EMEA/H/C/004882 Teva Pharma B.V., treatment of asthma and COPD, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Cinacalcet Accordpharma - cinacalcet - EMEA/H/C/005236 Accord Healthcare S.L.U., treatment of secondary hyperparathyroidism and hypercalcaemia, Generic, Generic of Mimpara, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Evenity - romosozumab - EMEA/H/C/004465 UCB Pharma S.A., Treatment of osteoporosis, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
GIVLAARI - givosiran - EMEA/H/C/004775, Orphan Alnylam Netherlands B.V., Treatment of acute hepatic porphyria (AHP) in adults and adolescents aged 12 years and older., New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Isturisa - osilodrostat - EMEA/H/C/004821, Orphan Novartis Europharm Limited, treatment of Cushing's syndrome, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Liumjev - insulin lispro - EMEA/H/C/005037 Eli Lilly Nederland B.V., Treatment of diabetes	For information only. Comments can be sent to the PL in case necessary.

mellitus in adults, Known active substance (Article 8(3) of Directive No 2001/83/EC)	
Nilemdo - bempedoic acid - EMEA/H/C/004958 FGK Representative Service GmbH, treatment of primary hypercholesterolaemia or mixed dyslipidaemia, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
NUBEQA - darolutamide - EMEA/H/C/004790 Bayer AG, treatment of non-metastatic castration resistant prostate cancer (nmCRPC), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Nustendi - bempedoic acid / ezetimibe - EMEA/H/C/004959 FGK Representative Service GmbH, treatment of primary hypercholesterolaemia or mixed dyslipidaemia, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Ruxience - rituximab - EMEA/H/C/004696 Pfizer Europe MA EEIG, treatment of non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukaemia (CLL), rheumatoid arthritis (RA), granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), and Pemphigus vulgaris (PV), Similar biological application (Article 10(4) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Rybelsus - semaglutide - EMEA/H/C/004953 Novo Nordisk A/S, treatment of type 2 diabetes mellitus, Known active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Staquis - crisaborole - EMEA/H/C/004863 Pfizer Europe MA EEIG, treatment of mild to moderate atopic dermatitis, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Trepulmix - treprostinil sodium - EMEA/H/C/005207, Orphan SciPharm Sarl, treatment of thromboembolic pulmonary hypertension (CTEPH), Hybrid application (Article 10(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Vaxchora - cholera vaccine, oral, live - EMEA/H/C/003876	For information only. Comments can be sent to the PL in case necessary.

Emergent Netherlands B.V., indicated for active immunisation against disease caused by Vibrio cholerae serogroup O1 in adults and children aged 6 years and older, New active substance (Article 8(3) of Directive No 2001/83/EC)	

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Adenuric - febuxostat - EMEA/H/C/000777/II/0056 Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.
BeneFIX - nonacog alfa - EMEA/H/C/000139/II/0161/G Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 20.02.2020, 05.12.2019.	Request for supplementary information adopted with a specific timetable.
Brineura - cerliponase alfa - EMEA/H/C/004065/II/0019, Orphan BioMarin International Limited, Rapporteur: Martina Weise Request for Supplementary Information adopted on 06.02.2020.	Request for supplementary information adopted with a specific timetable.
Buvidal - buprenorphine - EMEA/H/C/004651/II/0005 Camurus AB, Rapporteur: Peter Kiely Opinion adopted on 13.02.2020.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0085/G UCB Pharma S.A., Rapporteur: Kristina Dunder Opinion adopted on 13.02.2020. Request for Supplementary Information adopted on 12.12.2019.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
CRYSVITA - burosumab - EMEA/H/C/004275/II/0007/G, Orphan Kyowa Kirin Holdings B.V., Rapporteur: Kristina Dunder Opinion adopted on 20.02.2020. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 20.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 21.11.2019, 12.09.2019.	
Elaprase - idursulfase - EMEA/H/C/000700/II/0082 Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 20.02.2020. Request for Supplementary Information adopted on 12.12.2019, 12.09.2019.	Positive Opinion adopted by consensus on 20.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Eylea - aflibercept - EMEA/H/C/002392/II/0058 Bayer AG, Rapporteur: Alexandre Moreau Opinion adopted on 13.02.2020. Request for Supplementary Information adopted on 14.11.2019.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
IKERVIS - ciclosporin - EMEA/H/C/002066/II/0018 Santen Oy, Rapporteur: Peter Kiely Opinion adopted on 20.02.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 20.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ilumetri - tildrakizumab - EMEA/H/C/004514/II/0010/G Almirall S.A, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 20.02.2020. Request for Supplementary Information adopted on 28.11.2019.	Positive Opinion adopted by consensus on 20.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Inflectra - infliximab - EMEA/H/C/002778/II/0081/G Pfizer Europe MA EEIG, Duplicate, Duplicate of Remsima, Rapporteur: Outi Mäki-Ikola Opinion adopted on 06.02.2020. Request for Supplementary Information adopted on 28.11.2019.	Positive Opinion adopted by consensus on 06.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Natpar - parathyroid hormone - EMEA/H/C/003861/II/0020/G, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Bart Van der Schueren Opinion adopted on 20.02.2020. Request for Supplementary Information adopted on 07.11.2019.	Positive Opinion adopted by consensus on 20.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Onpattro - patisiran - EMEA/H/C/004699/II/0011/G, Orphan Alnylam Netherlands B.V., Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 06.02.2020.	Request for supplementary information adopted with a specific timetable.

Ozempic - semaglutide - EMEA/H/C/004174/II/0011 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.
Remicade - infliximab - EMEA/H/C/000240/II/0225/G Janssen Biologics B.V., Rapporteur: Kristina Dunder Opinion adopted on 13.02.2020.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Remsima - infliximab - EMEA/H/C/002576/II/0075/G Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola Opinion adopted on 06.02.2020. Request for Supplementary Information adopted on 28.11.2019.	Positive Opinion adopted by consensus on 06.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
RoActemra - tocilizumab - EMEA/H/C/000955/II/0093/G Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.
Rotarix - rotavirus vaccine (live, oral) - EMEA/H/C/000639/II/0116/G GlaxoSmithKline Biologicals S.A., Rapporteur: Bart Van der Schueren Opinion adopted on 13.02.2020.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Skilarence - dimethyl fumarate - EMEA/H/C/002157/II/0019 Almirall S.A, Rapporteur: Janet Koenig Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.
Somavert - pegvisomant - EMEA/H/C/000409/II/0091 Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race Opinion adopted on 06.02.2020. Request for Supplementary Information adopted on 05.12.2019.	Positive Opinion adopted by consensus on 06.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0020/G Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 06.02.2020.	Positive Opinion adopted by consensus on 06.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Request for Supplementary Information adopted on 05.12.2019.	
VIZAMYL - flutemetamol (18F) - EMEA/H/C/002557/II/0022/G GE Healthcare AS, Rapporteur: Maria Concepcion Prieto Yerro Opinion adopted on 06.02.2020.	Positive Opinion adopted by consensus on 06.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ziextenzo - pegfilgrastim - EMEA/H/C/004802/II/0005/G Sandoz GmbH, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 06.02.2020.	Request for supplementary information adopted with a specific timetable.
WS1524 **HyQvia-EMEA/H/C/002491/WS1524/0048** **Kiovig-EMEA/H/C/000628/WS1524/0090** Takeda Manufacturing Austria AG, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 20.02.2020. Request for Supplementary Information adopted on 19.09.2019, 14.03.2019.	Positive Opinion adopted by consensus on 20.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1720/G **Ambirix-EMEA/H/C/000426/WS1720/0104/G** **Twinrix Adult-EMEA/H/C/000112/WS1720/0139/G** **Twinrix Paediatric-EMEA/H/C/000129/WS1720/0140/G** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 27.02.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1744/G **Hexacima-EMEA/H/C/002702/WS1744/0095/G** **Hexaxim-EMEA/H/W/002495/WS1744/0100/G** **Hexyon-EMEA/H/C/002796/WS1744/0099/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 06.02.2020.	Positive Opinion adopted by consensus on 06.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Avamys - fluticasone furoate - EMEA/H/C/000770/II/0040 GlaxoSmithKline (Ireland) Limited, Rapporteur:	Request for supplementary information adopted with a specific timetable.

Ewa Balkowiec Iskra, "Update of section 4.8 of the SmPC in order to add bronchospasm and dyspnoea to the list of adverse drug reactions with a frequency unknown based on post-marketing experience. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet." Request for Supplementary Information adopted on 06.02.2020.	
Cablivi - caplacizumab - EMEA/H/C/004426/II/0021, Orphan Ablynx NV, Rapporteur: Filip Josephson"Submission of the results of the study ALX-0681-MS-01, a Modelling/Simulation study performed for the paediatric population as part of the approved Paediatric Investigation Plan (EMEA-001157-PIP-01-11-M02) for Cablivi" Request for Supplementary Information adopted on 27.02.2020.	See agenda 9.1 Request for supplementary information adopted with a specific timetable.
Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0007/G Sanofi Pasteur, Rapporteur: Bart Van der Schueren, "C.I.13: Submission of the final report from studies CYD63 and CYD64 listed as a category 3 study in the RMP. These are booster studies to evaluate the safety and immunogenicity of a booster dose of dengue vaccine administered in a subset of subjects who received third dose of dengue vaccine 4-5 years before, in Phase II studies." Opinion adopted on 13.02.2020.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Dovato - dolutegravir / lamivudine - EMEA/H/C/004909/II/0008 ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to update the safety and efficacy information following the week 48 results from TANGO study (204862); TANGO (204862) is an on-going 200-week, Phase III, randomized, open-label, active controlled, multicenter, parallel-group study, evaluating the efficacy, safety, and tolerability of switching to Dovato in HIV-1 infected adults who are virologically suppressed. The RMP version has not been submitted." Opinion adopted on 13.02.2020.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Dovato - dolutegravir / lamivudine -	Positive Opinion adopted by consensus on

EMEA/H/C/004909/II/0009 ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of section 5.1 in order to update the safety and efficacy following the week 96 results from 204861 (GEMINI-1) and 205543 (GEMINI-2) studies listed as a specific category 3 study in the RMP; these are two identical pivotal ongoing, randomized, double-blind, parallel group, 148-week, phase III studies to evaluate the efficacy, safety and tolerability of dolutegravir plus 3TC compared to dolutegravir plus tenofovir/emtricitabine in HIV-1-infected treatment naïve patients. The RMP version has not been submitted." Opinion adopted on 13.02.2020.	13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0058, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of sections 4.5 and 4.6 of the SmPC following the results from study CLL1017 (MEA 012.2). The PL is updated accordingly." Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.
Jivi - damoctocog alfa pegol - EMEA/H/C/004054/II/0004 Bayer AG, Rapporteur: Sinan B. Sarac, "Submission of the final Clinical Study Report PH-40657 for the pharmacokinetic study (study 19096) comparing pharmacokinetic parameters of Jivi vs. Elocta." Opinion adopted on 06.02.2020. Request for Supplementary Information adopted on 05.12.2019.	Positive Opinion adopted by consensus on 06.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kisqali - ribociclib - EMEA/H/C/004213/II/0020 Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and include safety information on toxic epidermal necrolysis. The Package Leaflet is updated accordingly." Opinion adopted on 13.02.2020.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kisqali - ribociclib - EMEA/H/C/004213/II/0022 Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC based on the final OS analysis from study CLEE011F2301 (MONALEESA-3), a randomised	Request for supplementary information adopted with a specific timetable.

double-blind, placebo-controlled, multicentre phase III clinical study in the treatment of men and postmenopausal women with hormone receptor positive, HER2-negative advanced breast cancer who had received no or only one line of prior endocrine treatment, in combination with fulvestrant versus fulvestrant alone." Request for Supplementary Information adopted on 13.02.2020.	
MabThera - rituximab - EMEA/H/C/000165/II/0169 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of the SmPC sections 4.8, 5.1 and 5.2 with the results of the Post-authorisation efficacy study (PAES) randomised phase 3 study (PEMPHIX WA29330) which further investigated the efficacy of Mabthera in the subgroup of patients with established PV as well as characterised its long term efficacy and safety on disease progression. Annex II and PL are updated accordingly. In addition, outstanding QRD comments from EMEA/H/C/00165/II/162 are being implemented." Opinion adopted on 27.02.2020. Request for Supplementary Information adopted on 12.12.2019.	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0031 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Jean-Michel Race, "Submission of the final clinical study report from the Phase 3b study M16-156 (A Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Glecaprevir (GLE)/Pibrentasvir (PIB) in Treatment-Naïve Adults in Brazil with Chronic Hepatitis C Virus (HCV) Genotype 1 – 6 Infection)." Opinion adopted on 13.02.2020.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Nivestim - filgrastim - EMEA/H/C/001142/II/0061 Pfizer Europe MA EEIG, Rapporteur: Outi Mäki-Ikola, "To update section 4.4 of the SmPC to add a warning on the content of a derivative of natural rubber latex in the needle cover formulation. The Package Leaflet are updated accordingly." Request for Supplementary Information adopted on 06.02.2020.	Request for supplementary information adopted with a specific timetable.

Perjeta - pertuzumab - EMEA/H/C/002547/II/0047 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Submission of the final report from study W020698 (CLEOPATRA), a phase III, randomized, double blind, placebo-controlled clinical trial to evaluate the efficacy and safety of pertuzumab + trastuzumab + docetaxel vs placebo + trastuzumab + docetaxel in previously untreated HER2-positive metastatic breast cancer." Request for Supplementary Information adopted on 06.02.2020.	Request for supplementary information adopted with a specific timetable.
PREVYMIS - letermovir - EMEA/H/C/004536/II/0013, Orphan Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to update the viral resistance profile that may be associated with a change in susceptibility to letermovir considering new intro pharmacology data based on the analysis of the patients' samples included in the study MK-8228.This study is a Phase III Randomized, Placebo-Controlled Clinical Trial to Evaluate the Safety and Efficacy of MK-8228 (Letermovir) for the Prevention of Clinically Significant Human Cytomegalovirus (CMV) Infection in Adult, CMV Seropositive Allogeneic Hematopoietic Stem Cell. This variation follows the recommendation dated 9th November 2017 that asked for the submission when available of the results to update the CMV phenotypic resistance analyses of all clinical isolates for subjects failing letermovir treatment and to explore the possibility to obtain additional pre-failure CMV genotypic data from available samples." Opinion adopted on 27.02.2020. Request for Supplementary Information adopted on 12.12.2019, 17.10.2019.	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PREVYMIS - letermovir - EMEA/H/C/004536/II/0014, Orphan Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to update the safety information with regard to the drug interaction information following the results from study MK-8228-039, a clinical pharmacology trial entitled "A Study to Assess the Effect of P-gp/BCRP Inhibition,	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

following Multiple Oral Doses of Itraconazole, on the Steady-State Pharmacokinetics of MK-8228 in Healthy Adult Subjects" listed as a category 3 study in the RMP. The RMP version has not been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to submit the protein binding report as part of the rifampin study MK-8228-038 as it was requested within the previous type II variation (EMEA/H/C/004536/II/0011) ." Opinion adopted on 13.02.2020. Request for Supplementary Information adopted on 05.12.2019.	
Qutenza - capsaicin - EMEA/H/C/000909/II/0048 Grunenthal GmbH, Rapporteur: Bruno Sepodes, "Update of sections 4.2 and 5.1 of the SmPC in order to amend the posology based on PACE and STRIDE studies. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 27.02.2020, 12.12.2019.	See agenda 9.1 Request for supplementary information adopted with a specific timetable.
Resolor - prucalopride - EMEA/H/C/001012/II/0049/G Shire Pharmaceuticals Ireland Limited, Rapporteur: Kristina Dunder, "Submission of the final report from study SH555-802 and an independent adjudication on all potential MACE from completed Phase 2/4 clinical studies in adult subjects. This is a the non-interventional pharmacoepidemiology safety with the primary objective to estimate, in real-world settings, the IRR and 95% CI for MACE in initiators of prucalopride compared with initiators of PEG (polyethylene glycol 3350), adjusting for potential confounders. More specifically, the study aimed to investigate whether the upper bound of the two-sided 95% CI for the adjusted IRR was less than 3.00. The study was designed as a multidatabase study with data from Germany, UK and Sweden with pooled results. German data was later discarded since due to disparate clinical profile of German patients compared to the others." Opinion adopted on 27.02.2020. Request for Supplementary Information adopted on 31.10.2019.	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Revatio - sildenafil - EMEA/H/C/000638/II/0086 Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 5.1 of the SmPC based on the final results from study A1481316; this is a multi-centre, randomised, placebo-controlled, double-blind, two-armed, parallel group study to evaluate efficacy and safety of iv sildenafil in the treatment of neonates with persistent pulmonary hypertension of the newborn (PPHN) or hypoxic respiratory failure and at risk for PPHN, with a long-term follow-up investigation of developmental progress 12 and 24 months after completion of study treatment. In addition some minor editorial updates to the Product Information are being proposed." Opinion adopted on 27.02.2020. Request for Supplementary Information adopted on 16.01.2020, 05.12.2019.	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
RoActemra - tocilizumab - EMEA/H/C/000955/II/0091 Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC for RoActemra 162 mg solution for injection in pre-filled pen in order to align with the approved indications for RoActemra 162 mg solution for injection in pre-filled syringe to include active systemic juvenile idiopathic arthritis (sJIA) and juvenile idiopathic polyarthritis from the age of 12 years; the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder took the opportunity to make minor editorial changes in sections 3, 4.2, 4.4 and 5.1 of the SmPC for RoActemra 162 mg solution for injection in pre-filled syringe and the Annex II." Opinion adopted on 27.02.2020.	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0021 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "C.I.13: Submission of the final report from study Zoster-063, listed as a category 3 study in the RMP version 2.0. The study was conducted to investigate the impact of reactogenicity on health-related quality of life in subjects ≥50 YOA following Shingrix vaccination."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 13.02.2020.	
Skyrizi - risankizumab - EMEA/H/C/004759/II/0008 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Peter Kiely, "Update of SmPC 5.1 'Pharmacodynamic Properties' of the Skyrizi SmPC. The change pertains to the addition of information on retreatment after withdrawal of risankizumab to the summary of the IMMhance clinical study (M15-992)." Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.
Soliris - eculizumab - EMEA/H/C/000791/II/0111, Orphan Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC (editorial changes) following variations EMEA/H/C/000791/II/0105 and EMEA/H/C/000791/II/0107 including interim and final results from studies ECU-NMO-302 and ECU-MG-302, respectively; these were open-label extensions of pivotal trials ECU-NMO-301 and ECU-MG-301 supporting the extension of indication for neuromyelitis optica spectrum disorder (NMOSD) with anti-aquaporin-4 (AQP4) antibodies and generalized myasthenia gravis (gMG), respectively. The Package Leaflet is updated accordingly. Editorial changes are also made to the Annex IID in line with version 19.3 of the RMP 19.3 agreed in conclusion of EMEA/H/C/000791/II/0105." Opinion adopted on 27.02.2020.	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
TAGRISSO - osimertinib - EMEA/H/C/004124/II/0032 AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.4 and 4.8 of the SmPC in order to include erythema multiforme as an adverse drug reaction following the review of the MAH internal safety data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity of this procedure to add the event frequency of Stevens-Johnson syndrome to align with the approved text in the SmPC." Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.

Tecentriq - atezolizumab - EMEA/H/C/004143/II/0034 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 5.1 of the SmPC in order to include updated overall survival data from study IMvigor 211 (GO29294), a phase III study to investigate the efficacy and safety of atezolizumab compared with chemotherapy in patients with locally advanced or metastatic urothelial bladder cancer after failure of platinum-containing chemotherapy." Opinion adopted on 13.02.2020.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0035 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to reflect the results of study GO29664, (iMATRIX) evaluate the safety and pharmacokinetics of Tecentriq in paediatric (<18, n=69) and young adult patients (18-30 years, n=18) with relapsed or progressive solid tumours as well as with Hodgkin's and non-Hodgkin's lymphoma. This study was agreed under the Paediatric Investigational Plan EMEA-001638-PIP01-14-M02 (EMA decision: P/0207/2019). The Package Leaflet is updated accordingly." Opinion adopted on 13.02.2020.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0054 MCM Vaccine B.V., Rapporteur: Bart Van der Schueren, "Update of section 4.8 of the Vaxelis SmPC in order to add Hypotonic Hyporesponsive Episode to the list of post-marketing adverse events, based on a cumulative assessment of post-marketing data from the Marketing authorisation holder (MAH) global safety database. The Package Leaflet is updated accordingly. In addition, the MAH made minor editorial changes to the product information." Opinion adopted on 13.02.2020.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vemlidy - tenofovir alafenamide - EMEA/H/C/004169/II/0023 Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, "Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC based on interim analysis data	Request for supplementary information adopted with a specific timetable.

at Week 24 from study GS-US-320-4035. This is a Phase 2, open-label study evaluating the efficacy and safety of tenofovir alafenamide (TAF) in virologically suppressed chronic hepatitis B subjects with renal and/or hepatic impairment who switch from tenofovir disoproxil fumarate and/or other oral antiviral agents to TAF 25 mg once daily. Supportive safety and pharmacokinetic data are also provided from Study GS-US-292-1825 (phase 3b trial in which Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide an fixed-dose TAF containing combination indicated for the treatment of HIV-1 infection, was evaluated in HIV-1 infected subjects with end stage renal disease). Study GS-US-320-4035 is included in the RMP version 4.2 under additional PhV activities." Request for Supplementary Information adopted on 06.02.2020.	
VEYVONDI - vonicog alfa - EMEA/H/C/004454/II/0010 Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus, "Variation to add hypersensitivity reactions (including anaphylaxis) in section 4.4 and 4.8 of the SmPC. Update of sections 4.4. and 4.8 of the SmPC to update the wording on hypersensitivity reactions (including anaphylaxis). Furthermore, sodium has been included in SmPC section 2 as "excipient with known effect" to be in line with the already approved information in section 4.4. of the SmPC. Finally, some minor changes to the Annex II have been proposed in line with the latest QRD template (version 10.1). The Package Leaflet has been updated accordingly." Opinion adopted on 20.02.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 20.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
VITRAKVI - larotrectinib - EMEA/H/C/004919/II/0001 Bayer AG, Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to remove the warning related to drug-drug interactions between larotrectinib and CYP2 substrates based on the results of study PH-40955 investigating the inductive potential of Larotrectinib on the expression of cytochrome P450 (CYP) enzymes. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 13.02.2020.	
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 opportunity to implement minor editorial changes to the SmPC and PIL." Request for Supplementary Information adopted on 13.02.2020, 21.11.2019, 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/II/0074 Bial - Portela & Cª, S.A., Rapporteur: Martina Weise, "Update of sections 4.2 and 5.2 of the SmPC in order to add the possibility to crush the tablets for patients unable to swallow whole tablets based on final results from study EP093-155; this is an interventional study to investigate and compare the relative bioavailability and bioequivalence of a crushed tablet and an intact tablet of ESL (800 mg); The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.
WS1683 **Elebrato Ellipta-EMEA/H/C/004781/ WS1683/0012** **Temybric Ellipta-EMEA/H/C/005254/ WS1683/0001** **Trelegy Ellipta-EMEA/H/C/004363/ WS1683/0010** GlaxoSmithKline Trading Services Limited, Lead Rapporteur: Peter Kiely, "Update of SmPC in order to add information in section 5.1 on survival data from the IMPACT study" Request for Supplementary Information adopted on 12.12.2019, 17.10.2019.	See agenda 2.3
WS1749 **AZILECT-EMEA/H/C/000574/ WS1749/0084** **Rasagiline ratiopharm-EMEA/H/C/ 003957/WS1749/0016** Teva B.V., Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, "Submission of the final report from study TV1030-CNS-50024 listed as a category 3 study in the RMP. This is a non-interventional retrospective cohort study which was conducted	Request for supplementary information adopted with a specific timetable.

using the United States Medicare research database to assess the potential risk of melanoma associated with the use of rasagilline mesylate in patients with Parkinson's disease." Request for Supplementary Information adopted on 13.02.2020.	
WS1762 **Dovato-EMEA/H/C/004909/WS1762/0007** **Juluca-EMEA/H/C/004427/WS1762/0018** **Tivicay-EMEA/H/C/002753/WS1762/0055** **Triumeq-EMEA/H/C/002754/WS1762/0076** ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson, "Update of sections 4.3 and 4.5 of the SmPC in order to add a new contraindication in relation to the co-administration of dolutegravir with medicinal products with narrow therapeutic windows that are substrates of organic cation transporter 2 (OCT2), including but not limited to fampridine (also known as dalfampridine). The Package Leaflet is updated accordingly. The RMP has not been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to remove the drug-drug interactions for products no longer authorised in the EU (boceprevir, dofetilide, nelfinavir), update the local MAH contacts in Belgium/Luxembourg, remove the inverted triangle for additional monitoring and add the date of first authorisation in the case of Dovato and add the date of last marketing authorisation renewal for Triumeq only." Opinion adopted on 06.02.2020.	Positive Opinion adopted by consensus on 06.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.3. CHMP-PRAC assessed procedures

Baraclude - entecavir - EMEA/H/C/000623/II/0064 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect the completion of the two paediatric studies AI463028 (Evaluation of the pharmacokinetics, safety, tolerability and efficacy of Entecavir (ETV) in pediatric subjects with chronic hepatitis B virus (HBV) infection who are HBeAg-Positive) and AI463189 (A Comparative Study of the Antiviral Efficacy and Safety of Entecavir (ETV) versus Placebo in Pediatric Subjects with Chronic Hepatitis B Virus (HBV) Infection who are HBeAg-Positive) and	Request for supplementary information adopted with a specific timetable.

section 5.3 to reflect the outcome of study AI463080 (Randomized, Observational Study of Entecavir to Assess Long-term Outcomes Associated with Nucleoside/Nucleotide Monotherapy for Patients with Chronic HBV Infection: The REALM Study). Section 5.2 of the SmPC is also updated to remove information on the pharmacokinetics of entecavir in lamivudine-experienced paediatric patients, at the request of the CHMP. The RMP version 15 has also been submitted, which implements Revision 2 of the EU-RMP template. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1 and to make minor editorial changes to the PI." Request for Supplementary Information adopted on 13.02.2020.	
Bavencio - avelumab - EMEA/H/C/004338/II/0013 Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Hans Christian Siersted, "Update of section 5.1 of the SmPC in order to update efficacy information following results from study EMR100070-003 Part B listed as a specific obligation in the Annex II; this is a Phase II, open-label, multicentre trial to investigate the clinical activity and safety of avelumab (MSB0010718C) in subjects with Merkel cell carcinoma. With this submission the company is also taking the opportunity to update annex-II proposing deletion of the specific obligation and proposing the switch from conditional to full marketing authorisation. The package leaflet and the RMP (version 2.1) are updated accordingly." Request for Supplementary Information adopted on 27.02.2020.	See agenda 9.1 Request for supplementary information adopted with a specific timetable.
Benlysta - belimumab - EMEA/H/C/002015/II/0076 GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information based on the final results from study BEL115467 listed as a imposed PASS in the Annex II; this is a Randomized, Double-Blind, Placebo-Controlled 52-Week Study to Assess Adverse Events of Special Interest in Adults with Active, Autoantibody-Positive Systemic Lupus	See agenda 9.1 Request for supplementary information adopted with a specific timetable.

Erythematosus Receiving Belimumab; the Package Leaflet is updated accordingly. The RMP version 36 has also been submitted. The MAH took the opportunity to make the following minor updates to the RMP: - Updated information on transplant study, updated information on BEL116543, added information on paediatric continuation study in Module SIV. - Updated exposure information and information for BEL116543 in Module SIV.2. - Update data on revised rates of pregnancy and lactation in Module SIV.3. - Correction of an error within Annex 3 and provision of the updated protocol Amendment 7 of a Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of belimumab plus Standard of Care versus Placebo plus standard of Care in Adult Subjects with Active Lupus Nephritis (BEL114054). This RMP also includes changes being reviewed in procedure II/0062, related to the use of Benlysta in paediatric patients, and BEL116027, evaluating the safety and efficacy of temporary discontinuation of belimumab. In addition, the Marketing authorisation holder took the opportunity to make minor editorial changes to the Annex II and the label." Request for Supplementary Information adopted on 27.02.2020.	
Biktarvy - bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449/II/0027 Gilead Sciences Ireland UC, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Liana Gross-Martirosyan, "Update of sections 4.8 and 5.1 of the Biktarvy SmPC to reflect pooled efficacy and safety data from the final clinical study reports of two antiretroviral therapy-naive adult studies through 144 weeks of treatment, GS-US-380-1489 (A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of GS-9883/Emtricitabine/ Tenofovir Alafenamide Versus Abacavir [ABC]/Dolutegravir [DTG]/Lamivudine [3TC] in HIV-1 Infected, Antiretroviral Treatment-Naive Adults) and GS-US-380-1490 (A Phase 3, Randomized, Double-Blinded Study to Evaluate the Safety and Efficacy of GS-9883/ Emtricitabine/Tenofovir	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Alafenamide Versus Dolutegravir + Emtricitabine/Tenofovir Alafenamide in HIV-1 Infected, Antiretroviral Treatment-Naive Adults). Both studies are listed as Category 3 studies in the RMP and this submission therefore fulfils MEA 001 and MEA 002. The RMP version 3.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to make some minor editorial changes to the PI and update Annex II with regards to PSUR requirements. Furthermore, the PI is brought in line with the latest QRD template version 10.1." Opinion adopted on 13.02.2020.	
Descovy - emtricitabine / tenofovir alafenamide - EMEA/H/C/004094/II/0044 Gilead Sciences Ireland UC, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ana Sofia Diniz Martins, "Submission of the final report from Study GS-US-311-1717 "A Phase 3b, Randomized, Double-Blind, Switch Study to Evaluate F/TAF in HIV-1 Infected Subjects who are Virologically Suppressed on Regimens Containing ABC/3TC" , listed as additional pharmacovigilance activity in the Descovy EU Risk Management Plan (RMP). This submission provides efficacy, clinical virology and safety data for virologically suppressed HIV-infected, who switch to regimens containing F/TAF from regimens containing abacavir (ABC)/lamivudine (3TC). No amendments are proposed to the Summary of Products Characteristics, product labelling and Patient Information Leaflet for the product. The RMP version 4.1 has been submitted." Opinion adopted on 27.02.2020. Request for Supplementary Information adopted on 12.12.2019.	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0036, Orphan Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Annika Folin, "Update of sections 4.8 and 5.1 of the SmPC based on data from the final CSR of the pivotal study GA04753g/GO01297/GADOLIN to fulfil a Category 3 PAM (MEA 006). The PL and RMP are updated accordingly." Opinion adopted on 13.02.2020. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 28.11.2019.	
Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0038, Orphan Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Annika Folin, "Submission of final CSR for study MO28543/GREEN to fulfil the post authorization commitment [MEA] 005, the RMP is updated with the deletion of the study under PhV plan, (RMP version 6.1)" Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.
Herceptin - trastuzumab - EMEA/H/C/000278/II/0158 Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Submission of the final report from study BO29159 (MetaPHER) a post-authorization safety measure Category 3 Non-Imposed Post-Approval Safety Study (NI-PASS), following approval of the Herceptin SC line extension procedure EMEA/H/C/278/X/60 to generate and evaluate additional safety and tolerability data for the approved triplet regimen (Herceptin+Perjeta+docetaxel) in the advanced breast cancer setting. In addition, bioanalytical supportive studies are presented. An updated version of the Herceptin Risk Management Plan (version 21) has also been submitted." Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.
Incresync - alogliptin / pioglitazone - EMEA/H/C/002178/II/0029 Takeda Pharma A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Incresync RMP (version 10.1) includes the following updates: (i) MAH's proposal for removal of additional risk minimisation measures and consequently the Drug Utilisation Study along with removal of relevant commitment (EMEA/H/C/002182/LEG/009). (ii) RMP updated in the new template in order to implement the GVP Module V Revision 2 template along with revising/removal of the safety concerns as summarised below: · The safety concerns for the alogliptin component have been updated. · The safety concerns for the pioglitazone	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

component have been aligned with the consolidated Pioglitazone family RMP (RMP V27.0 as part of the worksharing variation procedure [EMEA/H/C/XXXX/WS/1680]). ·The safety concerns for alogliptin/pioglitazone FDC have been updated. (iii) Targeted Adverse Event (AE) Follow-up Questionnaires related to AEs of severe hypersensitivity skin reactions, hepatic events, pancreatitis, bladder cancer, bone fractures, and macular oedema were also removed. (iv) RMP has also been updated to reflect the removal of the inverted black triangle as agreed as part of alogliptin renewal procedure (EMEA/H/C/002182/R/0019). Annex II of the PI has been updated accordingly, as well as local representative for Poland." Opinion adopted on 13.02.2020. Request for Supplementary Information adopted on 28.11.2019.	
Kisqali - ribociclib - EMEA/H/C/004213/II/0021 Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Hans Christian Siersted, "Update of sections 4.2 and 4.4 of the SmPC in order to add a warning on ILD/pneumonitis and related dose modification recommendations. The Package Leaflet is updated accordingly. The RMP version 4.0 has also been submitted." Request for Supplementary Information adopted on 27.02.2020.	Request for supplementary information adopted with a specific timetable.
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 8.0 has also been agreed. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the RMP in line with the template	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

revision 2 of the good Pharmacovigilance practice module V guideline and to align the PI to the QRD template version 10.1." Opinion adopted on 27.02.2020. Request for Supplementary Information adopted on 12.12.2019, 19.09.2019.	
Symkevi - tezacaftor / ivacaftor - EMEA/H/C/004682/II/0016, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, "Update of sections 4.8 and 5.1 of the SmPC in order to update the information based on final results from study VX14-661-110 listed as a category 3 study in the RMP; this is a Phase 3, multicenter, open label, rollover study for Studies 103, 106, 107, 108, 109, 111, 112, and 114 designed to evaluate the long-term safety and tolerability of TEZ/IVA treatment for 96 weeks in cystic fibrosis (CF) subjects 12 years and older, homozygous or heterozygous for the F508del CFTR mutation. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1. The RMP version 2.2 has also been submitted." Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.
Tamiflu - oseltamivir - EMEA/H/C/000402/II/0142 Roche Registration GmbH, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC following completion of the paediatric studies NV25719 and NV20234 and downstream population PK and PK/PD analysis, listed in the approved Tamiflu Paediatric Investigation Plan (PIP) (EMEA-000365-PIP01-08-M10); the study NV25719 was a prospective, open-label, randomized study which investigated PK and PD of two weight adjusted oseltamivir doses for the treatment of influenza-infected immunocompromised (IC) children less than 13 years of age. The study NV20234 was a prospective, double-blind, randomized trial which investigated safety and viral resistance to oseltamivir treatment in influenza-infected IC adults, adolescents and children. The purpose of this variation is to establish a dose recommendation for the treatment of paediatric	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

IC patients. The Package Leaflet and Labelling are updated accordingly. The updated RMP version 19 has also been submitted." Opinion adopted on 27.02.2020. Request for Supplementary Information adopted on 17.10.2019.	
Xultophy - insulin degludec / liraglutide - EMEA/H/C/002647/II/0034 Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, "Update of section 4.2 of the SmPC in order to change the wording "transfer from basal insulin" to "transfer from any insulin regimen", based on data from study NN9068-4184 (DUAL II Japan: A double-blinded trial comparing the efficacy and safety of insulin degludec/liraglutide and insulin degludec both in combination with metformin in Japanese subjects with type 2 diabetes mellitus inadequately controlled with basal or pre-mix/combination insulin therapy and oral anti-diabetic drugs) as well as data from the post-marketing setting. In addition, the MAH took the opportunity to make a minor correction in SmPC section 5.1 and to implement changes in the annexes in accordance with QRD template 10.1. The MAH provided an updated RMP version 9.0 as part of the application." Request for Supplementary Information adopted on 27.02.2020.	Request for supplementary information adopted with a specific timetable.
WS1704 **Alimta-EMEA/H/C/000564/WS1704/0058** **Pemetrexed Lilly-EMEA/H/C/004114/ WS1704/0010** Eli Lilly Nederland B.V., Lead Rapporteur: Alexandre Moreau, Lead PRAC Rapporteur: Ghania Chamouni, "Worksharing to update section 4.8 of the SmPC as requested by CHMP following the assessment of the PSUR covering the period between 05 February 2015 and 04 February 2018. To comply with SmPC guideline and latest QRD update, the Alimta and Pemetrexed Lilly SmPCs are updated combining multiple tables of ADRs into two tables: one for the ADRs reported in the pivotal registration trials and one for ADRs from the postmarketing period (both clinical trials and spontaneous reporting), organized by SOC with the respective frequency categories. The Package Leaflet is updated accordingly. In addition, an	Request for supplementary information adopted with a specific timetable.

updated RMP version 6.1 has been submitted to implement the revised GVP Module V (Rev 2) format as requested by CHMP following the assessment of the PSUR covering the period between 05 February 2015 and 04 February 2018." Request for Supplementary Information adopted on 20.02.2020, 28.11.2019.	

B.5.4. PRAC assessed procedures

PRAC Led **Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0040** Biofrontera Bioscience GmbH, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "To update the RMP for Ameluz to version 11.1 based on the new RMP template (GVP module V, rev.2), as well as the implementation of changes assessed and agreed by PRAC in the recently finalised PSUSA procedure (EMEA/H/C/002204/PSUSA/ 00010006/20180614)." Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Betmiga - mirabegron - EMEA/H/C/002388/II/0033** Astellas Pharma Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Final study report of the PASS Study 178-CL-114 – An evaluation of Cardiovascular Events in Users of Mirabegron and Other Treatments for Overactive Bladder." Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0086** UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from study (UP0038) listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study with the aim to evaluate the effectiveness of Cimzia risk minimisation educational materials for healthcare professionals and patients."	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 13.02.2020.	
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." Opinion adopted on 13.02.2020. Request for Supplementary Information adopted on 31.10.2019.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Constella - linaclotide - EMEA/H/C/002490/II/0043** Allergan Pharmaceuticals International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the final report from study "Linaclotide Utilization Study in Selected European Populations" listed as a category 3 study in the RMP. This is a Drug Utilisation Study (DUS) to address following safety concerns - The potential for off-label use and abuse/excessive use - Extent of use in pregnancy and lactation, and male patients - Assess the extent of off-label use and the extent of use in males and in pregnant females" Request for Supplementary Information adopted on 13.02.2020, 28.11.2019.	Request for supplementary information adopted with a specific timetable.
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 12.0 in order to delete all risks and additional risk minimisation measures, in line with GVP module V revision 2. Annex II of the Product	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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." Opinion adopted on 13.02.2020. Request for Supplementary Information adopted on 31.10.2019.	
PRAC Led **Fampyra - fampridine - EMEA/H/C/002097/II/0046** Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of sections 4.2, 4.3, 4.4, 4.8 and 5.1 of the SmPC in order to update the existing contraindication for renal impaired patients, update the frequency of seizure to uncommon and reflect safety information based on final results from study 218MS401 (LIBERATE) listed as category 3 study in the RMP; Study 218MS401 was a Phase IV prospective, noninterventional, multicentre, observational study in MS patients who began Fampyra treatment in the post-marketing setting. The Package Leaflet is updated accordingly. An updated RMP version 13.1 has also been submitted to align with the RMP Rev. 2 template." Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Firmagon - degarelix - EMEA/H/C/000986/II/0035** Ferring Pharmaceuticals A/S, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the FE 200486 CS39 Post Authorisation Safety Study (PASS) report; this was a Prospective Observational Safety Study in Patients with Advanced Prostate Cancer Treated with FIRMAGON (Degarelix) or a GnRH Agonist." Opinion adopted on 13.02.2020.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Rebif - interferon beta-1a - EMEA/H/C/000136/II/0144** Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

CHMP liaison: Filip Josephson, "C.I.11 for RMP: Submission of an updated RMP version 11 in order to comply with the Good Pharmacovigilance Practices (GVP) Module 5 RMP revision 2 requirements, and to ensure the appropriate time needed for effective review and analysis of all RMP Sections" Opinion adopted on 13.02.2020.	
PRAC Led **Retacrit - epoetin zeta - EMEA/H/C/000872/II/0094** Pfizer Europe MA EEIG, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Pfizer's biosimilar epoetin zeta list of safety concerns has been aligned to the Innovator's Eprex (reference product, INN epoetin alfa)." Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Saxenda - liraglutide - EMEA/H/C/003780/II/0025** Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report from study NN8022-4241, a retrospective drug utilisation study (DUS) undertaken to investigate patterns of use of liraglutide containing drugs in routine clinical practice, listed as a category 3 study in the RMP. An updated RMP version 31 was agreed during the procedure." Opinion adopted on 13.02.2020.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **SIRTURO - bedaquiline - EMEA/H/C/002614/II/0038, Orphan** Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "To update the RMP (version 5.1) to revise the Summary of Safety Concerns for Sirturo in response to a request received from PRAC/CHMP in the context of the assessment of the Renewal (EMEA/H/C/002614/R/0035) of the Conditional Marketing Authorisation of SIRTURO. As requested by the PRAC/CHMP, data on co-administration of bedaquiline and HIV-protease inhibitors are also summarised. No changes are proposed to the Product	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Information of SIRTURO." Opinion adopted on 13.02.2020.	
PRAC Led **Teysuno - tegafur / gimeracil / oteracil - EMEA/H/C/001242/II/0042** Nordic Group B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 9 in order to update safety specifications (re-classifying and removing risks from the list of important safety concerns as outlined in PSUSA/2875/201801)." Request for Supplementary Information adopted on 13.02.2020.	Request for supplementary information adopted with a specific timetable.
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, "Update of the RMP (finally agreed version 30.2) in line with the latest RMP template revision 2; as a consequence, Annex II of the PI is updated to reflect the removal of the additional risk minimisation activities (educational materials). In addition, the MAH 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)." Opinion adopted on 13.02.2020. Request for Supplementary Information adopted on 31.10.2019.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1747 Enbrel-EMEA/H/C/000262/WS1747/0231 LIFMIOR-EMEA/H/C/004167/WS1747/ 0025** Pfizer Europe MA EEIG, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of an updated RMP (version 7.0) in line with the latest GVP Module V RMP template (rev. 2) and revision of the list of safety concerns. In addition, the MAH took the opportunity to implement outcomes of previous procedures (type II variation EMEA/H/C/WS/1270 and PSUR EMEA/H/C/PSUSA/001295/201902) to remove	Request for supplementary information adopted with a specific timetable.

or consolidate risks. The MAH is also removing the addendum to RMP version 6.3., making clinical and post-marketing data updates in the RMP and reflecting the completion of post-authorisation studies." Request for Supplementary Information adopted on 13.02.2020.	

B.5.5. 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 Opinion adopted on 27.02.2020, 21.02.2020. Request for Supplementary Information adopted on 08.11.2019.	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Alofisel - darvadstrocel - EMEA/H/C/004258/II/0010/G, Orphan, ATMP Takeda Pharma A/S, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder Opinion adopted on 27.02.2020, 21.02.2020. Request for Supplementary Information adopted on 06.12.2019.	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0036, ATMP Amgen Europe B.V., Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen Request for Supplementary Information adopted on 21.02.2020.	Request for supplementary information adopted with a specific timetable.
Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0037, ATMP Amgen Europe B.V., Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen Opinion adopted on 27.02.2020, 21.02.2020.	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Yescarta - axicabtagene ciloleucel - EMEA/H/C/004480/II/0015, Orphan, ATMP Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus Request for Supplementary Information adopted on 21.02.2020.	Request for supplementary information adopted with a specific timetable.

B.5.6. 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 type II variations (C.I.4) to include: - Long-term efficacy and safety of Kymriah in relapsed/refractory DLBCL based on the 24 months follow-up results from study CCTL019C2201 (update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC) - Interim results from study CCTL019B2202 (update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC) - Interim results from study CCTL019B2205J (update section 5.2 of the SmPC) The Marketing authorisation holder (MAH) took the opportunity to clarify the wording of the indication to include patients over 25 years of age and to introduce some minor editorial corrections throughout the SmPC and the Package Leaflet. The MAH also updated sections 4.2, 4.4, 4.8 of the SmPC, Annex II and the Package Leaflet with regards to the acceptability of having 1 dose of tocilizumab per patient per centre for the management of cytokine release syndrome. In addition, the MAH requested updates to sections 2.2 and 6.5 of the SmPC, the labelling and to the package leaflet to accommodate the administration of additional infusion bags, when applicable. The requested group of variations proposed amendments to the Summary of Product Characteristics, Annex II, Annex IIIA and Package Leaflet and to the Risk Management Plan (RMP). The RMP version 2.1 has been agreed." The CHMP opinion was adopted via written procedure. Request for Supplementary Information adopted on 06.12.2019.	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.7. PRAC assessed ATMP procedures

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

WS1699 **Hexacima-EMEA/H/C/002702/WS1699/0093** **Hexaxim-EMEA/H/W/002495/WS1699/0098** **Hexyon-EMEA/H/C/002796/WS1699/0097** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 27.02.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1729 **Juluca-EMEA/H/C/004427/WS1729/0020** **Tivicay-EMEA/H/C/002753/WS1729/0056** **Triumeq-EMEA/H/C/002754/WS1729/0077** ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson Opinion adopted on 13.02.2020.	Positive Opinion adopted by consensus on 13.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1734 **Riarify-EMEA/H/C/004836/WS1734/0005** **Trimbow-EMEA/H/C/004257/WS1734/0010** **Trydonis-EMEA/H/C/004702/WS1734/0005** Chiesi Farmaceutici S.p.A., Lead Rapporteur: Janet Koenig, "To provide an updated Enviromental Risk Assessment (ERA) report." Opinion adopted on 27.02.2020. Request for Supplementary Information adopted on 12.12.2019.	Positive Opinion adopted by consensus on 27.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1738/G **Dovato-EMEA/H/C/004909/WS1738/0011/G** **Juluca-EMEA/H/C/004427/WS1738/0021/G** **Tivicay-EMEA/H/C/002753/WS1738/0057/G** **Triumeq-EMEA/H/C/002754/WS1738/0078/G** ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson Opinion adopted on 20.02.2020.	Positive Opinion adopted by consensus on 20.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1746 **Biktarvy-EMEA/H/C/004449/WS1746/0026** **Descovy-EMEA/H/C/004094/WS1746/0045** **Genvoya-EMEA/H/C/004042/WS1746/0067** **Odefsey-EMEA/H/C/004156/WS1746/0044** **Vemlidy-EMEA/H/C/004169/WS1746/0022** Gilead Sciences Ireland UC, Lead Rapporteur: Jean-Michel Race Opinion adopted on 06.02.2020.	Positive Opinion adopted by consensus on 06.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1751/G **Keppra-EMEA/H/C/000277/WS1751/0185/G** UCB Pharma S.A., Lead Rapporteur: Koenraad Norga Request for Supplementary Information adopted on 20.02.2020.	Request for supplementary information adopted with a specific timetable.
WS1759/G **Blitzima-EMEA/H/C/004723/WS1759/0030/G** **Ritemvia-EMEA/H/C/004725/WS1759/0030/G** **Truxima-EMEA/H/C/004112/WS1759/0033/G** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz Opinion adopted on 06.02.2020.	Positive Opinion adopted by consensus on 06.02.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Feraccru - ferric maltol - EMEA/H/C/002733/II/0024 Norgine B.V., Rapporteur: Maria Concepcion Prieto Yerro, "To update sections 4.4 and 5.1 of the SmPC in order to update safety and efficacy information based on final results from study ST 10-01-304 this is a phase 3b, randomized, controlled, multicentre study with oral ferric maltol (Feraccru) or intravenous iron (ferric carboxymaltose; FCM), for the treatment of iron deficiency anaemia in subjects with inflammatory bowel disease."	

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

Protopic - tacrolimus - EMEA/H/C/000374/II/0083/G LEO Pharma A/S, Rapporteur: Peter Kiely, PRAC Rapporteur: Rhea Fitzgerald"Update of sections 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC following results from two non-interventional post-authorisation safety studies: JOELLE study (Joint European Longitudinal Lymphoma and skin cancer Evaluation, category 3) and APPLES study (a prospective pediatric longitudinal evaluation to assess the long-term safety of tacrolimus ointment for the treatment of atopic dermatitis, category 3). The Package Leaflet is updated accordingly. The RMP version 15.1. has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1."	Request by the applicant for an extension of the clock stop to respond to the RSI adopted on. The CHMP agreed to the clock stop extension.
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 Request for Supplementary Information adopted on 24.10.2019.	Request for a revised timetable. The CHMP agreed to the revised timetable via written procedure on 27.02.2020.

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

indacaterol / mometasone furoate - EMEA/H/C/005516 treatment of asthma
salmeterol xinafoate / fluticasone propionate - EMEA/H/C/005591 for treatment of asthma List of Questions adopted on 27.02.2020.
estetrol / drospirenone - EMEA/H/C/005336 oral contraceptive
estetrol / drospirenone - EMEA/H/C/005382 oral contraception
bevacizumab - EMEA/H/C/005556

treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer. First-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer. First line treatment of patients with advanced and/or metastatic renal cell cancer.
pitolisant - EMEA/H/C/005117 Treatment of Excessive Daytime Sleepiness (EDS) in patients with Obstructive Sleep Apnoea (OSA)
sodium thiosulfate - EMEA/H/C/005130, PUMA for the prevention of ototoxicity induced by cisplatin (CIS) chemotherapy in patients 1 month to < 18 years of age with localized, non-metastatic, solid tumours.
tirbanibulin mesilate - EMEA/H/C/005183 topical field treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis
sildenafil - EMEA/H/C/005439 treatment of erectile dysfunction

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

Diacomit - stiripentol - EMEA/H/C/000664/X/0032 BIOCODEX, Rapporteur: Alar Irs, PRAC Rapporteur: Maia Uusküla, "Extension application to add a new strength of 100 mg capsules. The RMP (version 2.0) is updated in accordance."
Elebrato Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004781/X/0014/G GlaxoSmithKline Trading Services Limited, Duplicate, Duplicate of Trelegy Ellipta, Rapporteur: Peter Kiely, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Annika Folin, "Extension application to introduce a new strength (184mcg/55mcg/22mcg) grouped with a type II variation (C.I.6.a) to add a new indication (asthma). Whilst the new indication is applicable also to

the existing presentations (EU/1/17/1237/001-3), the new strength is indicated only for the treatment of asthma. The RMP (version 2.2) is updated in accordance.”
Plegridy - peginterferon beta-1a - EMEA/H/C/002827/X/0056 Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ulla Wändel Liminga, “Extension application to introduce a new route of administration (intramuscular use) for the 125 µg solution for injection.”
Temybric Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/005254/X/0004/G GlaxoSmithKline Trading Services Limited, Informed Consent of Trelegy Ellipta, Rapporteur: Peter Kiely, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Annika Folin, “Extension application to introduce a new strength (184mcg/55mcg/22mcg) grouped with a type II variation (C.I.6.a) to add a new indication (asthma). Whilst the new indication is applicable also to the existing presentations (EU/1/19/13781237/001-3), the new strength is indicated only for the treatment of asthma. The RMP (version 2.2) is updated in accordance.”
Trelegy Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004363/X/0012/G GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Annika Folin, “Extension application to introduce a new strength (184mcg/55mcg/22mcg) grouped with a type II variation (C.I.6.a) to add a new indication (asthma). Whilst the new indication is applicable also to the existing presentations (EU/1/17/1236/001-3), the new strength is indicated only for the treatment of asthma. The RMP (version 2.2) is updated in accordance.”

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

bulevirtide - EMEA/H/C/004854, Orphan
MYR GmbH, indicated for the treatment of chronic hepatitis delta virus (HDV) infection in adult patients with compensated liver disease.
List of Questions adopted on 28.01.2020.

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

SCENESSE - afamelanotide - EMEA/H/C/002548/S/0032, Orphan
Clinuvel Europe Limited, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber

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

Cotellic - cobimetinib - EMEA/H/C/003960/R/0019
Roche Registration GmbH, Rapporteur: Filip Josephson, Co-Rapporteur: Koenraad Norga, PRAC Rapporteur: Menno van der Elst

Entresto - sacubitril / valsartan - EMEA/H/C/004062/R/0031
Novartis Europharm Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Anette Kirstine Stark

Hetlioz - tasimelteon - EMEA/H/C/003870/R/0018, Orphan
Vanda Pharmaceuticals Germany GmbH, Rapporteur: Jayne Crowe, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Adam Przybylkowski

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/R/0039, ATMP
Amgen Europe B.V., Rapporteur: Olli Tenhunen, Co-Rapporteur: Rune Kjeken, PRAC Rapporteur: Brigitte Keller-Stanislawski

Kyprolis - carfilzomib - EMEA/H/C/003790/R/0044, Orphan
Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Nikica Mirošević Skvrce

Nucala - mepolizumab - EMEA/H/C/003860/R/0031

GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Brigitte Keller-Stanislawski

Omidria - phenylephrine / ketorolac - EMEA/H/C/003702/R/0015
Omeros Ireland Limited, Rapporteur: Jayne Crowe, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Jan Neuhauser

Pemetrexed medac - pemetrexed - EMEA/H/C/003905/R/0008
medac Gesellschaft fur klinische Spezialpraparate mbH, Generic, Generic of Alimta, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ghania Chamouni

Pemetrexed Sandoz - pemetrexed - EMEA/H/C/004011/R/0008
Sandoz GmbH, Generic, Generic of Alimta, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ghania Chamouni

RAVICTI - glycerol phenylbutyrate - EMEA/H/C/003822/R/0034, Orphan
lmmedica Pharma AB, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Ilaria Baldelli

Votubia - everolimus - EMEA/H/C/002311/R/0065, Orphan
Novartis Europharm Limited, Rapporteur: Janet Koenig, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Martin Huber

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

Dupixent - dupilumab - EMEA/H/C/004390/II/0027
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Kimmo Jaakkola, "Extension of indication to include atopic dermatitis patients from 6 years to 11 years. Consequently, the sections 4.1, 4.2, 4.8, 5.1 and 5.2 are updated. The PL is updated accordingly."

Imbruvica - ibrutinib - EMEA/H/C/003791/II/0059, Orphan
Janssen-Cilag International NV, Rapporteur:

Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "Extension of indication in chronic lymphocytic leukaemia (CLL) to add combination with rituximab as follows: In combination with rituximab or obinutuzumab for the treatment of adult patients with previously untreated CLL.
This extension of the approved CLL indication is based on results from the Phase 3 Eastern Cooperative Oncology Group-American College of Radiology Imaging Network (ECOG ACRIN) Study E1912 (also referred to as PCYC-1126e-CA).
The SmPC is revised to include information related to the new indication. The PL has been revised accordingly. Minor editorial changes have been implemented in Annex II and Annex IIIA. An updated RMP has been submitted."

Nordimet - methotrexate - EMEA/H/C/003983/II/0016

Nordic Group B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Martin Huber, "Extension of indication to include the treatment of mild to moderate Crohn's disease either alone or in combination with corticosteroids in patients refractory or intolerant to thiopurines for Nordimet;
as a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 5.0 has also been submitted. The MAH took the opportunity to update the RMP with changes related to GVP V version 2 template and the outcome of MTX referral."

NovoThirteen - catridecacog - EMEA/H/C/002284/II/0026/G

Novo Nordisk A/S, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Ghania Chamouni, "Extension of indication to include treatment of bleeding episodes in patients with congenital factor XIII A-subunit deficiency as well as minor surgery based on the results of study NN1841-3868 and the PRO-RBDD registry. As a consequence, sections 4.1, 4.2, 4.4, 4.6, 5.1, 5.2 of the SmPC and the RMP version 15 has been submitted. Annex IID and the package leaflet have been updated accordingly. Furthermore, the PI is brought in line with the latest QRD template version. Minor editorial updates have also been made."

Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)
OPDIVO - nivolumab - EMEA/H/C/003985/II/0080 Bristol-Myers Squibb Pharma EEIG, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension of indication to include treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC) after prior fluoropyrimidine- and platinum-based chemotherapy. 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. Version 16.0 of the RMP has also been submitted."
Remsima - infliximab - EMEA/H/C/002576/II/0082 Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, "Extension of indication to add Crohn's disease, ulcerative colitis, ankylosing spondylitis, psoriatic arthritis and psoriasis to the Remsima SC pharmaceutical form to be in line with the IV formulation."
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0022 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sonja Hrabcik, "Extension of indication to include a new population for Shingrix; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated in order to delete a warning and to add new safety and efficacy information. The Package Leaflet is updated in accordance. The RMP version 2.1 has also been submitted."
Spravato - esketamine - EMEA/H/C/004535/II/0001/G Janssen-Cilag International N.V., Rapporteur: Martina Weise, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kirsti Villikka, "C.I.6(a): Extension of indication to include a new indication for Spravato for the rapid reduction of depressive symptoms in adult patients with a moderate to severe depressive

episode of MMD who have current suicidal ideation with intent.
As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 the SmPC are updated. The RMP version 2.1 has also been submitted.
B.II.e.5.a.2: Addition of a new pack size corresponding to 4 weeks of treatment in the new indication.
The Package Leaflet and labelling are updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to clarify the wording in Annex II.D."

WS1769
Iscover-EMEA/H/C/000175/WS1769/0140
Plavix-EMEA/H/C/000174/WS1769/0138
sanofi-aventis groupe, Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Extension of indication to include adult patients with high risk Transient Ischemic Attack (TIA) (ABCD2 score ≥4) or minor Ischemic Stroke (IS) (NIHSS ≤3) within 24 hours of either the TIA or IS event.
The new indication is based on the results of two double-blind, randomised, placebo-controlled phase III trials (studies POINT & CHANCE); as a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated, the PL is updated accordingly. Version 1.0 of the RMP has also been submitted."

WS1782
Lacosamide UCB-EMEA/H/C/005243/WS1782/0006
Vimpat-EMEA/H/C/000863/WS1782/0088
UCB Pharma S.A., Lead Rapporteur: Filip Josephson, Lead Co-Rapporteur: Daniela Melchiorri, Lead PRAC Rapporteur: Ulla Wändel Liminga, "Extension of indication to include the treatment as adjunctive therapy of primary generalised tonic-clonic seizures in adults, adolescents and children from 4 years of age with idiopathic generalised epilepsy for Lacosamide UCB and Vimpat; consequently, 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 15.0 has also been submitted.
Furthermore, the PI is brought in line with the latest QRD template version 10.1. The MAH also takes the opportunity to align the PI of

Lacosamide UCB with the PI of Vimpat and to implement some corrections in BG, CS, DA, FR, DE, HU, PL and ES."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Entyvio - vedolizumab - EMEA/H/C/002782/II/0048
Takeda Pharma A/S, Rapporteur: Daniela Melchiorri

HyQvia - human normal immunoglobulin - EMEA/H/C/002491/II/0055
Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus

Kiovig - human normal immunoglobulin - EMEA/H/C/000628/II/0098
Takeda Manufacturing Austria AG, Rapporteur: Jan Mueller-Berghaus

Mepsevii - vestronidase alfa - EMEA/H/C/004438/II/0013/G, Orphan
Ultragenyx Germany GmbH, Rapporteur: Johann Lodewijk Hillege

Obizur - susoctocog alfa - EMEA/H/C/002792/II/0027
Baxalta Innovations GmbH, Rapporteur: Andrea Laslop

Ogivri - trastuzumab - EMEA/H/C/004916/II/0013
Mylan S.A.S, Rapporteur: Koenraad Norga

Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0007
Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus

Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0010/G
Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus

Orencia - abatacept - EMEA/H/C/000701/II/0137/G
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola

Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0157/G
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Puregon - follitropin beta - EMEA/H/C/000086/II/0106/G
Merck Sharp & Dohme B.V., Rapporteur: Peter Kiely

Ritonavir Mylan - ritonavir - EMEA/H/C/004549/II/0007/G
Mylan S.A.S, Generic, Generic of Norvir, Rapporteur: John Joseph Borg

Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0026
GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren

Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0027/G
GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren

Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0055
MCM Vaccine B.V., Rapporteur: Bart Van der Schueren

Zaltrap - aflibercept - EMEA/H/C/002532/II/0055/G
sanofi-aventis groupe, Rapporteur: Filip Josephson

WS1736/G
Elebrato Ellipta-EMEA/H/C/004781/ WS1736/0015/G
Temybric Ellipta-EMEA/H/C/005254/ WS1736/0003/G
Trelegy Ellipta-EMEA/H/C/004363/ WS1736/0013/G
GlaxoSmithKline Trading Services Limited, Lead Rapporteur: Peter Kiely

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

AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0028
sanofi-aventis groupe, Rapporteur: Martina Weise, "To update section 4.6 of the SmPC with additional information in relation to human experience of use of teriflunomide during

pregnancy, from an analysis of the data recorded in the global safety database and available sources (clinical trial cases, registries and cohort studies, literature and post-marketing pregnancy reports). The MAH also took the opportunity to update sections 2 and 4.4 of the SmPC to align with the updated annex of the guideline excipients with regards to sodium. The Labelling and Package Leaflet are updated accordingly.”	
Bridion - sugammadex - EMEA/H/C/000885/II/0036 Merck Sharp & Dohme B.V., Rapporteur: Outi Mäki-Ikola, “update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC with information on morbidly obese patients (based on study report P146MK8616 - a phase 4 randomized, active-comparator controlled trial to study the efficacy and safety of sugammadex (MK-8616) for the reversal of neuromuscular blockade induced by either rocuronium bromide or vecuronium bromide in morbidly obese subjects) and information related to the excipient sodium in accordance with the revised Annex to the EC guideline on excipients. The Patient Leaflet is updated accordingly. The MAH also took the opportunity to include the changes related to the new EMA QRD template version 10.1 and to implement some editorial changes.”	
Brintellix - vortioxetine - EMEA/H/C/002717/II/0025 H. Lundbeck A/S, Rapporteur: Bart Van der Schueren, “Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC to reflect the outcomes of the paediatric clinical study 12710A (a paediatric efficacy and safety study in adolescent MDD patients) and the study 12708A (paediatric pharmacokinetics and tolerability study in children and adolescent patients with DSM-IV diagnosis of depressive and anxiety disorder). In addition, the MAH took the opportunity to propose minor amendments to the labelling and to update the list of local representatives in the Package Leaflet.”	
Esmya - ulipristal acetate - EMEA/H/C/002041/II/0048	See agenda 9.1

Gedeon Richter Plc., Rapporteur: Kristina Dunder, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information based on a new case of liver transplantation following exposure to Esmya; the Package Leaflet and Labelling are updated accordingly"

Faslodex - fulvestrant - EMEA/H/C/000540/II/0068

AstraZeneca AB, Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information based on the results from study Phase 3 Study A5481023 (PALOMA-3) a randomized controlled study of fulvestrant and palbociclib combination. In addition, the MAH took the opportunity to make a number of editorial changes to the PI to comply with the new QRD template v10.1 and the addition of the respective strength and pharmaceutical form to the corresponding Marketing Authorisation Number."

Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0037/G

MSD Vaccins, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC based on the 2nd interim report from studies V503-002-20 (MEA 005) and V503-021 (MEA 004) listed as a category 3 in the RMP and on final results from study V501-015-21-01 (qHPV); these are effectiveness and immunogenicity long-term follow-up (LTFU) studies from the 9-valent HPV and 4-valent HPV (qHPV) vaccines programs in women 16-26YOA. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.1. In addition, one linguistic comment received from the Czech NCA on the PI during procedure EMEA/H/C/003852/II/033 will be implemented as well."

Gliolan - 5-aminolevulinic acid - EMEA/H/C/000744/II/0018/G

medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Bruno Sepodes, "To update section 4.4 of the SmPC to

add a warning (false positive and false negative fluorescence) following an analysis of the MAHs safety database.
To update section 4.2 of the SmPC to exclude re-administration if surgery is delayed by less than 12 hours."

Herceptin - trastuzumab - EMEA/H/C/000278/II/0160
Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.7 of the SmPC in order to add "dizziness and somnolence" to the recommendations on the effects on the patient's ability to drive and use machines. Update of section 4.8 of the SmPC to remove Herpes zoster, Erysipelas, Cellulitis Common, Sepsis, Thinking abnormal, Ataxia, Paresis, Brain oedema, Pericarditis, Bradycardia and Hepatic failure as adverse drug reactions. An update of the frequencies of adverse reactions is proposed in accordance to a change in the company core datasheet (CDS) for Herceptin: Anaphylactic reaction and Anaphylactic shock is changed to frequency Rare, Wheezing is changed to frequency Uncommon, Pneumonitis is changed to frequency Uncommon and Palpitation is changed to frequency Common. The MAH is taking the opportunity to update section 2 of the Herceptin PL to ensure compliance with the guidance on Excipients in the Labelling and Package Leaflet of medicinal products for Human Use (SANTE 2017-11668). The Package Leaflet is updated accordingly."

Kyprolis - carfilzomib - EMEA/H/C/003790/II/0043, Orphan
Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of section 4.8 of the SmPC in order to include cardiomyopathy as a new adverse drug reaction with uncommon frequency following a signal evaluation triggered by a request from the Therapeutic Goods Administration (TGA) Australian authority. The RMP version 11.0 has also been submitted. In addition, the MAH took the opportunity to make some minor editorial changes to the PI."

Opsumit - macitentan - EMEA/H/C/002697/II/0035/G, Orphan
Janssen-Cilag International N.V., Rapporteur: Maria Concepcion Prieto Yerro, "Update of

section 4.5 of the SmPC in order to update the drug-drug interaction information of macitentan with Breast cancer resistance protein (BCRP) substrate drugs based on final results from studies AC-055-122 and AC-055-123; these are single-center, open-label, one-sequence, two-treatment studies investigating the effect of macitentan at steady state on the pharmacokinetics of rosuvastatin and riociguat respectively in healthy male subjects. In addition, a minor editorial change was introduced in section 5.1."	
Perjeta - pertuzumab - EMEA/H/C/002547/II/0048 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of sections 4.2 and 4.4 of the SmPC in order to add safety information on elderly patients based on a safety review. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor amendments to section 4.7 of the SmPC and to update the PL in accordance with the excipient guideline and in line with the SmPC."	
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0040 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC to include the adverse drug reactions hyperthyroidism and hypertension, identified in study IMvigor130. The package leaflet is proposed to be updated accordingly."	
Xyrem - sodium oxybate - EMEA/H/C/000593/II/0088 UCB Pharma S.A., Rapporteur: Bruno Sepodes, "Update of sections 4.4. and 4.8 of the SmPC in order to update the safety information to add choking sensation; the Package Leaflet is updated accordingly."	
WS1718 **Eviplera-EMEA/H/C/002312/WS1718/0101** **Odefsey-EMEA/H/C/004156/WS1718/0045** Gilead Sciences Ireland UC, Lead Rapporteur: Bruno Sepodes, "Update of section 4.6 of the Eviplera and Odefsey SmPCs in order to reflect rilpivirine data from the Antiretroviral Pregnancy Registry (APR) Interim Report issued in December 2019. The Eviplera Package Leaflet is	

updated in accordance. In addition, the Worksharing applicant (WSA) took the opportunity to bring the PI in line with the latest QRD template version 10.1 and to update the PI in line with the Annex to the European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use' (EMA/CHMP/302620/2017 Rev.1) for both products."

B.6.10. CHMP-PRAC assessed procedures

Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0055

Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Rhea Fitzgerald, "Update of SmPC section 4.8 following results of safety study in children. Additionally, the applicant took the opportunity to update the SmPC in line with the latest version of the QRD template v10.1. The PL is updated accordingly.
In addition, the RMP is updated and version 7,1 is submitted."

Palynziq - pegvaliase - EMEA/H/C/004744/II/0007/G, Orphan

BioMarin International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, "Update of sections 4.4, 4.8 and 5.1 of the SmPC based on final results from studies 1655-003, a long-term extension of a Phase 2, open-label, dose-finding study and 165-302 a Phase 3, randomised, double-blind, placebo-controlled, four-arm, discontinuation study which are listed in the RMP as category 3 studies. The RMP version 2.0 has also been submitted. In addition, the SmPC was amended with minor editorial changes."

Tremfya - guselkumab - EMEA/H/C/004271/II/0020

Janssen-Cilag International N.V., Rapporteur: Melinda Sobor, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.4 and 4.8 to include anaphylactic reactions. Additionally the RMP is updated"

B.6.11. PRAC assessed procedures

PRAC Led **BeneFIX - nonacog alfa - EMEA/H/C/000139/II/0163** Pfizer Europe MA EEIG, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of the RMP to remove LETE (Less than therapeutic effect) as an important identified risk. In addition, in the light of GVP Module V Revision 2,1 the MAH proposes to remove patient populations that were previously identified as Missing information."	
PRAC Led **Ceplene - histamine dihydrochloride - EMEA/H/C/000796/II/0040** Noventia Pharma Srl, Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, "Submission of an updated RMP version 8.1 in order to include the information about the termination of the non-interventional study (NIS) of category 3 Ceplene-3290 and of the PAES Ceplene Cohort Study 3306. -RMP has been adapted to the new RMP template (GVP V rev.2, mandatory since 31 March 2018). -The safety concerns (Part II Modules SVII and SVIII, Part V, Part VI) have been changed. A new important potential risk, named "Drug effect decreased as a consequence of drug interaction", has been added to the list of safety concerns. -Part III and Part IV have been updated to include information about the termination of the non-interventional study (NIS) of category 3 Ceplene-3290 and of the PAES Ceplene Cohort Study 3306. -updated information about the other ongoing studies included in the Pharmacovigilance Plan, "Ceplene-3292" and "Ceplene-3298", have been included in Part III and related parts/modules. -Details about the Marketing Authorization Holder have been updated accordingly upon implementation of transfer from previous Marketing Authorisation Holder, Meda AB, (positive decision received 08 December 2017)"	
PRAC Led **Lemtrada - alemtuzumab -**	

EMEA/H/C/003718/II/0031
Sanofi Belgium, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an update the RMP (version 7.0) incorporating all amendments and additional activities defined in the Article 20 referral procedure (EMEA/H/A-20/1483/C/3718/0028)."

PRAC Led
Siklos - hydroxycarbamide -
EMEA/H/C/000689/II/0045
Addmedica S.A.S., Rapporteur: Koenraad Norga, PRAC Rapporteur: Laurence de Fays, PRAC-CHMP liaison: Bart Van der Schueren, "Update of sections 4.2, 4.3, 4.4, 4.5, 4.6, 4.8 and 4.9 of the SmPC as a consequence of the final study results of the non-interventional cohort study ESCORT-HU (European Sickle Cell Disease Cohort – Hydroxyurea) and harmonisation with other HU products. In addition, Annex II is amended to delete the paragraph about the treatment guide for physicians. The PIL is updated in accordance with the changes to the SmPC. The RMP is updated to reflect the finalisation of the ESCORT-HU study."

PRAC Led
Spectrila - asparaginase -
EMEA/H/C/002661/II/0017
medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Jan Neuhauser, PRAC-CHMP liaison: Andrea Laslop, "Update of the Risk Management Plan (version 12) for Spectrila in accordance with GVP Module V Rev 2 including the implementation of the new RMP template and the new definition of safety concerns. The QPPV and the Milestones / Timelines for the clinical study MC-Spectrila.1/ALL were updated in accordance to the newly applied DLP for this Risk Management Plan."

PRAC Led
Taxotere - docetaxel -
EMEA/H/C/000073/II/0136/G
Sanofi Mature IP, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "C.I.3:

Update of sections 4.4 and 4.8 of the SmPC to add a warning and safety information about tumour lysis syndrome based on a cumulative safety review requested as part of the last PSUR; The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor corrections to the SmPC and update the list of local representatives in the Package Leaflet. C.I.3: Update of section 4.8 of the SmPC to add safety information about myositis based on cumulative safety review requested as part of the last PSUR; the Package Leaflet is updated accordingly."	
PRAC Led **WS1773** **Exelon-EMEA/H/C/000169/WS1773/0128** **Prometax-EMEA/H/C/000255/WS1773/0128** Novartis Europharm Limited, Lead Rapporteur: Alexandre Moreau, Lead PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP v 10.0 to reflect the results of the Drug Utilisation Study CENA713D2409 (submitted and assessed in variation WS-1557, opinion adopted in July 2019) and to reassess all important risks in accordance of GVP revision 2. In addition, as requested by the PRAC following the assessment of the PSUSA/00002654/201901, some safety concerns have been removed."	
PRAC Led **WS1775** **Renagel-EMEA/H/C/000254/WS1775/0114** **Renvela-EMEA/H/C/000993/WS1775/0051** **Sevelamer carbonate Winthrop-EMEA/H/C/ 003971/WS1775/0024** Genzyme Europe BV, Lead Rapporteur: Bart Van der Schueren, Lead PRAC Rapporteur: Laurence de Fays, PRAC-CHMP liaison: Bart Van der Schueren, "Submission of an updated RMP version 10 in order to remove the important potential risk "sevelamer crystals associated with serious gastrointestinal disorders" from the list of safety concerns in the RMP of sevelamer hydrochloride/carbonate products, as agreed by the CHMP during the procedure for the renewal	

of the marketing authorization for Sevelamer Carbonate Winthrop (EMEA/H/C/003971/R/0022).”

B.6.12. CHMP-CAT assessed procedures

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

WS1745 **Biktarvy-EMEA/H/C/004449/WS1745/0028** **Descovy-EMEA/H/C/004094/WS1745/0046** **Vemlidy-EMEA/H/C/004169/WS1745/0025**	Gilead Sciences Ireland UC, Lead Rapporteur: Bruno Sepodes, “To update section 2 of the Product Information Annexes (PIs) of the medicinal products concerned, to align the pregnancy language between the summary of product characteristics (SmPC) and the patient information leaflet (PIL). In addition, the MAH has taken this opportunity to: · Introduce an update to the sodium wording in Section 6 of the PIL for Descovy, Biktarvy and Vemlidy. This update is in line with the excipient guidance. · Implement minor linguistic amendments (MLAs) for Descovy to the below languages: CS, ES, FI, MT, NL, NO, PT, RO, SV”
WS1765 **Halimatoz-EMEA/H/C/004866/WS1765/0018** **Hefiya-EMEA/H/C/004865/WS1765/0018** **Hyrimoz-EMEA/H/C/004320/WS1765/0018**	Sandoz GmbH, Lead Rapporteur: Milena Stain, “To update section 5.1 of the SmPC in line with the reference product to reflect results from the final report from study M11-327: A Multicenter Open-Label Study of the Long-term Safety and Efficacy of the Human Anti-TNF Monoclonal Antibody Adalimumab in Subjects with Non-

infectious Intermediate Uveitis, Posterior Uveitis, or Panuveitis; listed as a category 3 study in the RMP of the reference product. Furthermore editorial changes and a brief description of the study design were added to section 5.1 of the SmPC.”
WS1770/G **Infanrix hexa-EMEA/H/C/000296/** **WS1770/0271/G** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren
WS1789/G **AZILECT-EMEA/H/C/000574/** **WS1789/0086/G** **Rasagiline ratiopharm-EMEA/H/C/** **003957/WS1789/0018/G** Teva B.V., Lead Rapporteur: Bruno Sepodes

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. Timetables – 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. Ongoing procedures

G.3. PRIME

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

G.3.1. List of procedures concluding at 24-27 February 2020 CHMP plenary:

Ophthalmology		
1.	**Adenovirus associated viral vector serotype 5 containing the human RPGR gene** ATMP; Treatment of X linked Retinitis Pigmentosa owing to defects in Retinitis Pigmentosa GTPase Regulator	The CHMP granted eligibility to PRIME and adopted the critical summary report.
Cardiovascular diseases		
2.	Treatment as an adjunct to diet for the secondary prevention of major adverse	The CHMP denied eligibility to PRIME and adopted the critical summary report.

	cardiac events and congestive heart failure in patients with type 2 diabetes mellitus (T2DM), and recent acute coronary syndrome (ACS) in combination with standard of care including high-intensity statins	
Neurology		
3.	Treatment of non-arteritic anterior ischemic optic neuropathy (NAION)	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Endocrinology-Gynaecology-Fertility-Metabolism		
4.	Treatment of polycystic ovary syndrome in non-obese adolescent girls	The CHMP denied eligibility to PRIME and adopted the critical summary report.
5.	Treatment of new-onset type 1 diabetes in patients at risk of imminent loss of the residual β-cell function	The CHMP denied eligibility to PRIME and adopted the critical summary report.

G.3.2. List of procedures starting in February 2020 for March 2020 CHMP adoption of outcomes

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