02 March 2020
EMA/CHMP/71515/2020
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Final Minutes of the meeting on 09-12 December 2019

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced the restricted involvement of some meeting participants in upcoming discussions as included in the pre-meeting list of participants and restrictions. See (current) December 2019 CHMP minutes for the list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session held 9 – 12 December 2019 (to be published post January 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 09-12 December 2019

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 11 – 14 November 2019

The CHMP adopted the minutes via written procedure on 20.12.2019.

CHMP ORGAM Minutes for 02 December 2019

The Minutes of the December 2019 CHMP ORGAM meeting held on 02 December 2019, together with all decisions taken at that meeting, were adopted.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. crisaborole - EMEA/H/C/004863

treatment of mild to moderate atopic dermatitis

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday 11 December 2019 at time 11:00

List of Outstanding Issues adopted on 29.05.2019, 28.02.2019. List of Questions adopted on 20.09.2018.

An oral explanation was held on Wednesday 11 December 2019. The presentation by the company focused on the clinical data supporting their new formulation.

2.1.2. Recarbrio - imipenem / cilastatin / relebactam - EMEA/H/C/004808

Merck Sharp & Dohme B.V.; indicated for the treatment of bacterial infections due to gram-negative microorganisms

Scope: Possible oral explanation/Opinion

Action: Possible oral explanation to be held on Tuesday 10 December 2019 at time 16:00

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

List of Outstanding Issues adopted on 17.10.2019. List of Questions adopted on 28.03.2019.

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

See 3.1

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

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

Merck Sharp & Dohme B.V.

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

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

Oral explanation

Action: Oral explanation to be held on Tuesday 10 December 2019 at 09:00

Request for Supplementary Information adopted on 14.11.2019, 19.09.2019, 29.05.2019.

An oral explanation was held on Tuesday 10 December 2019. The presentation by the company focused on clinical data supporting the extension of indication.

See 5.1

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

Recordati Rare Diseases

Rapporteur: Fátima Ventura

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

Oral explanation

Action: Oral explanation to be held on Wednesday 11 December 2019 at 09:00

List of Outstanding Issues adopted on 19.09.2019. List of Questions adopted on 28.03.2019.

An oral explanation was held on Wednesday 11 December 2019. The presentation by the MAH mainly focused on safety data in relation to the new formulation and post authorisation measures.

See 4.1

2.4. Referral procedure oral explanations

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

MAH various

Rapporteur: Ondrej Slanar, Co-rapporteur: Janet Koenig

Scope: Oral explanation, opinion

Action: Oral explanation to be held on Tuesday 10 December 2019 at 11:00

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

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

An oral explanation was held on Tuesday 10 December 2019. The presentation of the company focused on clinical data supporting the indication prophylaxis in transrectal prostate biopsy.

See 10.6

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. AMSPARITY - adalimumab - EMEA/H/C/004879

Pfizer Europe MA EEIG; treatment of juvenile idiopathic arthritis, paediatric plaque psoriasis, paediatric Crohn's disease, adolescent hidradenitis suppurativa, paediatric uveitis, treatment of rheumatoid arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, hidradenitis suppurativa (HS), crohn's disease, ulcerative colitis, uveitis

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 17.10.2019. List of Questions adopted on 28.03.2019.

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

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

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

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

The summary of opinion was circulated for information.

3.1.2. Azacitidine Accord - azacitidine - EMEA/H/C/005147

Accord Healthcare S.L.U.; Treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML) and acute myeloid leukemia (AML) and AML with >30% marrow blasts according to the WHO classification.

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 14.11.2019, 17.10.2019. List of Questions adopted on 29.05.2019.

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

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

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

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

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report.

3.1.3. BEOVU - brolucizumab - EMEA/H/C/004913

Novartis Europharm Limited; treatment of neovascular (wet) age-related macular degeneration (AMD)

Scope: Opinion

Action: For adoption

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

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

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

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

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

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

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

The summary of opinion was circulated for information.

3.1.4. Dexmedetomidine Accord - dexmedetomidine - EMEA/H/C/005152

Accord Healthcare S.L.U.; light to moderate sedation

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 19.09.2019. List of Questions adopted on 26.04.2019.

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

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

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

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

The summary of opinion was circulated for information.

3.1.5. Recarbrio - imipenem / cilastatin / relebactam - EMEA/H/C/004808

Merck Sharp & Dohme B.V.; indicated for the treatment of bacterial infections due to gram-negative microorganisms

Scope: Possible oral explanation/Opinion

Action: Possible oral explanation to be held on Tuesday 10 December 2019 at time 16:00

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

List of Outstanding Issues adopted on 17.10.2019. List of Questions adopted on 28.03.2019.

See 2.1

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

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

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

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

The CHMP noted the letter of recommendation dated 11 December 2019.

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. arsenic trioxide - EMEA/H/C/005235

treatment of relapsed acute promyelocytic leukaemia (APL)

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.

3.2.2. azacitidine - EMEA/H/C/005075

Treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukaemia (CMML) and acute myeloid leukaemia (AML)

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 17.10.2019. 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 2nd list of outstanding issues with a specific timetable.

3.2.3. azacitidine - EMEA/H/C/004984

treatment of adult patients who are not eligible for haematopoietic stem cell transplantation (HSCT)

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.

3.2.4. cinacalcet - EMEA/H/C/005236

treatment of secondary hyperparathyroidism and hypercalcaemia

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 17.10.2019. 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 2nd list of outstanding issues with a specific timetable.

3.2.5. 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 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.

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

Active immunisation against influenza in the elderly (65 years of age and older) and in children 6 months to less than 6 years of age.

Scope: List of outstanding issues, responses by VWP to questions from CHMP

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.

3.2.7. givosiran - Orphan - EMEA/H/C/004775

Accelerated assessment

Alnylam Netherlands B.V.; Treatment of acute hepatic porphyria (AHP) in adults and adolescents aged 12 years and older.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 15.10.2019.

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.

3.2.8. rituximab - EMEA/H/C/005387

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

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues 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.

3.2.9. rituximab - EMEA/H/C/004807

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

Scope: List of outstanding issues

Action: For adoption

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

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

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

3.2.10. entrectinib - EMEA/H/C/004936

treatment of adult and paediatric patients with neurotrophic tyrosine receptor kinase (NTRK) fusion-positive locally advanced or metastatic solid tumours and treatment of patients with ROS1-positive, advanced non-small cell lung cancer (NSCLC).

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 17.10.2019. 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 2nd list of outstanding issues with a specific timetable.

3.2.11. rituximab - EMEA/H/C/004696

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 13.12.2018.

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

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

3.2.12. semaglutide - EMEA/H/C/004953

treatment of type 2 diabetes mellitus

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 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.

3.2.14. tigecycline - EMEA/H/C/005114

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

Scope: List of outstanding issues

Action: For adoption

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

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

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

3.2.15. treprostinil sodium - Orphan - EMEA/H/C/005207

SciPharm Sarl; treatment of thromboembolic pulmonary hypertension (CTEPH)

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.

3.2.16. 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: 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.

3.2.17. lifitegrast - EMEA/H/C/004653

treatment of moderate to severe dry eye disease in adults for whom prior artificial tears have not been sufficient

Scope: List of outstanding issues

Action: For adoption

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.

3.2.18. ozanimod - EMEA/H/C/004835

Treatment of multiple sclerosis

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.

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

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

Scope: List of outstanding issues

Action: For information

List of Outstanding Issues adopted on 21.06.2019. List of Questions adopted on 22.02.2019.

The CHMP was updated on discussions at the CAT.

The Committee adopted a 2nd 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. arsenic trioxide - EMEA/H/C/005218

treatment of relapsed acute promyelocytic leukaemia (APL)

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. satralizumab - Orphan - EMEA/H/C/004788

Roche Registration GmbH; treatment of adult and adolescent patients from 12 years of age with neuromyelitis optica spectrum disorders (NMOSD)

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

The CHMP adopted the similarity assessment report.

3.3.3. fampridine - EMEA/H/C/005359

treatment of Multiple Sclerosis

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.4. filgotinib - EMEA/H/C/005113

treatment of adult patients with moderately to severely active rheumatoid arthritis

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. rilpivirine - EMEA/H/C/005060

treatment of human immunodeficiency virus type 1 (HIV-1)

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. rivaroxaban - EMEA/H/C/005279

prevention of atherothrombotic events

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. cabotegravir - EMEA/H/C/004976

treatment of human immunodeficiency virus type 1 (HIV-1)

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. dasatinib - EMEA/H/C/005446

treatment of leukaemia

Scope: Letter by the applicant dated 05.12.2019 requesting an extension of the clock stop to respond to the list of questions adopted on 17.10.2019

Action: For adoption

List of Questions adopted on 17.10.2019.

The CHMP agreed to the request by the applicant for an extension of the clock stop to respond to the list of questions adopted on 17.10.2019.

3.4.2. dasatinib - EMEA/H/C/005317

treatment of leukaemia

Scope: Letter by the applicant dated 05.12.2019 requesting an extension of the clock stop to respond to the list of questions adopted on 17.10.2019

Action: For adoption

List of Questions adopted on 17.10.2019.

The CHMP agreed to the request by the applicant for an extension of the clock stop to respond to the list of questions adopted on 17.10.2019.

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

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

Scope: Letter by the applicant dated 5 December 2019 requesting an extension of the clock stop to respond to the list of questions adopted on 19.09.2019

Action: For adoption

List of Questions adopted on 19.09.2019.

The CHMP agreed to the request by the applicant for an extension of the clock stop to respond to the list of questions adopted on 19.09.2019.

3.4.4. teriparatide - EMEA/H/C/005233

treatment of osteoporosis

Scope: letter by the applicant requesting an extension of the clock stop to respond to the list of questions adopted on 25.07.2019

Action: For adoption

List of Questions adopted on 25.07.2019.

The CHMP agreed to the request by the applicant dated 10.12.2019 for an extension of the clock stop to respond to the list of questions adopted on 25.07.2019

3.4.5. bupivacaine - EMEA/H/C/004586

Indicated for prolonged acute pain management and reduction in need for opioids in adults compared to immediate-release bupivacaine.

Scope: letter by the applicant dated 13.11.2019 requesting an extension of the clock stop to respond to the List of Questions adopted on 17.10.2019.

List of Questions adopted on 17.10.2019

The CHMP agreed to an extension of the clock stop to respond to the List of Questions adopted on 17.10.2019.

3.4.6. fenfluramine - Orphan - EMEA/H/C/003933

Zogenix GmbH; treatment of seizures associated with Dravet syndrome in children aged 2 years to 17 years and adults.

Scope: Request by the applicant for an extension of the clock stop to respond to the List of Questions adopted on 27.06.2019.

List of Questions adopted on 27.06.2019.

The CHMP agreed to an extension of the clock stop to respond to the List of Questions adopted on 27.06.2019.

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

No items

3.6. Initial applications in the decision-making phase

3.6.1. Spravato - esketamine - EMEA/H/C/004535

Janssen-Cilag International N.V.; treatment-resistant depression

Scope: Response letters to third parties

Action: For adoption

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

Opinion on 17.10.2019. List of Outstanding Issues adopted on 25.07.2019. List of Questions adopted on 28.02.2019.

The CHMP agreed to the response letters to third parties.

3.7. Withdrawals of initial marketing authorisation application

3.7.1. Idhifa - enasidenib - Orphan - EMEA/H/C/004324

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

Scope: Withdrawal of marketing authorisation application

Action: For information

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

List of Outstanding Issues adopted on 19.09.2019, 26.04.2019. List of Questions adopted on 18.10.2018.

The CHMP noted the withdrawal of the marketing authorisation application.

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

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

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

Helsinn Birex Pharmaceuticals Limited

Rapporteur: Peter Kiely, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Ilaria Baldelli

Scope: "Addition of a new strength for Akynzeo, fixed combination of fosnetupitant (pro-drug of netupitant) and palonosetron, of 235 mg/0.25 mg, associated with a new pharmaceutical form powder for concentrate for solution for infusion and a new route of administration for intravenous use."

Action: For adoption

List of Outstanding Issues adopted on 14.11.2019, 19.09.2019. List of Questions adopted on 28.03.2019.

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

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

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

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

Recordati Rare Diseases

Rapporteur: Fátima Ventura

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

Action: For adoption

List of Outstanding Issues adopted on 19.09.2019. List of Questions adopted on 28.03.2019.

See 2.3

An oral explanation was held on Wednesday 11 December 2019. The presentation by the MAH mainly focused on safety data in relation to the new formulation and post authorisation measures.

The CHMP noted the letter from the MAH notifying about the withdrawal of its extension application.

4.1.3. Dificlir - fidaxomicin - EMEA/H/C/002087/X/0034/G

Astellas Pharma Europe B.V.

Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to introduce a new pharmaceutical form associated with a new strength: 40mg/ml, and a new pharmaceutical form: Granules for oral suspension for the treatment of Clostridioides difficile infections (CDI) also known as C. difficile-associated diarrhoea (CDAD) in adults and paediatric patients from birth to < 18 years of age. C.I.6.a - to extend the indication for the film-coated tablet formulation in paediatric patients with a body weight of at least 12.5 kg. Sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC for film-coated tablets are updated to support the extended indication. The RMP (version 11.0), the labelling and the package leaflet (PL) are updated accordingly. The PL is also being amended to include a statement that Dificlir is essentially 'sodium-free', in accordance with the Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. The details of the local representative of the MAH in the Czech Republic and Malta are also updated."

Action: For adoption

List of Outstanding Issues adopted on 17.10.2019. List of Questions adopted on 29.05.2019.

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

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

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

4.1.4. IBRANCE - palbociclib - EMEA/H/C/003853/X/0018

Pfizer Europe MA EEIG

Rapporteur: Filip Josephson

Scope: "Extension application to introduce a new pharmaceutical form (film-coated tablets) associated with new strengths."

Action: For adoption

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.

4.1.5. Kymriah - tisagenlecleucel - Orphan - ATMP - EMEA/H/C/004090/X/0010

Novartis Europharm Limited

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

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

Action: For adoption

List of Questions adopted on 13.09.2019.

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.

4.1.6. Vyndaqel - tafamidis - Orphan - EMEA/H/C/002294/X/0049/G

Pfizer Europe MA EEIG

Rapporteur: Jean-Michel Race, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension application to:
- introduce a new strength (tafamidis 61 mg soft capsules, pack-size of 30 and 90 capsules) including a new indication "treatment of transthyretin amyloidosis in adult patients with wild-type or hereditary cardiomyopathy to reduce all-cause mortality and cardiovascular-related hospitalisation (ATTR-CM)"
- introduce qualitative change in declared active substance (tafamidis) not defined as a new active substance;
grouped with a type II variation (C.I.4) to update section 4.6 of the Vyndaqel (tafamidis meglumine) 20 mg soft capsules SmPC to add wording pertaining to the Tafamidis Enhanced Surveillance for Pregnancy Outcomes (TESPO) programme.
Submission of an updated RMP version 9.0 in order to include the proposed new dosage/indication, review of the additional data collected from the ATTR-CM clinical program and post marketing reporting, reclassification of the safety concerns, remove of HCP educational leaflet.
Relevant changes are proposed for Annex II.
In addition, the MAH is proposing an update to Section 16 Information in Braille of Annex IIIa - Labelling (carton) to differentiate between the dosage forms."

Action: For adoption

List of Outstanding Issues adopted on 17.10.2019. List of Questions adopted on 29.05.2019.

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

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

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

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. 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 Questions adopted on 25.07.2019.

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

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. Darzalex - daratumumab - Orphan - EMEA/H/C/004077/X/0032

Janssen-Cilag International NV

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

Scope: "Extension application to introduce a new pharmaceutical form (solution for injection), a new strength (1800 mg) and a new route of administration (subcutaneous route). The RMP version 7.0 was updated in accordance."

Action: For adoption

The Committee discussed the issues identified in this application, mainly concerning the pharmacokinetics in relation to body weight of the different subgroups and in this context the appropriate posology.

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

4.3.2. Jorveza - budesonide - Orphan - EMEA/H/C/004655/X/0007/G

Dr. Falk Pharma GmbH

Rapporteur: Martina Weise, Co-Rapporteur: Tomas Radimersky, PRAC Rapporteur: Zane Neikena

Scope: "Extension application to add a new strength of 0.5 mg for budesonide orodispersible tablets, grouped with:
- A type II variation (C.I.6) - Extension of indication to include the maintenance of remission for Jorveza (0.5 mg and 1 mg orodispersible tablets); as a consequence, sections 4.2, 4.8 and 5.1 of the SmPC are updated to reflect the recommended daily dose and duration of treatment of Jorveza for the maintenance of remission, to update the list of adverse reactions and the clinical efficacy and safety information based on the results of the phase III clinical study BUL-2/EER. The relevant sections of the PL are updated accordingly. In addition, a revised RMP (version 2.0) has been submitted to reflect the results of this study and to align with the GVP Module V (rev 2) template. The MAH also took the opportunity to bring the product information in line with the latest QRD template (version 10.1).
- A type IB variation (B.II.e.5.a.2) – To add a new pack-size of 200 x 1 orodispersible tablets (unit dose) in a blister for Jorveza 1 mg orodispersible tablet (EU/1/17/1254/006)"

Action: For adoption

The Committee discussed the issues identified in this application, which related to some quality and clinical aspects.

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. Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0039/G

Biofrontera Bioscience GmbH

Rapporteur: Janet Koenig, Co-Rapporteur: Peter Kiely

Scope: "C.I.6.a - To modify the approved therapeutic indication to include the treatment of mild to severe actinic keratosis on extremities, trunk and neck. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC and sections 1 and 4 of the PL are updated accordingly.
C.I.4 - To update section 5.1 of the SmPC based on follow-up data from study ALA-AK-CT009; this is a randomized, observer-blind, intra-individual phase III study to evaluate the

safety and efficacy of Ameluz in combination with daylight PDT (photodynamic therapy) in comparison with Metvix for the treatment of mild to moderate actinic keratosis."

Action: For adoption

The Committee discussed the issues identified in this application, mainly relating to the wording of the indication and posology.

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

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

Novartis Europharm Limited

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

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

Action: For adoption

The Committee discussed the issues identified in this application, mainly relating to the wording of the indication and the appropriate patient population.

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

5.1.3. Cyramza - ramucirumab - EMEA/H/C/002829/II/0033

Eli Lilly Nederland B.V.

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Kolbeinn Gudmundsson (IS) (MNAT with FI for Quality, FI for Non-Clinical, LT for Clinical Pharmacology), PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication for Cyramza, to include in combination with erlotinib, the first-line treatment of adult patients with metastatic non-small cell lung cancer with activating epidermal growth factor receptor (EGFR) mutations.
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 accordingly.
The RMP version 9 has also been submitted."

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.

5.1.4. Darzalex - daratumumab - Orphan - EMEA/H/C/004077/II/0030

Janssen-Cilag International NV

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of indication in combination with bortezomib, thalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant (ASCT) for Darzalex; as a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP (version 6.4) has also been agreed."

Action: For adoption

Request for Supplementary Information adopted on 17.10.2019, 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 recommendation dated 10 December 2019.

The summary of opinion was circulated for information.

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

Janssen-Cilag International N.V.

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

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

Action: For adoption

Request for Supplementary Information adopted on 19.09.2019.

The Committee discussed the issues identified in this application. The members noted that the MAH withdrew the request for 1 year of market protection for a new indication.

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.

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

Eisai GmbH

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

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

Action: For adoption

The Committee discussed the issues identified in this application, mainly relating to the appropriate patient population and in particular the paediatric age groups and the related posology as well as long-term safety.

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

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

Merck Sharp & Dohme B.V.

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

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

Action: For adoption

Request for Supplementary Information adopted on 14.11.2019, 19.09.2019, 29.05.2019.

See 2.3

An oral explanation was held on Tuesday 10 December 2019. The presentation by the company focused on clinical data supporting the extension of indication.

The CHMP noted the withdrawal letter from the MAH notifying about the withdrawal of its Type II variation application.

5.1.8. MabThera - rituximab - EMEA/H/C/000165/II/0162

Roche Registration GmbH

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

Scope: "Extension of indication to include the treatment of paediatric patients (aged ≥ 2 to <18 years old) with active polyangiitis (Wegener's) (GPA) and microscopic polyangiitis (MPA), for MA numbers EU/1/98/067/001-002 for MabThera; following efficacy and safety data from Clinical study report (CSR) WA25615 (also known as Paediatric Polyangiitis and Rituximab Study [PePRS]) which was conducted to fulfil the measure of the Paediatric Investigational Plan (PIP: EMEA-000308-PIP02-11-M01) agreed upon in the context of rituximab development for treatment of adult patients with GPA and MPA (RAVE study). The CSR for Study 1: WA 25615 was submitted on 30th Oct 2018 as the Post Approval Measure submission according to Article 46 requirement. Linked to this variation the final compliance check procedure to close the PIP has started 3rd January 2019.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and sections 2, 3 and 4 of the Package Leaflet are updated accordingly. Furthermore, the PI is brought in line with the latest QRD template (version 10) and the opportunity is taken to combine the SmPC and PIL for 100 mg and 500 mg IV as they are identical except for strength specifications.
In addition, the applicant took the opportunity to implement minor editorial changes in the SmPC. The RMP version 20.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 17.10.2019, 29.05.2019.

The Committee discussed the issues identified in this application, mainly relating to a post authorisation safety study to further investigate the long-term safety in the maintenance setting.

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

5.1.9. OFEV - nintedanib - Orphan - EMEA/H/C/003821/II/0027

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 other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype based on the results of pharmacology studies and the double-blind, randomised, placebo-controlled phase III trial (INBUILD). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to reflect the use of Ofev in the new indication. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to introduce minor formatting changes in the PI. Furthermore, the PI is brought in line with the latest QRD template version 10.1. The RMP version 9.0 has also been submitted." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

List of questions to an ad-hoc expert group. See also OFEV II/26.

Call for nomination of experts to the ad-hoc expert group.

Action: For adoption

The Committee discussed the issues identified in this application, mainly relating to the appropriate patient population in relation to the study population.

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

The CHMP adopted the list of questions to the ad-hoc expert group.

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

Janssen-Cilag International NV

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

Scope: "Grouping of an extension of indication to include patients 12 years of age and older and weighing more than 30 kg for SIRTURO and a Type II variation to change an existing recommendation about the management of a bedaquiline overdose in section 4.9 of the SIRTURO SmPC. The extension of indication is supported by the Week 24 analysis of Cohort 1 (adolescent subjects aged ≥12 to <18 years) of Study TMC207-C211. Based on these data, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are also updated. The Package Leaflet is updated in accordance. An updated version of the RMP was included in the submission."

Action: For adoption

Request for Supplementary Information adopted on 17.10.2019, 19.09.2019, 29.05.2019, 31.01.2019.

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.

5.1.11. Stelara - ustekinumab - EMEA/H/C/000958/II/0073

Janssen-Cilag International NV

Rapporteur: Jayne Crowe, Co-Rapporteur: Mark Ainsworth, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Extension of indication to include the treatment of children aged 6 to 12 years with moderate to severe psoriasis for Stelara solution for injection; as a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Section 4.8 for Stelara concentrate for solution for infusion is updated accordingly. Minor editorial changes are made to section 4.5 for both formulations.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 16.1 has also been submitted."

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.

5.1.12. Taltz - ixekizumab - EMEA/H/C/003943/II/0030

Eli Lilly Nederland B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include treatment of adult patients with active axial spondyloarthritis; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC and relevant sections of the PL are updated. The PI was also brought in line with the latest QRD template version 10.1. In addition, an updated RMP version 6.1 has also been submitted." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

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

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

5.1.13. Votubia - everolimus - Orphan - EMEA/H/C/002311/II/0061

Novartis Europharm Limited

Rapporteur: Janet Koenig

Scope: "To modify the approved therapeutic indication (adjunctive treatment of patients aged 2 years and older whose refractory partial-onset seizures, with or without secondary generalisation, are associated with tuberous sclerosis complex, TSC) to include the new population of patients from 6 months to less than 2 years of age.
As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC and sections 1 and 2 of the PL are updated accordingly. Furthermore, the PI is brought in line with the latest QRD template version 10.1."

Action: For adoption

The Committee discussed the issues identified in this application, mainly concerning the posology and the exposure-response relationship in the new paediatric population.

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

5.1.14. 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 than 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."

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019, 15.11.2018.

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

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

5.1.15. Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0048

Pfizer Ireland Pharmaceuticals

Rapporteur: Alar Irs

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

Action: For adoption

The Committee discussed the issues identified in this application, mainly relating to the clinical data and the wording of the indication.

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. 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."

Request by the applicant for an extension of clock stop to respond to the RSI adopted on 19.09.2019.

Action: For adoption

Request for Supplementary Information adopted on 19.09.2019, 28.03.2019, 18.10.2018.

The CHMP **did not agree** to the request by the applicant for an extension of clock stop to respond to the RSI adopted on 19.09.2019.

5.2.2. 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)

List of questions to an ad-hoc expert group. See also OFEV II/27.

Call for nomination of experts to the ad-hoc expert group.

Action: For adoption

Request for Supplementary Information adopted on 14.11.2019, 27.06.2019.

The CHMP adopted the list of questions to the ad-hoc expert group.

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

Celgene Europe BV

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 and sections 1, 2 and 4 of the PL are updated accordingly. The updated RMP version 12.0 has also been submitted." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Change in timetable.

Request for Supplementary Information adopted on 17.10.2019.

The CHMP adopted the amended timetable.

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. Autologous T cells transduced with retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor - ATMP - H0005102

Treatment of adult patients with relapsed or refractory mantle cell lymphoma

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. selpercatinib - Orphan - H0005375

Eli Lilly Nederland B.V.; RET-mutant medullary thyroid cancer (MTC), advanced RET fusion-positive non-small cell lung cancer (NSCLC), advanced RET fusion-positive thyroid cancer

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. selumetinib - H0005244

treatment of paediatric patients aged 3 years and above, with symptomatic and/or progressive neurofibromatosis type 1 (NF1) inoperable plexiform neurofibromas (PN)

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

Action: For adoption

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

8.2. Priority Medicines (PRIME)

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

8.2.1. List of applications received

Action: For information

The CHMP noted the list of applications received.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 6 recommendations for eligibility to PRIME: 2 were 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. Xiapex – collagenase clostridium histolyticum – EMEA/H/C/002048

Swedish Orphan Biovitrum AB (publ); treatment of Dupuytren's contracture/ Peyronie's disease in adult patients

Rapporteur: Janet Koenig, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Martin Huber

Scope: Notification by the MAH about the withdrawal of the marketing authorisation.

Action: For information

The CHMP noted the withdrawal of marketing authorisation.

9.1.2. Fortacin - lidocaine / prilocaine - EMEA/H/C/002693/II/0030

Recordati Ireland Ltd

Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon

Scope: "Change in the legal status of Fortacin from 'medicinal product subject to medical prescription' to 'medicinal product not subject to medical prescription' in view of the safety profile of Fortacin, the post-marketing experience already available with other medicinal products containing amide local anaesthetics and in view of making the product more accessible to the target population. Furthermore, the PI is being brought in line with the latest QRD template (version 10.1). The RMP version 3.1 has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application, mainly relating to some clinical aspects and the RMP.

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

9.1.3. Kromeya – Adalimumab – EMEA/H/C/005158

Fresenius Kabi Deutschland GmbH

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Romaldas Maciulaitis, PRAC Rapporteur: Ulla Wändel Liminga

Scope: Notification by the MAH about the withdrawal of the marketing authorisation.

Action: For information

The CHMP noted the withdrawal of marketing authorisation.

9.1.4. 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.

Scope: Request to consult the SAG-HIV/viral diseases

Action: For adoption

The Committee discussed the issues identified in this application, regarding a possible increased risk of NTD with peri-conceptional exposure to dolutegravir.

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

The CHMP agreed to consult the SAG-HIV/viral diseases and adopted a list of questions to this group.

The CHMP agreed to consult the PRAC. The list of questions to PRAC will be adopted at a later time.

9.1.5. 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"

Action: For adoption

Request for Supplementary Information adopted on 17.10.2019.

The Committee discussed the issues identified in this application, mainly concerning the wording of section 5.1 of the SmPC.

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

9.1.6. PD1/PD-L1 targeting agents

Scope: LEG procedure

Action: For adoption

The CHMP agreed to consult the Biostatistics Working Party and adopted a list of questions to this group.

9.1.7. Infanrix hexa – diphtheria (d), tetanus (t), pertussis (acellular, component) (pa), hepatitis b (rdna) (hbv), poliomyelitis (inactivated) (ipv) and haemophilus influenzae type b (hib) conjugate vaccine (adsorbed) - PAM – EMEA/H/C/000296

GlaxoSmithkline Biologicals SA

Rapporteur: Bart van der Schueren, Co-Rapporteur: Jan Mueller-Berghaus

Scope: VWP response to questions from CHMP

Action: For adoption

The CHMP adopted the VWP response.

9.1.8. 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

Scope: "Submission of a group of 3 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 Annex II and the Package Leaflet are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to clarify the wording of the indication to include patients over 25 years of age and to introduce some minor editorial corrections throughout the SmPC and the Package Leaflet. The RMP version 2.0 has also been submitted."

Action: For adoption

The CHMP was updated on discussions at the CAT.

The Committee agreed to the request for supplementary information with a specific timetable as adopted by the CAT.

10. Referral procedures

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

No items

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

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

MAHs: various

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

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

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

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

Action: For adoption

The CHMP adopted a list of questions to the MAHs.

The CHMP adopted lists of questions to the BWP, SWP and QWP.

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

The CHMP adopted the procedural timetable.

Adoption of LoQs to WPs: December CHMP (9-12 December 2019)

BWP meeting: 20-23 January 2020

SWP meeting: 27 January 2020 (tbc, usually Monday of CHMP)

QWP meeting: 4-6 February 2020

Ad-hoc expert meeting: 28 February 2020

Ad-hoc expert meeting minutes: 13 March 2020

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

No items

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

No items

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

No items

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

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

MAH various

Rapporteur: Ondrej Slanar, Co-Rapporteur: Janet Koenig

Scope: Oral Explanation, opinion

Action: Oral explanation to be held on Tuesday 10 December 2019 at 11:00

Need to re-evaluate the benefit-risk ratio of the approved indications considering the

current scientific knowledge. Furthermore, the appropriate dose and duration of administration for both oral and intravenous formulations need to be discussed as well as the adequacy of safety relevant information and information about pharmacological properties.

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

See 2.4

An oral explanation was held on Tuesday 10 December 2019. The presentation of the company focused on clinical data supporting the indication prophylaxis in transrectal prostate biopsy.

The CHMP adopted a 4th list of outstanding issues with a specific timetable.

Submission of responses: 06 February 2020

Re-start of the procedure: 27 February 2020

Joint Assessment report circulated to CHMP: 06 March 2020

Comments: 13 March 2020

Updated joint assessment report circulated to CHMP: 19 March 2020

CHMP opinion: March 2020 CHMP

10.6.2. Methocarbamol/Paracetamol– EMEA/H/A-31/1484

FAES FARMA, S.A., DiaMed Beratungsgesellschaft fuer pharmazeutische Unternehmen mbH

Rapporteur: Romaldas Maciulaitis, Co-Rapporteur: Jorge Camarero Jimenez

Scope: 2nd List of Outstanding Issues

Action: For adoption

Review of the benefit-risk balance following notification by BfArM in Germany on 27 May 2019 of a referral under Article 31 of Directive 2001/83/EC.

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

Submission of responses: 06 February 2020

Re-start of the procedure: 27 February 2020

Rapporteurs' joint assessment report circulated to CHMP: 03 March 2020

Comments: 10 March 2020

Updated Rapporteurs' joint assessment report circulated to CHMP: 16 March 2020

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

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

MAH various

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

Action: For adoption

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.

The CHMP adopted a list of outstanding issues to MAHs with a specific timetable.

Submission of responses: 09 January 2020

Re-start of the procedure: 30 January 2020

Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 07 February 2020

Comments: 14 February 2020

Updated Rapporteur/co-rapporteur joint assessment report circulated to CHMP: 20 February 2020

CHMP list of outstanding issues/opinion: February 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

December 2019 Early Notification System on envisaged CHMP/CMDh outcome accompanied

by communication to the general public.

Action: For information

The CHMP noted the document.

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

14.1.1. Seating plan for CHMP under Croatian Presidency of the Council of the European Union, 1 January – 30 June 2020

CHMP Seating Plan, 1 January – 30 June 2020, under Croatian EU presidency

Action: For information

The CHMP noted the new seating plan.

14.1.2. CHMP Workplan 2020

Action: For discussion

The CHMP discussed the proposed topics on the work plan.

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 25-28 November 2019

Action: For information

The CHMP noted the Summary of recommendations and advice.

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for December 2019

Action: For adoption

The CHMP adopted the EURD list.

CHMP-PRAC cooperation group

Call for volunteers

Action: For information

Three members from the CHMP volunteered to participate in this group.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 04-06 December 2019

Action: For information

The CHMP noted the draft minutes.

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 18-19 November 2019

Action: For information

The CHMP noted the report.

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at December 2019 PDCO

Action: For information

The CHMP noted the information.

Report from the PDCO meeting held on 09-11 December 2019

Action: For information

The CHMP noted the report.

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 03-05 December 2019

Action: For information

The CHMP noted the report.

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

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 09-11 December 2019

Action: For information

The CHMP noted the report.

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

14.3.1. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 25-28 November 2019. Table of conclusions

Action: For information

The CHMP noted the report.

Scientific advice letters:

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

14.3.2. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP December 2019 meeting to CHMP for adoption:

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

Action: For adoption

The CHMP adopted the BWP reports.

Questions from CMDh to BWP on DCP application for medicinal product

Action: For adoption

The CHMP agreed to the consultation of the BWP.

14.3.3. Antimicrobial Advice Ad Hoc Expert Group (AMEG)

Scope: Scientific advice on the AMEG categorisation of antimicrobials in the European Union; overview of comments

Background information: request from the EC for the update of the AMEG advice on the impact on public health and animal health of the use of antibiotics in animals (link); further extension for the deadline to submit the advice

Action: For adoption

The CHMP adopted the scientific advice by majority (28 positive out of 32 votes).

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

The divergent position (Sinan B Sarac, Alar Irs, Daniela Melchiorri, Melinda Sobor, Kolbeinn Gudmundsson) was appended to the opinion.

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

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

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

Action: For information

The CHMP noted the report.

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. EMA relocation – move to the new building

Action: For information

The CHMP was updated on procedural aspects in relation to the move to the new building in Amsterdam.

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 December 2019 CHMP meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Harald Enzmann	Chair	Germany	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Milena Stain	Alternate	Austria	No interests declared	
Bart Van der Schueren	Member	Belgium	No interests declared	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Margareta Bego	Member	Croatia	No interests declared	
Loizos Panayi	Member	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Tomas Radimersky	Alternate	Czech Republic	No interests declared	
Sinan B. Sarac	Member	Denmark	No interests declared	
Mark Ainsworth	Alternate	Denmark	No interests declared	
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	
Eleftheria Nikolaidi	Alternate	Greece	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Melinda Sobor	Member	Hungary	No restrictions applicable to this meeting	
Agnes Gyurasics	Alternate	Hungary	No interests declared	
Kolbeinn Gudmundsson	Member	Iceland	No interests declared	
Jayne Crowe	Member	Ireland	No interests declared	
Peter Kiely	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No restrictions applicable to this meeting	
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	
Bruno Sepodes	Member (Vice-Chair)	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meeting	
Simona Badoi	Member	Romania	No interests declared	
Francisek Drafi	Member	Slovakia	No interests declared	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Maria Concepcion Prieto Yerro	Member	Spain	No interests declared	
Jorge Camarero Jiménez	Alternate	Spain	No participation in final deliberations and voting on:	EMEA/H/C/004936 EMEA/H/C/004788 MabThera - EMEA/H/C/000165/II/0162
Kristina Dunder	Member	Sweden	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Filip Josephson	Alternate	Sweden	No interests declared	
Nithyanandan Nagercoil	Member	United Kingdom	No restrictions applicable to this meeting	
Christian Gartner	Co-opted member	Austria	No restrictions applicable to this meeting	
Koenraad Norga	Co-opted member	Belgium	No participation in final deliberations and voting on:	WS1683 Infanrix hexa - EMEA/H/C/000296
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	
Andreas Brønden	Expert in person*	Denmark	No part in discussions, final deliberations and voting as appropriate as regards:	H0005244
Anne Hasle Buur	Expert in person*	Denmark	No interests declared	
Andre Elferink	Expert in person*	Netherlands	No interests declared	
Erik Hergarden	Expert in person*	Netherlands	No interests declared	
Ingrid Schellens	Expert in person*	Netherlands	No interests declared	
Leon van Aerts	Expert in person*	Netherlands	No interests declared	
Nienke Rodenhuis	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	
Agustin Portela	Expert in person*	Spain	No interests declared	
Alicia Perez	Expert in person*	Spain	No interests declared	
Isabella Berger	Expert in person*	Spain	No interests declared	
Minne Casteels	Expert - via telephone*	Belgium	No restrictions applicable to this meeting	
Livia Puljak	Expert via telephone*	Croatia	No interests declared	
Benedicte Hay	Expert via telephone*	France	No interests declared	
Lamisse Bouti	Expert via telephone*	France	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Olivier Le Blaye	Expert - via telephone*	France	No restrictions applicable to this meeting	
Anna Cunney	Expert via telephone*	Ireland	No interests declared	
Finbarr Leacy	Expert via telephone*	Ireland	No interests declared	
Benita Cullen	Expert via telephone*	Ireland	No interests declared	
Danila Renzo	Expert - via telephone*	Italy	No interests declared	
Valeria Zoccano	Expert - via telephone*	Italy	No interests declared	
Henrica (Ria) Nibbeling	Expert - via telephone*	Netherlands	No interests declared	
Janneke van Leeuwen	Expert - via telephone*	Netherlands	No interests declared	
Johannes Hendrikus Ovelgonne	Expert - via telephone*	Netherlands	No interests declared	
Johannes Petrus Theodorus Span	Expert - via telephone*	Netherlands	No interests declared	
Lieke Sandberg Smits	Expert - via telephone*	Netherlands	No interests declared	
Viktoriia Starokozhko	Expert - via telephone*	Netherlands	No restrictions applicable to this meeting	
Helen Jukes	Expert - via telephone*	United Kingdom	No interests declared	
Linda Trauffler	Expert - via Adobe*	Austria	No interests declared	
Antero Kallio	Expert - via Adobe*	Finland	No restrictions applicable to this meeting	
Vincent Gazin	Expert - in person*	France	No interests declared	
Andrea Dercks-Müller	Expert - via Adobe*	Germany	No interests declared	
Andreas Wilhelm Grummel	Expert - via Adobe*	Germany	No interests declared	
Christine Greiner	Expert - via Adobe*	Germany	No interests declared	
Ellen Pantke	Expert - via Adobe*	Germany	No restrictions applicable to this meeting	
Elmer Schabel	Expert - via Adobe*	Germany	No interests declared	
Marion Haberkamp	Expert - via Adobe*	Germany	No interests declared	
Sylvia Kuehn	Expert - via Adobe*	Germany	No restrictions applicable to this meeting	
Consuelo Mejias Pavon	Expert - via Adobe*	Spain	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Macarena Rodriguez Mendizabal	Expert - via Adobe*	Spain	No interests declared	
Maria del Pilar Rayon	Expert - via Adobe*	Spain	No interests declared	
Tania Lopez Garrido	Expert - via Adobe*	Spain	No interests declared	
Kristian Wennmalm	Expert - via Adobe*	Sweden	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)*

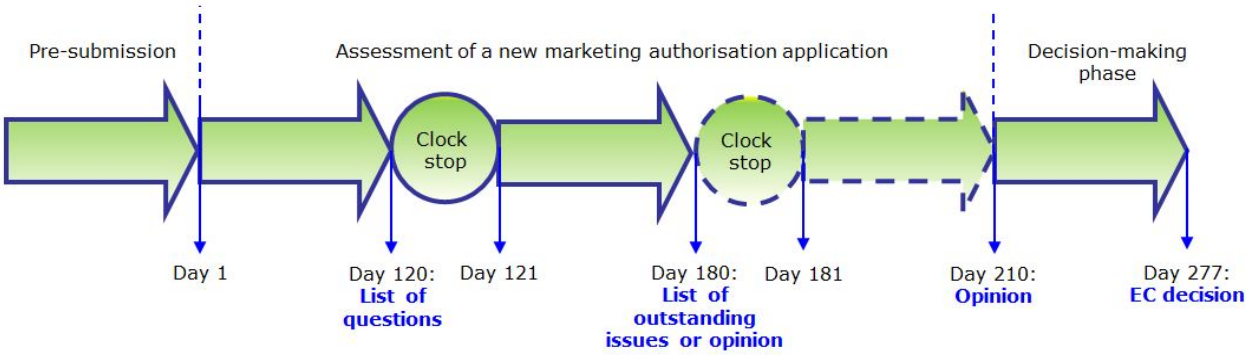
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

02 March 2020
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Annex to 09-12 December 2019 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 December 2019: **For adoption**	Adopted.

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

Final Outcome of Rapporteurship allocation for December 2019: **For adoption**	Adopted.

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

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

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

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

Brineura - cerliponase alfa - EMEA/H/C/004065/S/0018, Orphan BioMarin International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga 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.
Ceplene - histamine dihydrochloride - EMEA/H/C/000796/S/0039 Noventia Pharma Srl, Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald	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.
Strensiq - asfotase alfa - EMEA/H/C/003794/S/0041, Orphan Alexion Europe SAS, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Rhea Fitzgerald	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

Quinsair - levofloxacin - EMEA/H/C/002789/R/0022 Chiesi Farmaceutici S.p.A., Rapporteur: Ondřej Slanař, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maria del Pilar Rayon Request for Supplementary Information adopted on 17.10.2019.	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 an additional five-year renewal was required. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Aripiprazole Mylan Pharma - aripiprazole - EMEA/H/C/003803/R/0013 Mylan S.A.S, Generic, Generic of Abilify, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ana Sofia Diniz Martins	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.
Duloxetine Mylan - duloxetine - EMEA/H/C/003981/R/0021 Mylan S.A.S, Generic, Generic of Cymbalta, Rapporteur: John Joseph Borg, PRAC Rapporteur: Maria del Pilar Rayon	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.
EVOTAZ - atazanavir / cobicistat - EMEA/H/C/003904/R/0031 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Adrien Inoubli Request for supplementary information adopted on 12.12.2019.	Request for supplementary information adopted with a specific timetable.
Keytruda - pembrolizumab - EMEA/H/C/003820/R/0081 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-	Request for supplementary information adopted with a specific timetable.

Berghaus, PRAC Rapporteur: Menno van der Elst Request for supplementary information adopted on 12.12.2019.	
Lenvima - lenvatinib - EMEA/H/C/003727/R/0031 Eisai GmbH, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin Request for supplementary information adopted on 12.12.2019.	Request for supplementary information adopted with a specific timetable.
Lixiana - edoxaban - EMEA/H/C/002629/R/0023 Daiichi Sankyo Europe GmbH, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Adrien Inoubli	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.	Request for supplementary information adopted with a specific timetable.
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.	Request for supplementary adopted with a specific timetable.
Pregabalin Mylan - pregabalin - EMEA/H/C/004078/R/0014 Mylan S.A.S, Generic, Duplicate, Generic of Lyrica, Duplicate of Pregabalin Mylan Pharma, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Liana Gross-Martirosyan Request for supplementary information adopted on 12.12.2019.	Request for supplementary information adopted with a specific timetable.
Pregabalin Mylan Pharma - pregabalin - EMEA/H/C/003962/R/0012 Mylan S.A.S, Generic, Generic of Lyrica, Rapporteur: Alexandre Moreau, PRAC	Request for supplementary information adopted with a specific timetable.

Rapporteur: Liana Gross-Martirosyan Request for supplementary information adopted on 12.12.2019.	
Voriconazole Hikma - voriconazole - EMEA/H/C/003737/R/0010 Hikma Farmaceutica (Portugal), S.A., Generic, Generic of Vfend, Rapporteur: Natalja Karpova, PRAC Rapporteur: Liana Gross-Martirosyan Request for supplementary information adopted on 12.12.2019.	Request for supplementary information adopted with a specific timetable.

B.2.3. Renewals of Conditional Marketing Authorisations

Bosulif - bosutinib - EMEA/H/C/002373/R/0039 Pfizer Europe MA EEIG, Rapporteur: Janet Koenig, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Martin Huber	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Cometriq - cabozantinib - EMEA/H/C/002640/R/0032, Orphan Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Menno van der Elst Request for supplementary information adopted on 14.11.2019.	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.
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.	Request for supplementary information adopted with a specific timetable.

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its December 2019 meeting:	
EMEA/H/C/PSUSA/00000226/201905 (apixaban) CAPS: **Eliquis** (EMEA/H/C/002148) (apixaban), Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Period Covered From: 18/05/2018 To:17/05/2019"	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 4.5 of the SmPC to add fluconazole to the list of inhibitors, which are not considered strong inhibitors of both CYP3A4 and P-gp. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00002491/201904 (pramipexole) CAPS: **Mirapexin** (EMEA/H/C/000134) (pramipexole), Boehringer Ingelheim International GmbH, Rapporteur: Mark Ainsworth **Sifrol** (EMEA/H/C/000133) (pramipexole), Boehringer Ingelheim International GmbH, Rapporteur: Mark Ainsworth NAPS: **Calmolan** - G.L. PHARMA GMBH PRAC Rapporteur: Anette Kirstine Stark, "From: 06/04/2016 To: 06/04/2019"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the medicinal products containing the above referred active substance(s), concerning the following change(s): Updates of section 4.4 of the SmPC to add a warning on risk factors of DAWS and section 4.2 to add a warning on DAWS when discontinuing or tapering pramipexole. Update of section 3 of the Package leaflet to add information on the risk and symptoms of DAWS when discontinuing or tapering pramipexole. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010540/201903 (olanzapine) CAPS: **Olazax Disperzi** (EMEA/H/C/001088) (olanzapine), Glenmark Pharmaceuticals s.r.o., Rapporteur: Alexandre Moreau **Zalasta** (EMEA/H/C/000792) (olanzapine), KRKA, d.d., Novo mesto, Rapporteur: Nevenka Trsinar Brodt	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the medicinal products containing the above referred active substance(s), concerning the following

Zypadhera (EMEA/H/C/000890) (olanzapine), Eli Lilly Nederland B.V., Rapporteur: Outi Mäki-Ikola **Zyprexa** (EMEA/H/C/000115) (olanzapine), Eli Lilly Nederland B.V., Rapporteur: Outi Mäki-Ikola **Zyprexa Velotab** (EMEA/H/C/000287) (olanzapine), Eli Lilly Nederland B.V., Rapporteur: Outi Mäki-Ikola NAPS: **OLANZAPIN KRKA** - KRKA, D.D., NOVO MESTO PRAC Rapporteur: Kimmo Jaakkola, "From: 01/04/2016 To: 31/03/2019"	change(s): Update of section 4.8 of the SmPC to add salivary hypersecretion with a frequency of uncommon. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010577/201905 (insulin glargine / lixisenatide) CAPS: **Suliqua** (EMEA/H/C/004243) (insulin glargine / lixisenatide), sanofi-aventis groupe, Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, "From 21/11/2018 To: 21/05/2019"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of sections 4.8 and 4.2 of the SmPC to introduce 'cutaneous amyloidosis' to the list of adverse drug reactions with a frequency 'unknown' and add a relevant detailed description and to amend method of administration instructions accordingly. The Package Leaflet is updated accordingly. The MAH also took the opportunity to add lipodystrophy to section 4.8 of the SmPC in line with the information in the Package Leaflet. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010596/201904 (cerliponase alfa) CAPS: **Brineura** (EMEA/H/C/004065) (cerliponase alfa), BioMarin International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga, "From: 27/10/2018 To: 26/04/2019"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of sections 4.4 and 4.8 of the SmPC to add 'anaphylactic reaction'. 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/00010699/201905 (erenumab)	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the

CAPS: **Aimovig** (EMEA/H/C/004447) (erenumab), Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Kirsti Villikka, "Period Covered From: 16/11/2018 To: 16/05/2019"	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 anaphylaxis and angioedema and to add warning on hypersensitivity reactions. 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/00010723/201904 (durvalumab) CAPS: **Imfinzi** (EMEA/H/C/004771) (durvalumab), AstraZeneca AB, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: David Olsen, "From: 30/10/2018 To: 30/04/2019"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of sections 4.2, 4.4 and 4.8 of the SmPC to add pemphigoid as an adverse reaction with a frequency uncommon (0.2%). The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.

B.4. EPARs / WPARs

Clopidogrel/Acetylsalicylic acid Mylan - clopidogrel / acetylsalicylic acid - EMEA/H/C/004996 Mylan S.A.S, indicated for the secondary prevention of atherothrombotic events, Generic, Generic of DuoPlavin, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Deferasirox Accord - deferasirox - EMEA/H/C/005156 Accord Healthcare S.L.U., treatment of chronic iron overload, Generic, Generic of EXJADE, Generic application (Article 10(1) 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	For information only. Comments can be sent to the PL in case necessary.

(Article 8(3) of Directive No 2001/83/EC)	
Mayzent - siponimod - EMEA/H/C/004712 Novartis Europharm Limited, treatment of secondary progressive multiple sclerosis (SPMS), 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.
Polivy - polatuzumab vedotin - EMEA/H/C/004870, Orphan Roche Registration GmbH, treatment of mature B cell lymphomas, 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.
Sunosi - solriamfetol - EMEA/H/C/004893 Jazz Pharmaceuticals Ireland Limited, is indicated to improve wakefulness in patients with narcolepsy or obstructive sleep apnoea., 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.
Tavlesse - fostamatinib - EMEA/H/C/005012 Rigel Pharmaceuticals B.V., indicated for the treatment of thrombocytopenia, 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.

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

Alprolix - eftrenonacog alfa - EMEA/H/C/004142/II/0026, Orphan Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Apidra - insulin glulisine - EMEA/H/C/000557/II/0082/G Sanofi-Aventis Deutschland GmbH, Rapporteur: Mark Ainsworth Request for Supplementary Information adopted on 21.11.2019.	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	Request for supplementary information adopted with a specific timetable.

Mueller-Berghaus Request for Supplementary Information adopted on 05.12.2019.	
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0085/G UCB Pharma S.A., Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 12.12.2019.	Request for supplementary information adopted with a specific timetable.
Cinryze - C1 esterase inhibitor (human) - EMEA/H/C/001207/II/0071/G Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 28.11.2019. Request for Supplementary Information adopted on 19.09.2019.	Positive Opinion adopted by consensus on 28.11.2019. 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 Request for Supplementary Information adopted on 21.11.2019, 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Elaprase - idursulfase - EMEA/H/C/000700/II/0082 Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 12.12.2019, 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Esperoct - turoctocog alfa pegol - EMEA/H/C/004883/II/0002, Orphan Novo Nordisk A/S, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 21.11.2019.	Request for supplementary information adopted with a specific timetable.
Eylea - aflibercept - EMEA/H/C/002392/II/0055/G Bayer AG, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 12.12.2019, 07.11.2019.	Request for supplementary information adopted with a specific timetable.
Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0008 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz Opinion adopted on 28.11.2019.	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Fulphila - pegfilgrastim - EMEA/H/C/004915/II/0005/G Mylan S.A.S, Rapporteur: Martina Weise Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 28.11.2019.	
Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0037, Orphan Roche Registration GmbH, Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 12.12.2019.	Request for supplementary information adopted with a specific timetable.
GONAL-f - follitropin alfa - EMEA/H/C/000071/II/0145/G Merck Europe B.V., Rapporteur: Johann Lodewijk Hillege Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 10.10.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0111/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 12.12.2019.	Request for supplementary information adopted with a specific timetable.
Ilumetri - tildrakizumab - EMEA/H/C/004514/II/0010/G Almirall S.A, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 28.11.2019.	Request for supplementary information adopted with a specific timetable.
Inflectra - infliximab - EMEA/H/C/002778/II/0081/G Pfizer Europe MA EEIG, Duplicate, Duplicate of Remsima, Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 28.11.2019. Clockstop extension Adopted.	Request for supplementary information adopted with a specific timetable.
Kalydeco - ivacaftor - EMEA/H/C/002494/II/0080, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Maria Concepcion Prieto Yerro Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 24.10.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kyprolis - carfilzomib - EMEA/H/C/003790/II/0040, Orphan Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez Opinion adopted on 28.11.2019.	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Lamzede - velmanase alfa - EMEA/H/C/003922/II/0007, Orphan	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP

Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 12.09.2019.	Members were in agreement with the CHMP recommendation.
LIBTAYO - cemiplimab - EMEA/H/C/004844/II/0003 Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Sinan B. Sarac Opinion adopted on 28.11.2019. Request for Supplementary Information adopted on 24.10.2019.	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Mozobil - plerixafor - EMEA/H/C/001030/II/0040/G, Orphan Genzyme Europe BV, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 17.10.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
NeuroBloc - botulinum toxin type B - EMEA/H/C/000301/II/0104/G Sloan Pharma S.a.r.l, Rapporteur: Bruno Sepodes Request for Supplementary Information adopted on 05.12.2019, 31.10.2019, 26.09.2019.	Request for supplementary information adopted with a specific timetable.
NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0033/G Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 05.12.2019.	Request for supplementary information adopted with a specific timetable.
Noxafil - posaconazole - EMEA/H/C/000610/II/0059 Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau Opinion adopted on 21.11.2019. Request for Supplementary Information adopted on 12.09.2019.	Positive Opinion adopted by consensus on 21.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
OPDIVO - nivolumab - EMEA/H/C/003985/II/0076/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez Request for Supplementary Information adopted on 28.11.2019. Letter from the applicant dated 13.12.2019 requesting a clock stop extension. **For**	Request for supplementary information adopted with a specific timetable.

information.	
OPDIVO - nivolumab - EMEA/H/C/003985/II/0078 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez Opinion adopted on 12.12.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0053/G Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 28.11.2019.	Request for supplementary information adopted with a specific timetable.
Pelgraz - pegfilgrastim - EMEA/H/C/003961/II/0013/G Accord Healthcare S.L.U., Rapporteur: Sol Ruiz Opinion adopted on 05.12.2019. Request for Supplementary Information adopted on 31.10.2019.	Positive Opinion adopted by consensus on 05.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pheburane - sodium phenylbutyrate - EMEA/H/C/002500/II/0025 Eurocept International B.V., Rapporteur: Jayne Crowe Opinion adopted on 28.11.2019.	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Posaconazole AHCL - posaconazole - EMEA/H/C/005028/II/0001 Accord Healthcare S.L.U., Generic, Generic of Noxafil, Rapporteur: Kolbeinn Gudmundsson Opinion adopted on 05.12.2019.	Positive Opinion adopted by consensus on 05.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0180/G Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 07.11.2019, 12.09.2019.	Positive Opinion adopted by consensus on 12.12.2019. 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 Request for Supplementary Information adopted on 28.11.2019. Clockstop extension Adopted.	Request for supplementary information adopted with a specific timetable.
Repaglinide Accord - repaglinide - EMEA/H/C/002318/II/0009/G	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP

Accord Healthcare S.L.U., Generic, Generic of NovoNorm, Rapporteur: Melinda Sobor Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 10.10.2019, 26.04.2019.	Members were in agreement with the CHMP recommendation.
Ruconest - conestat alfa - EMEA/H/C/001223/II/0052 Pharming Group N.V, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 21.11.2019.	Request for supplementary information adopted with a specific timetable.
SomaKit TOC - edotreotide - EMEA/H/C/004140/II/0011, Orphan Advanced Accelerator Applications, Rapporteur: Maria Concepcion Prieto Yerro Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Somavert - pegvisomant - EMEA/H/C/000409/II/0091 Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race Request for Supplementary Information adopted on 05.12.2019.	Request for supplementary information adopted with a specific timetable.
Symtuza - darunavir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004391/II/0020 Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege Opinion adopted on 12.12.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
TEPADINA - thiotepa - EMEA/H/C/001046/II/0034, Orphan ADIENNE S.r.l., Rapporteur: Alexandre Moreau Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 14.11.2019, 19.09.2019.	Positive Opinion adopted by consensus on 12.12.2019. 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 Request for Supplementary Information adopted on 05.12.2019.	Request for supplementary information adopted with a specific timetable.
Viramune - nevirapine - EMEA/H/C/000183/II/0141/G Boehringer Ingelheim International GmbH, Rapporteur: Bruno Sepodes	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 10.10.2019.	
WS1726 **Nuwiq-EMEA/H/C/002813/WS1726/0033** **Vihuma-EMEA/H/C/004459/WS1726/0015** Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 28.11.2019.	Positive Opinion adopted by consensus on 28.11.2019. 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

Baraclude - entecavir - EMEA/H/C/000623/II/0063 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, "Submission of responses to the final clinical study report (CSR) from a Paediatric Safety and Efficacy Study (AI463189), a comparative study of the antiviral efficacy and safety of Entecavir (ETV) versus placebo in paediatric subjects with chronic Hepatitis B Virus (HBV) infection who are HBeAg positive, in order to provide additional clarification regarding the on-treatment and long-term follow-up haematology findings. The final CSR for AI463189 was already submitted and assessed within the context of procedure EMEA/H/C/000623/P46/010." Request for Supplementary Information adopted on 05.12.2019, 10.10.2019.	Request for supplementary information adopted with a specific timetable.
Bydureon - exenatide - EMEA/H/C/002020/II/0066 AstraZeneca AB, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC to include information about the new ADR drug-induced thrombocytopenia (DITP) based on spontaneous reports post-marketing. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes in line with the latest QRD template."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 21.11.2019.	
BYETTA - exenatide - EMEA/H/C/000698/II/0071 AstraZeneca AB, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC to include information about the new ADR drug-induced thrombocytopenia (DITP) based on spontaneous reports post-marketing. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes in line with the latest QRD template." Request for Supplementary Information adopted on 21.11.2019.	Request for supplementary information adopted with a specific timetable.
Dovato - dolutegravir / lamivudine - EMEA/H/C/004909/II/0001 ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegavir. The SmPC is updated accordingly. The RMP is not submitted." Request for Supplementary Information adopted on 12.12.2019, 14.11.2019.	Request for supplementary information adopted with a specific timetable.
Edurant - rilpivirine - EMEA/H/C/002264/II/0036 Janssen-Cilag International NV, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.6 of the SmPC based on the most recent data described in the ARV Pregnancy Registry (APR). In addition, the Marketing authorisation holder (MAH) took the opportunity to update the Package Leaflet to include information on the sodium excipient, as per the revised Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' and the list of local representatives, as well as to make	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

minor editorial changes in the SmPC and in the Package Leaflet." Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 12.09.2019.	
Eurartesim - piperaquine tetraphosphate / artenimol - EMEA/H/C/001199/II/0036 Alfasigma S.p.A., Rapporteur: Janet Koenig, "Update of sections 4.2 and 5.1 of the SmpC with reference to the posology in patients weighing ≥ 100 kg. Update of sections 4.4 and 4.6 of the SmPC with recommendations during pregnancy. Annex II has been updated to reflect the closure of the Eurartesim Pregnancy Registry (as endorsed by CHMP in procedure II/32). The package leaflet is amended accordingly and the list of local representatives has also been updated in the Package leaflet." Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 07.11.2019, 19.09.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Eviplera - emtricitabine / rilpivirine / tenofovir disoproxil - EMEA/H/C/002312/II/0100 Gilead Sciences Ireland UC, Rapporteur: Johann Lodewijk Hillege, "Submission of the final study report for the drug utilisation study EDMS-ERI-139775027, an observational cohort study to assess the compliance of rilpivirine use with the SmPC, implemented using data from the EuroSIDA study cohort. The study is listed as a Category 3 study in the Eviplera RMP and submission of the final study report fulfils PAM MEA 011.5." Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 12.09.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/II/0082 Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, "Update of section 5.3 of the SmPC in order to add new information on ledipasvir carcinogenicity based on the final results from study TX-256-2016; this was a 104-week oral gavage carcinogenicity study in rats. In addition, the MAH took the opportunity to bring the Product Information in line with the current QRD template version 10.1."	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 12.12.2019.	
Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0110/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include the number of PID patients, to include prescriber information and tolerability information for manual push infusion, to update prescriber information on device-assisted infusion and to include safety information, based on final results from study IgPro20_4004, an open-label study to evaluate the safety and tolerability of higher infusion parameters of Hizentra infused manually or with pump assistance in PID patients. Update of sections 4.2 and 4.8 of the SmPC in order to update the number of PID patients and to include safety information based on final results from study IgPro_4005, a phase 4, open-label, single-sequence, crossover study to investigate the tolerability, safety and efficacy of biweekly Hizentra dosing in PID patients. Section 4.8 of the SmPC is further updated to present the adverse drug reactions frequency per infusion. The Package Leaflet is updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the list of local representative in the Package Leaflet, to make some editorial updates in sections 4.2, 5.1 and 5.2 of the SmPC and to bring the PI in line with the latest QRD template version 10.1." Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 17.10.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0053, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC with final results on PFS by investigator assessment in Study PCYC-1112-CA, including PFS2 and overall survival data until study closure per protocol at 65-months follow-up. The Annex II is updated accordingly with deletion of ANX 003. The contact details of the local representatives have been updated in the Package Leaflet. Minor editorial revisions have been proposed throughout the PI." Opinion adopted on 05.12.2019. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 05.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 03.10.2019.	
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." Request for Supplementary Information adopted on 05.12.2019.	Request for supplementary information adopted with a specific timetable.
Juluca - dolutegravir / rilpivirine - EMEA/H/C/004427/II/0016 ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegavir. The SmPC is updated accordingly. The RMP is not submitted." Request for Supplementary Information adopted on 12.12.2019, 14.11.2019.	Request for supplementary information adopted with a specific timetable.
Lorviqua - lorlatinib - EMEA/H/C/004646/II/0002 Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, "Update of section 4.5 of the SmPC in order to further reflect the induction potential of lorlatinib on CYP2C9, P-gp, CYP2B6 and UGT1A1 substrates based on the results from the drug-drug interaction sub-study of B7461001. Furthermore, the MAH corrected information regarding ADRs in sections 4.4 and 4.8 of the SmPC and clarification regarding linearity/non-linearity of lorlatinib PK in section 5.2 of the SmPC. 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 for Supplementary Information adopted on 12.12.2019.	Request for supplementary information adopted with a specific timetable.
MabThera - rituximab -	Request for supplementary information adopted

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." Request for Supplementary Information adopted on 12.12.2019.	with a specific timetable.
Mepsevii - vestronidase alfa - EMEA/H/C/004438/II/0009, Orphan Ultragenyx Germany GmbH, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8. 5.1 and 5.2 of the SmPC following final results from paediatric study UX003-CL203, an open –label study of vestrodinase alfa enzyme replacement therapy in MPS 7 patients less than 5 years old." Request for Supplementary Information adopted on 12.12.2019.	Request for supplementary information adopted with a specific timetable.
Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0010/G, Orphan Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, "A group of two type II variations, to submit the non-clinical in vitro study reports PFZ-07 and 6000572 relating to the effects of gemtuzumab ozogamicin on platelet development as well as on human platelet function." Request for Supplementary Information adopted on 21.11.2019, 10.10.2019.	Request for supplementary information adopted with a specific timetable.
Nerlynx - neratinib - EMEA/H/C/004030/II/0007 Pierre Fabre Medicament, Rapporteur: Bruno Sepodes, "Update of section 5.1 of the SmPC to update the results of the multicentre, randomised, double-blind, placebo-controlled, pivotal phase III study, ExteNET (3004) in women with early-stage HER2-positive breast cancer who had completed adjuvant treatment with trastuzumab, based on a re-analysis conducted with corrected stratification factors. Furthermore, the MAH took the opportunity to make some corrections in section 4.4 of the	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

SmPC." Opinion adopted on 12.12.2019.	
Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0003 Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, "Submission of the final report from Population PK and PK/PD Modelling Report (POR-PKPD-ADEX-321) listed as a category 2 study in the RMP/Specific Obligation 004 in Annex II." Request for Supplementary Information adopted on 12.12.2019.	Request for supplementary information adopted with a specific timetable.
Ongentys - opicapone - EMEA/H/C/002790/II/0020 Bial - Portela & Cª, S.A., Rapporteur: Martina Weise, "Update of sections 4.5 and 5.2 of the SmPC to add information on drug interaction and pharmacokinetic properties of opicapone based on final results from drug interaction studies NBI-OPC-1708 and NBI-OPC-1707. Study NBI-OPC-1708 is a phase 1, open-label, one-sequence crossover, drug-interaction study to evaluate and compare the pharmacokinetics of repaglinide when administered alone and concomitantly with opicapone. Study NBI-OPC-1707 is a Phase 1, randomized, open-label, 2-period crossover drug interaction study of the effect of administration of single dose of quinidine on the pharmacokinetics of opicapone." Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 24.10.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Portrazza - necitumumab - EMEA/H/C/003886/II/0017 Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Rugile Pilviniene, "Submission of the exploratory biomarker analysis from 4 clinical studies (I4X-MC-JFCU, I4X-MC-JFCQ, I4X-MC-JFCP, I6A-MC-CBBE) listed as a category 3 measure in the RMP. The RMP version 8.1 has also been submitted." Request for Supplementary Information adopted on 28.11.2019.	Request for supplementary information adopted with a specific timetable.
Praluent - alirocumab - EMEA/H/C/003882/II/0051 sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC to add a new warning on angioedema and	Positive Opinion adopted by consensus on 05.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

update of section 4.8 of the SmPC to add 'angioedema' as a new adverse drugs reaction, based on safety review of post-marketing cases and cases from study EFC11570 (OUTCOMES study); the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make some formatting changes throughout the product information." Opinion adopted on 05.12.2019.	
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." Request for Supplementary Information adopted on 12.12.2019, 17.10.2019.	Request for supplementary information adopted with a specific timetable.
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, 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	Request for supplementary information adopted with a specific timetable.

(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)." Request for Supplementary Information adopted on 05.12.2019.	
PREVYMIS - letermovir - EMEA/H/C/004536/II/0016/G, Orphan Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "C.I.4 (type II) – Update of sections 4.4 and 6.6 of the SmPC to include the recommendation to use an in-line filter at the point of administration for finished product Prevymis 240 mg and 480 mg concentrate for solution for infusion (EU/1/17/1245/003-004). The package leaflet and labelling are updated accordingly. B.II.d.1.z (type IB) C.1.11.z (type IB) - Change in the due date of the Annex II condition for the medicinal product Prevymis 240 mg and 480 mg concentrate for solution for infusion (EU/1/17/1245/003-004) from 31 May 2020 to 31 May 2021." Request for Supplementary Information adopted on 12.12.2019.	Request for supplementary information adopted with a specific timetable.
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 12.12.2019.	Request for supplementary information adopted with a specific timetable.
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	Request for supplementary information adopted with a specific timetable.

after completion of study treatment. In addition some minor editorial updates to the Product Information are being proposed." Request for Supplementary Information adopted on 05.12.2019.	
Soliris - eculizumab - EMEA/H/C/000791/II/0107, Orphan Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez, "Submission of the final report from study ECU-MG-302, a phase III, open-label, extension trial of ECU-MG-301 to evaluate the safety and efficacy of eculizumab in subjects with refractory generalized myasthenia gravis (EudraCT 2013-002191-41)." Opinion adopted on 12.12.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Strensiq - asfotase alfa - EMEA/H/C/003794/II/0043/G, Orphan Alexion Europe SAS, Rapporteur: Daniela Melchiorri, "Type IB B.II.f.1.z. – To extend the time out of refrigeration (TOR) of the Strensiq vials from 1 to 3 hours. Section 6.3 of the SmPC and the Package Leaflet are updated accordingly. In addition, the MAH took the opportunity to align the annexes with the latest QRD template v. 10.1 and to update the Package Leaflet section "How to inject Strensiq" with the clarification of the steps for injection, in order to align the instructions for injection with the EU RMP educational materials." Opinion adopted on 12.12.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Symkevi - tezacaftor / ivacaftor - EMEA/H/C/004682/II/0012/G, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.5 and 5.2 of the SmPC in order to provide information on drug-drug interactions and pharmacogenetic data based on final results from two post-authorisation measures (PAMs) studies: VX18-661-011 (an open-label phase 1 study to examine the effects of combination of tezacaftor and ivacaftor on the pharmacokinetics and safety of pitavastatin in healthy subjects) and pharmacokinetics study P088 (pharmacogenetic study of TEZ and IVA exposure with respect to CYP3A4*22 genotype)." Opinion adopted on 12.12.2019. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 19.09.2019.	
Symtuza - darunavir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004391/II/0021/G Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ana Sofia Diniz Martins, "C.I.13: Submission of the final report from study GS-US-311-1717, listed as a category 3 study in the RMP. This is a randomized, double-blind, active-controlled study to evaluate the safety and efficacy of switching to emtricitabine/tenofovir alafenamide (F/TAF) versus continuing abacavir/lamivudine (ABC/3TC) in HIV-1 infected subjects who were virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable regimen containing ABC/3TC after 96 weeks. The RMP version 6.1 has also been submitted. C.I.11.z: Submission of an updated RMP version 6.1 in order to postpone the due date of the final report from study GS-US-292-0109 from Q4 2019 to Q2 2021." Opinion adopted on 12.12.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0030 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC to reflect the outcome of anti-drug antibody (ADA) analyses conducted across studies POPLAR, OAK, IMpower 150, IMpower 130, IMPower 131, IMpower 132, IMvigor 211, IMmotion 151, IMpower 133 and IMpassion 130, further to the CHMP recommendation." Request for Supplementary Information adopted on 05.12.2019.	Request for supplementary information adopted with a specific timetable.
Tivicay - dolutegravir - EMEA/H/C/002753/II/0052 ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at	Request for supplementary information adopted with a specific timetable.

conception. This surveillance system captures all antiretroviral exposure including dolutegavir. The SmPC is updated accordingly. The RMP is not submitted." Request for Supplementary Information adopted on 12.12.2019, 14.11.2019.	
Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/II/0069 ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegavir. The SmPC is updated accordingly. The RMP is not submitted." Request for Supplementary Information adopted on 12.12.2019, 14.11.2019.	Request for supplementary information adopted with a specific timetable.
Verzenios - abemaciclib - EMEA/H/C/004302/II/0006 Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add interstitial lung disease (ILD)-like events (including pneumonitis) as new adverse drug reactions together with a related warning and dose adjustments recommendations. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1 and make few corrections to the PL to bring it in line with the SmPC." Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 14.11.2019, 19.09.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Verzenios - abemaciclib - EMEA/H/C/004302/II/0008 Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC to include the results of the interim OS analysis	Request for supplementary information adopted with a specific timetable.

from study MONARCH 2, a randomised, double-blind, placebo-controlled, phase 3 study of fulvestrant with or without abemaciclib, for women with hormone receptor positive, HER2 negative locally advanced or metastatic breast cancer." Request for Supplementary Information adopted on 05.12.2019.	
Xagrid - anagrelide - EMEA/H/C/000480/II/0086 Shire Pharmaceuticals Ireland Limited, Rapporteur: Alexandre Moreau, "Update of section 4.8 of the SmPC to include the adverse drug reaction Prinzmetal angina with a frequency not known. The PIL is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes throughout the product information." Request for Supplementary Information adopted on 21.11.2019.	Request for supplementary information adopted with a specific timetable.
Xaluprine - mercaptopurine - EMEA/H/C/002022/II/0022, Orphan Nova Laboratories Ireland Limited, Rapporteur: Filip Josephson, "Update of sections 4.4, 4.8 and 4.9 of the SmPC to add further information on hepatic toxicity. The MAH took the opportunity to implement minor editorial changes to the SmPC and PIL." Request for Supplementary Information adopted on 21.11.2019, 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Xarelto - rivaroxaban - EMEA/H/C/000944/II/0068 Bayer AG, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC based on results from the pantoprazole/placebo randomization part of the COMPASS study; this is part of a double-blind, double-dummy randomized trial in which pantoprazole is being compared with placebo in patients participating in the trial who are not receiving a proton-pump inhibitor. In addition, an amendment to the COMPASS Clinical Study Report is submitted to correct values caused by a programming error in the statistical outputs in this study. No changes on the approved label are proposed due to this correction." Opinion adopted on 28.11.2019. Request for Supplementary Information adopted on 03.10.2019.	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Yondelis - trabectedin - EMEA/H/C/000773/II/0058 Pharma Mar, S.A., Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, "Update of section 4.4 of the SmPC in order to add a warning based on results from study Cardiac Safety Report [Protocols ET743-SAR-3007, ET743-OVA-301, ET743-OVC-3006; Phase 3. JNJ-17027907; R270741 (trabectedin)] following the PSUSA procedure EMEA/H/C/PSUSA/00003001/201809; the Package Leaflet is updated accordingly." Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 19.09.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zessly - infliximab - EMEA/H/C/004647/II/0011 Sandoz GmbH, Rapporteur: Bjorg Bolstad, "Submission of the final CSR for the efficacy and safety study GP11-301; the report includes results from treatment period 3, where all subjects continued to receive open-label Zessly treatment for an additional 24 weeks (Week 54 until Week 78)." Opinion adopted on 05.12.2019.	Positive Opinion adopted by consensus on 05.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zoely - nomegestrol acetate / estradiol - EMEA/H/C/001213/II/0050 Theramex Ireland Limited, Rapporteur: Jean-Michel Race, "Update of sections 4.3 and 4.4 of the SmPC in order to add a new contraindication and a new warning regarding meningioma, upon request by PRAC following the assessment of Post-authorisation measure "LEG 014". The Package Leaflet is being updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in the Netherlands and Portugal in the Package Leaflet." Request for Supplementary Information adopted on 12.12.2019, 14.11.2019, 19.09.2019.	Request for supplementary information adopted with a specific timetable.
Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0058 Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez, "To update section 5.1 of the SmPC based on final results from study PCR3011 (Lattitude); this is a randomised, double-blind, placebo-controlled study designed to determine the efficacy of abiraterone acetate and low-dose prednisone in men with metastatic	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

hormone-naive prostate cancer. The MAH took the occasion to update the product information as per the latest QRD version and to update local representative for Spain and Hungary in the package leaflet." Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 10.10.2019.	
WS1636/G **Mekinist-EMEA/H/C/002643/WS1636/0035/G** **Tafinlar-EMEA/H/C/002604/WS1636/0040/G** Novartis Europharm Limited, Lead Rapporteur: Filip Josephson, "Update of section 5.1 of the Mekinist (trametinib) and Tafinlar (dabrafenib) SmPC to include the 5-years overall survival (OS) results from study MEK115306 (COMBI-d), a phase III, randomised, double-blinded study comparing the combination of dabrafenib and trametinib to dabrafenib and placebo in first-line therapy for subjects with unresectable or metastatic BRAF V600/K mutation-positive cutaneous melanoma and the 5-years overall survival (OS) results from study MEK116513 (COMBI-v), a phase III, open-label, 2 arm, randomised study comparing dabrafenib and trametinib combination therapy with vemurafenib monotherapy in BRAF V600 mutation-positive metastatic melanoma." Opinion adopted on 21.11.2019. Request for Supplementary Information adopted on 03.10.2019.	Positive Opinion adopted by consensus on 21.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
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.	Request for supplementary information adopted with a specific timetable.
WS1689 **Leganto-EMEA/H/C/002380/WS1689/0031**	Request for supplementary information adopted with a specific timetable.

Neupro-EMEA/H/C/000626/WS1689/0085 UCB Pharma S.A., Lead Rapporteur: Bruno Sepodes, "Update of section 4.8 of the SmPC in order to include "Rhabdomyolysis" as undesirable effect with frequency "not known" and widen the scope of an existing undesirable effect "increased CPK" based on new pharmacovigilance data. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant took the opportunity to correct some minor editorial discrepancies found within the package leaflets of Germany, Italy, France and Sweden." Request for Supplementary Information adopted on 28.11.2019.	
WS1702 **Fertavid-EMEA/H/C/001042/WS1702/0046** **Puregon-EMEA/H/C/000086/WS1702/0104** Merck Sharp & Dohme B.V., Lead Rapporteur: Peter Kiely, "Update of section 4.4 of the SmPC in order to revise the existing warning on Ovarian Hyperstimulation Syndrome (OHSS) based on post-marketing data and literature review. The package leaflet is updated accordingly. In addition, the worksharing applicant took the opportunity to update the list of local representatives in the package leaflet and made some editorial changes in the Product Information." Opinion adopted on 28.11.2019.	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1714 **OPDIVO-EMEA/H/C/003985/WS1714/0077** **Yervoy-EMEA/H/C/002213/WS1714/0073** Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.2 and 4.4 of the SmPC in order to update the safety information on myocarditis management for nivolumab monotherapy or for nivolumab in combination with ipilimumab therapy." Opinion adopted on 12.12.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1722 **OFEV-EMEA/H/C/003821/WS1722/0029** **Vargatef-EMEA/H/C/002569/WS1722/0028** Boehringer Ingelheim International GmbH, Lead	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to add alopecia with a frequency uncommon for Ofev and very common for Vargatef and headache with a frequency of common for both Ofev and Vargatef as new adverse drug reactions based on an overall assessment of the safety data for the nintedanib products. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to include the latest renewal date for Vargatef." Opinion adopted on 12.12.2019.	

B.5.3. CHMP-PRAC assessed procedures

AJOVY - fremanezumab - EMEA/H/C/004833/II/0003 TEVA GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Kirsti Villikka, "Update of section 4.8 of the SmPC in order to update the safety information based on final results from study TV48125-CNS-30051 listed as a category 3 study in the RMP; A Multicenter, Randomized, Double-Blind, Parallel-Group Study Evaluating the Long-Term Safety, Tolerability, and Efficacy of Subcutaneous Administration of TEV-48125 for the Preventive Treatment of Migraine. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted." Opinion adopted on 28.11.2019.	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Benlysta - belimumab - EMEA/H/C/002015/II/0073 GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from study BEL116027 listed as a category 3 study in the RMP. This is a multi-centre, open-label, non-randomized, efficacy and safety study to evaluate treatment holidays and rebound phenomenon after treatment with belimumab 10 mg/kg in subjects with low SLE disease activity. The RMP is updated to version 34 to reflect the study results." Opinion adopted on 12.12.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Bydureon - exenatide - EMEA/H/C/002020/II/0064 AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

sections 4.2 and 4.4 of the SmPC in order to remove the limitation of use in patients with moderate renal impairment (creatinine clearance [CrCl] 30 to 50 ml/min) based on pooled data from 8 EQW/EQWS studies undertaken in patients with mild renal impairment/chronic kidney disease stage 2 or moderate renal impairment/chronic kidney disease stage 3, and update of section 5.1 of the SmPC to include the results of a subgroup analysis from EXSCEL (Study D5551C00003/BCB109) in a subset of patients with moderate renal impairment. In addition, the MAH took the opportunity to introduce GFR as the main indicator of renal function rather than CrCl. The Package Leaflet has been updated accordingly and the MAH has taken the opportunity to implement some minor changes in the labelling. An updated RMP version 34 was provided with the application, which includes consequential changes as well as a proposal for the removal of Acute Renal Failure (ARF) as an Important Identified Risk based on the GVP V Rev2 guidance. In addition, upon request following the assessment of II/54, a Pan EU epidemiological study to monitor events of pancreatic cancer has been included as an additional planned pharmacovigilance activity." Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 17.10.2019.	
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	Request for supplementary information adopted with a specific timetable.

labelling and Patient Information Leaflet for the product. The RMP version 4.1 has been submitted." Request for Supplementary Information adopted on 12.12.2019.	
Fortacin - lidocaine / prilocaine - EMEA/H/C/002693/II/0030 Recordati Ireland Ltd, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, "Change in the legal status of Fortacin from 'medicinal product subject to medical prescription' to 'medicinal product not subject to medical prescription' in view of the safety profile of Fortacin, the post-marketing experience already available with other medicinal products containing amide local anaesthetics and in view of making the product more accessible to the target population. Furthermore, the PI is being brought in line with the latest QRD template (version 10.1). The RMP version 3.1 has also been submitted." Request for Supplementary Information adopted on 12.12.2019.	Request for supplementary information adopted with a specific timetable.
Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0033 MSD Vaccins, Rapporteur: Kristina Dunder, PRAC Rapporteur: Jean-Michel Dogné, "Update of sections 4.2, 4.6, 4.8 and 5.1 of the SmPC in order to update the safety and immunogenicity information based on final results from study V503-P004 listed as a category 3 study in the RMP (MEA007); this is an open-label phase III clinical trial to study the immunogenicity and tolerability of Gardasil 9 in adult women (27 to 45 year-olds) compared to young adult women (16 to 26 year-olds); the Package Leaflet is updated accordingly. The RMP version 4.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.4 of the SmPC according to the Guideline on quality aspects included in the product information for vaccines for human use (EMA/CHMP/BWP/133540/2017), and to include editorial changes in section 5.1 of the SmPC" Opinion adopted on 28.11.2019. Request for Supplementary Information adopted on 03.10.2019.	Positive Opinion adopted by consensus on 28.11.2019. 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 [MEA] PAM. The PL and RMP are updated accordingly." Request for Supplementary Information adopted on 28.11.2019.	Request for supplementary information adopted with a specific timetable.
Giotrif - afatinib - EMEA/H/C/002280/II/0031 Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "Update of sections 4.4 and 4.8 of the SmPC in order to introduce a warning and to add gastrointestinal (GI) perforation as an additional adverse drug reaction based on summaries of clinical trial and post-marketing safety data, respectively. The Package Leaflet and the RMP (agreed version 8.1) are updated accordingly. The RMP also includes the update of the RMP due to the GVP revision 2 template. In addition, the MAH took the opportunity to update the list of the local representatives in the package leaflet." Opinion adopted on 28.11.2019. Request for Supplementary Information adopted on 03.10.2019, 11.07.2019.	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0052, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of section 4.8 of the SmPC based on final results from study PAM 3038-1, which assessed long term safety data collected from predefined cohorts of subjects treated with ibrutinib for up to 5 years or until disease progression or unacceptable toxicity at the recommended daily doses of 420 mg/day for CLL/SLL and 560 mg/day for MCL (MEA 025)." Opinion adopted on 05.12.2019. Request for Supplementary Information adopted on 03.10.2019.	Positive Opinion adopted by consensus on 05.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Incresync - alogliptin / pioglitazone - EMEA/H/C/002178/II/0029 Takeda Pharma A/S, Rapporteur: Johann	Request for supplementary information adopted with a specific timetable.

Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Incresync RMP (version 10.0) includes the following updates: (i) MAH's proposal for removal of aRMMs and consequently the Drug Utilisation Study (DUS) 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 component have been aligned with the consolidated Pioglitazone family RMP (RMP V27.0 as agreed with EMA 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, malignancies (including pancreatic 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/002178/R/0023). Annex II of the PI has been updated accordingly." Request for Supplementary Information adopted on 28.11.2019.	
Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0048/G Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, "C.1.4: Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information on the risk of Left Ventricular Dysfunction (LVD) based on the final results from study BO39807 listed as a category 3 study in the RMP. This is an observational study of cardiac events in patients with HER2-positive metastatic breast cancer who have a Left Ventricular Ejection Fraction (LVEF) between 40%-49% prior to initiating treatment with Kadcyla; the RMP version 11.1 is approved.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

C.I.13: Submission of the final report from study BO28408 listed as a category 3 study in the RMP addressing cardiac safety, safety in elderly patients, and immunogenicity. This is a randomised, multicenter, open-label, two-arm, phase III neoadjuvant study evaluating the efficacy and safety of trastuzumab emtansine plus pertuzumab compared with chemotherapy plus trastuzumab and pertuzumab for patients with HER2-Positive Breast Cancer." Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 05.09.2019.	
Lokelma - sodium zirconium cyclosilicate - EMEA/H/C/004029/II/0013 AstraZeneca AB, Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to update the clinical information based final results from study DIALIZE. This was a Phase 3b, multicentre, prospective, randomised, double-blind, placebo-controlled study to reduce incidence of pre-dialysis hyperkalaemia with sodium zirconium cyclosilicate. The Package Leaflet and Labelling are updated accordingly. The RMP version 2.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement the new excipient statement for sodium in section 4.4 of the SmPC, section 2 of Labelling and section 2 of the Package Leaflet. Furthermore, minor editorial changes were introduced in section 2 of the Package leaflet." Request for Supplementary Information adopted on 12.12.2019, 19.09.2019.	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 6.3 has	Request for supplementary information adopted with a specific timetable.

also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the RMP in line with the template revision 2 of the good Pharmacovigilance practice module V guideline." Request for Supplementary Information adopted on 12.12.2019, 19.09.2019.	
Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0075 Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, "Update of sections 4.4 and 5.1 of the Summary of Product Characteristics in order to reflect change in the existing warning on immunogenicity and immunomodulation and add new clinical information on infantile onset patients (IOPD) immune tolerance induction based on data on use of immune tolerance induction in infantile onset Pompe disease patients from two exploratory Phase 4 studies (AGLU03707 / MSC12817 and companion study AGLU03807/ MSC12892) and the Duke Center of Excellence Observational Study (01562). The updated RMP version 9.0 has also been submitted." Opinion adopted on 28.11.2019. Request for Supplementary Information adopted on 03.10.2019.	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0002 Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "C.I.13: Submission of the Final Study Report for ANNEXA-4 Study ("Prospective, Open-Label Study of Andexanet Alfa in Patients Receiving a Factor Xa Inhibitor Who Have Acute Major Bleeding") listed as category 2 study in the RMP. This is an interventional non-randomized, multicentre, prospective, open-label, single-group study in patients with acute major bleeding. The results of ANNEXA-4 were requested to be submitted as Specific Obligation in the context of Conditional Marketing Authorisation. The RMP version 1.1 has also been submitted." Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 19.09.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Orencia - abatacept -	Positive Opinion adopted by consensus on

EMEA/H/C/000701/II/0134 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, "As a result of the outcome of the Article P46 064, update of sections 4.8 and 5.1 of the SmPC for Orencia solution for injection in pre-filled syringe based on the final 24-month results from study IM101301; this was an open-label study to assess pharmacokinetics, safety and efficacy of SC abatacept in pJIA with no formal hypothesis testing. Update of section 4.8 of the SmPC for Orencia powder for concentrate for solution for infusion based on the final 24-month results from study IM101301. The PL for Orencia solution for injection in pre-filled syringe has been updated to reflect the removal of the IFU booklet, as requested by the CHMP as part of the procedure EMEA/H/C/000701/X/0117/G. The RMP version 27.1 was updated with clinical trial exposure data from the 2-year data for 2 to 5 years old cohort in study IM101301. The presentation of identified and potential risks was updated with study IM101301 data on infections, injection reactions, malignancies and autoimmune symptoms in the 2 to 5 years old cohort and 6-17 years old cohort. In addition, the MAH took the opportunity to update the Annex II and to update section 4.4 of the SmPCs in line with the latest QRD template version 10.1 for all registered presentations. In addition, the list of local representatives in the PLs has been updated." Opinion adopted on 12.12.2019.	12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Rapiscan - regadenoson - EMEA/H/C/001176/II/0034/G GE Healthcare AS, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "Update of sections 4.4, 4.5, 4.9 and 5.1 of the SmPC regarding co-administration with methylxanthines due to the risk of seizure based on a review of the safety database and CCDS update; Update of section 5.1 of the SmPC regarding the use of regadenoson in patients with inadequate stress test based on results from study 3606-CL-3004 and CCDS update. In addition, the Marketing authorisation holder (MAH) took the opportunity to make small	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

corrections in section 4.4 of the SmPC. The RMP version (11.4) has also been submitted in order to fulfil LEG 016." Opinion adopted on 28.11.2019. Request for Supplementary Information adopted on 05.09.2019.	
Sancuso - granisetron - EMEA/H/C/002296/II/0056/G Kyowa Kirin Holdings B.V., Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Rugile Pilviniene, "update of the SmPC section 5.2. to add pharmacokinetic information concluded from a completed paediatric PK study, 392MD/44/C. The RMP has been updated accordingly The RMP has also been updated to implement RMP template EMA/PRAC/613102/2015 Rev 2 and includes the addition or deletion of safety concerns ((identified risks, potential risks, missing information) not previously assessed or requested by a competent authority. The MAH took the opportunity to update the Pregnancy information in section 4.6 of Annex I to align with the QRD statements provided in the QRD product information template. Minor QRD updates have also been made to the English language annex in line with version 10.1 of the QRD template." Request for Supplementary Information adopted on 12.12.2019.	Request for supplementary information adopted with a specific timetable.
Vemlidy - tenofovir alafenamide - EMEA/H/C/004169/II/0020 Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, PRAC Rapporteur: Ilaria Baldelli, "Update of sections 4.8 and 5.1 of the SmPC based on safety information from interim results at Week 48 of a phase 3, randomized, double blind study (GS-US-320-4018) conducted to evaluate the efficacy and safety of switching from tenofovir disoproxil fumarate (TDF) 300 mg QD to tenofovir alafenamide (TAF) 25 mg QD in subjects with CHB who are virologically suppressed, listed as a category 3 study in the RMP; the Package Leaflet is updated accordingly. The RMP version 5.0 has also been submitted." Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 17.10.2019, 25.07.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Zoely - nomegestrol acetate / estradiol - EMEA/H/C/001213/II/0051 Theramex Ireland Limited, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Adrien Inoubli, "To update the RMP to version 9.1 as requested in the outcome of the imposed PASS protocol adopted by the PRAC in June 2019 for a prospective observational study to assess the risk of venous thromboembolic events (VTE) and arterial thromboembolic events (ATE) in nomegestrel/estradiol users compared with the risk of VTE in users of combined oral contraceptives (COCs)-containing levonorgestrel, including the change of the due date from June 2020 to April 2021. The RMP is also updated in line with GVP V revision 2. As a consequence, annex II is updated. The MAH also took the opportunity to amend the package leaflet in order to update the list of local representatives." Opinion adopted on 28.11.2019.	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
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 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 28.11.2019.	Request for supplementary information adopted with a specific timetable.

B.5.4. PRAC assessed procedures

PRAC Led **BLINCYTO - blinatumomab - EMEA/H/C/003731/II/0033, Orphan** Amgen Europe B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Eva Jirsová, PRAC-CHMP liaison: Ondřej Slanař, "Submission of an updated RMP version 11 in line with the guideline on Good Pharmacovigilance Practices (GVP) Module V on RMP. In accordance with the RMP update, the protocol for Category 1 PASS 20150136 has been updated and the enrolment period for the study has been extended by 1 year. The milestones in the RMP were updated accordingly. In addition, the RMP includes a proposed update to the milestone of the Category 3 PASS 20180138." Request for Supplementary Information adopted on 28.11.2019.	Request for supplementary information adopted with a specific timetable.
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 rug Utilisation Study (DUS) 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 28.11.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Darzalex - daratumumab - EMEA/H/C/004077/II/0033, Orphan** Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, PRAC-CHMP liaison: Bruno Sepodes, "Submission of final study results of a non-interventional PASS to investigate the effectiveness of Darzalex educational materials concerning the potential risk of daratumumab to interfere with blood	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

typing analysis; this commitment was requested as PAM-001. An updated RMP (v.5.4) to reflect the completion of the study is included in the submission." Opinion adopted on 28.11.2019.	
PRAC Led **Daxas - roflumilast - EMEA/H/C/001179/II/0038** AstraZeneca AB, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Amendment of safety concerns and removal of additional risk minimisation measures. Minor changes are implemented in section 4.4 of SmPC and PL according to QRD template." Request for Supplementary Information adopted on 28.11.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Hemangiol - propranolol - EMEA/H/C/002621/II/0019** PIERRE FABRE DERMATOLOGIE, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Update of section 4.4 of the SmPC to amend the existing warning on hypoglycaemia and of the Package Leaflet to amend the existing warnings on hypotension/bradycardia and hypoglycaemia following the completion of a Drug Utilisation Study (DUS) performed in Germany and France to evaluate off-label use and effectiveness of RMM in a real-life clinical setting (MEA 002); the Annex II to the Opinion is updated in accordance. In addition, editorial amendments are made to section 4.4 of the SmPC and to the Package Leaflet. The RMP version 3.5 has also been agreed." Opinion adopted on 28.11.2019. Request for Supplementary Information adopted on 05.09.2019, 16.05.2019, 14.02.2019.	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Iclusig - ponatinib - EMEA/H/C/002695/II/0053, Orphan** Incyte Biosciences Distribution B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Filip Josephson, "Submission of an updated RMP version 20 in order to remove the study	Request for supplementary information adopted with a specific timetable.

AP24534-14-401, a Postmarketing Observational Registry to Evaluate the Incidence of and Risk Factors for Vascular Occlusive Events Associated With Iclusig (Ponatinib) in Routine Clinical Practice in the US (OMNI) from the Pharmacovigilance plan. In addition, in the framework of variation type II/51, it was considered that the distribution of the educational material was not needed anymore. The MAH is therefore also taking the opportunity to amend the RMP to remove reference to these measures." Request for Supplementary Information adopted on 28.11.2019.	
PRAC Led **Inflectra - infliximab - EMEA/H/C/002778/II/0079** Pfizer Europe MA EEIG, Duplicate, Duplicate of Remsima, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of the final clinical study report for C1231002 (PERSIST) study, an observational cohort study designed to evaluate real life drug persistence in biologic naive rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis patients receiving CT-P13 or those switched to CT-P13 from stable treatment with Remicade (reference medicinal product)." Request for Supplementary Information adopted on 28.11.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Inflectra - infliximab - EMEA/H/C/002778/II/0080** Pfizer Europe MA EEIG, Duplicate, Duplicate of Remsima, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of the final clinical study report for C1231001 (CONNECT-IBD) study; a non-interventional study designated as a Post Authorisation Safety Study conducted voluntarily to capture data from real-world clinical practice to characterise the population and document drug utilisation patterns. In addition, available safety data and data on the effectiveness of CT-P13 in the context of standard of care utilisation of Remicade (reference medicinal product) was collected in patients with Crohn's disease or ulcerative colitis."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 28.11.2019.	
PRAC Led **Instanyl - fentanyl - EMEA/H/C/000959/II/0052** Takeda Pharma A/S, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 19.2 in order to update information relating to educational material." Request for Supplementary Information adopted on 28.11.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Kisplyx - lenvatinib - EMEA/H/C/004224/II/0030** Eisai GmbH, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Bjorg Bolstad, "Submission of an updated RMP version 11.3 as a result of interim analysis and updated final report submission dates added for study E7080-G000-307. The protocol for study E7080-G000-307 has been updated to version 06, dated 10 September 2019, to include an interim analysis for profession-free survival and overall survival." Request for Supplementary Information adopted on 28.11.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Luveris - lutropin alfa - EMEA/H/C/000292/II/0082** Merck Europe B.V., Rapporteur: Mark Ainsworth, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 3.1 (subsequently updated to version 4.0) for Luveris in order to adapt the RMP template to Good Pharmacovigilance Practice (GVP) Module V, rev 2., with consequential removal of important identified risks, important potential risks as well as modification of the missing information on hypogonadotropic hypogonadal women with severe LH and FSH deficiency of advanced maternal age, as well as other minor changes." Opinion adopted on 28.11.2019. Request for Supplementary Information adopted on 05.09.2019.	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Led **M-M-RVAXPRO - measles, mumps and rubella vaccine (live) - EMEA/H/C/000604/II/0096** MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP (version 4.1) in order to - Align to the new EU RMP template and EMA guideline on good pharmacovigilance practices (GVP) Module V (Rev. 2); - Remove the important potential risk "a potential change in the safety profile related to the replacement of human serum albumin (HAS) with recombinant human albumin (rHA)"; - Remove the missing information related to "exposure during pregnancy"." Opinion adopted on 28.11.2019.	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Mavenclad - cladribine - EMEA/H/C/004230/II/0009** Merck Europe B.V., Rapporteur: Mark Ainsworth, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, PRAC-CHMP liaison: Bruno Sepodes, "Submission of the final CSR for the PREMIERE registry (EMR700568-012), which is a category 3 study in the RMP. The PREMIERE study is a prospective, observational, long-term safety registry of Multiple Sclerosis patients who have participated in cladribine clinical studies. It collected long-term safety data from patients previously participating in 1 out of 5 clinical trials (protocol numbers: 25643, 26593, 27820, 27967 and 28821) and aiming to further characterise the following safety concerns: malignancies, severe infections, Tuberculosis, opportunistic infections, progressive multifocal leukoencephalopathy (PML), severe (grade ≥3) lymphopenia, pregnancy outcomes." Opinion adopted on 28.11.2019.	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Onivyde pegylated liposomal - irinotecan hydrochloride trihydrate - EMEA/H/C/004125/II/0015, Orphan** Les Laboratoires Servier, PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Ingrid Wang, "Submission of an updated RMP version 3.0 in order to update the RMP further to the last	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PSUSA procedures (PSUSA/00010534/201804 and (PSUSA/00010534/201810) and in accordance with GVP Module V Rev.2" Opinion adopted on 28.11.2019. Request for Supplementary Information adopted on 03.10.2019.	
PRAC Led **Qarziba - dinutuximab beta - EMEA/H/C/003918/II/0015, Orphan** EUSA Pharma (Netherlands) B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "To update the RMP for Qarziba to version 9.0 to remove from the RMP as missing information Drug-drug interaction, Use in adolescents, adults and elderly, Use in patients with an ethnic origin other than Caucasian, Use in patients with hepatic and renal impairment and Potential harm from overdose." Request for Supplementary Information adopted on 28.11.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Remsima - infliximab - EMEA/H/C/002576/II/0073** Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of the final clinical study report for C1231001 (CONNECT-IBD) study; a non-interventional study designated as a Post Authorisation Safety Study conducted voluntarily to capture data from real-world clinical practice to characterise the population and document drug utilisation patterns. In addition, available safety data and data on the effectiveness of CT-P13 in the context of standard of care utilisation of Remicade (reference medicinal product) was collected in patients with Crohn's disease or ulcerative colitis." Request for Supplementary Information adopted on 28.11.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Remsima - infliximab - EMEA/H/C/002576/II/0074** Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola,	Request for supplementary information adopted with a specific timetable.

"Submission of the final clinical study report for C1231002 (PERSIST) study, an observational cohort study designed to evaluate real life drug persistence in biologic naive rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis patients receiving CT-P13 or those switched to CT-P13 from stable treatment with Remicade (reference medicinal product)." Request for Supplementary Information adopted on 28.11.2019.	
PRAC Led **Selincro - nalmefene - EMEA/H/C/002583/II/0025** H. Lundbeck A/S, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission for the Final Study Reports for the PASS 15649A: Use of Nalmefene (Selincro in European databases: Cohort design using longitudinal electronic medical records or claims databases and PASS 14910A a non-interventional multi-country prospective cohort study to investigate the pattern of use of Selincro and frequency of selected adverse reactions in routine clinical practice. The RMP version 8.0 (dated 4 November 2019) has been updated accordingly and is therefore acceptable." Opinion adopted on 28.11.2019. Request for Supplementary Information adopted on 31.10.2019, 05.09.2019.	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1680** **Actos-EMEA/H/C/000285/WS1680/0082** **Competact-EMEA/H/C/000655/WS1680/0074** **Glubrava-EMEA/H/C/000893/WS1680/0060** **Glustin-EMEA/H/C/000286/WS1680/0081** **Tandemact-EMEA/H/C/000680/WS1680/0060** Takeda Pharma A/S, Lead Rapporteur: Peter Kiely, Lead PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, "Submission of an updated RMP (version 27.1) in order to update and consolidate within a single RMP the RMPs for Pioglitazone, Pioglitazone/Metformin fixed dose combination (FDC) and Pioglitazone/Glimepiride FDC. The list of safety concerns has also been reviewed and consolidated RMP version updated with	Positive Opinion adopted by consensus on 28.11.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

information agreed/approved as part of the PSUR procedure (EMEA/H/C/PSUSA/00002417/201807) with regards to discontinuation of pioglitazone aRMMs." Opinion adopted on 28.11.2019. Request for Supplementary Information adopted on 03.10.2019.	
PRAC Led **WS1711** **Aluvia-EMEA/H/W/000764/WS1711/0112** **Kaletra-EMEA/H/C/000368/WS1711/0181** AbbVie Deutschland GmbH & Co. KG, Lead PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Jean-Michel Race, "To update the RMP for Kaletra and Aluvia (LPV/r) to version 9.0 in order to comply with the current revision 2 of the template. At the same time, the MAH took the opportunity to review the safety information contained in the RMP, removed an important potential risk of drug interaction with telaprevir and boceprevir (HCV protease inhibitors) and missing information regarding use of LPV/r in elderly patients. In addition, the MAH has added information regarding the requirement for a pharmacovigilance (PV) cohort as part of LEG 121 to the RMP." Request for Supplementary Information adopted on 28.11.2019.	Request for supplementary information adopted with a specific timetable.

B.5.5. CHMP-CAT assessed procedures

Alofisel - darvadstrocel - EMEA/H/C/004258/II/0010/G, Orphan, ATMP Takeda Pharma A/S, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder Request for Supplementary Information adopted on 06.12.2019.	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, "Submission of a group of 3 type II variations	Request for supplementary information adopted with a specific timetable.

(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 Annex II and the Package Leaflet are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to clarify the wording of the indication to include patients over 25 years of age and to introduce some minor editorial corrections throughout the SmPC and the Package Leaflet. The RMP version 2.0 has also been submitted." Request for Supplementary Information adopted on 06.12.2019.	

B.5.7. PRAC assessed ATMP procedures

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

WS1667/G **Corbilta-EMEA/H/C/002785/WS1667/0019/G** **Levodopa/Carbidopa/Entacapone Orion-EMEA/H/C/002441/WS1667/0028/G** **Stalevo-EMEA/H/C/000511/WS1667/0089/G** Orion Corporation, Lead Rapporteur: Outi Mäki-Ikola Opinion adopted on 05.12.2019.	Positive Opinion adopted by consensus on 05.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1684/G **Infanrix hexa-EMEA/H/C/000296/WS1684/0264/G** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 12.12.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1687 **Fiasp-EMEA/H/C/004046/WS1687/0017** **NovoMix-EMEA/H/C/000308/WS1687/0100** **NovoRapid-EMEA/H/C/000258/WS1687/0130** **Ryzodeg-EMEA/H/C/002499/WS1687/0037**	Positive Opinion adopted by consensus on 05.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder Opinion adopted on 05.12.2019. Request for Supplementary Information adopted on 10.10.2019.	
WS1694 **Infanrix hexa-EMEA/H/C/000296/ WS1694/0265** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 12.12.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1706 **Enurev Breezhaler-EMEA/H/C/002691/ WS1706/0030** **Seebri Breezhaler-EMEA/H/C/002430/ WS1706/0030** **Tovanor Breezhaler-EMEA/H/C/002690/ WS1706/0034** Novartis Europharm Limited, Duplicate, Duplicate of Seebri Breezhaler, Lead Rapporteur: Mark Ainsworth, "To introduce a modification of the Instructions for Use (IFU) for the Breezhaler devices affecting the labeling (SmPC and PL) through simplification of its content and layout - condensing textual instructions, optimizing illustrations, and clustering of content to aid comprehension of the procedure of use." Opinion adopted on 12.12.2019. Request for Supplementary Information adopted on 07.11.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1708 **Hirobriz Breezhaler-EMEA/H/C/001211/ WS1708/0055** **Onbrez Breezhaler-EMEA/H/C/001114/ WS1708/0053** **Oslif Breezhaler-EMEA/H/C/001210/ WS1708/0053** Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth, "To introduce a modification of the Instructions for Use (IFU) for the Breezhaler devices affecting the labeling (SmPC and PL) through simplification of its content and layout - condensing textual instructions, optimizing illustrations, and clustering of content to aid comprehension of the procedure of use. In addition both the packaging and IFU in the SmPC and PL have included device-specific information in precise locations in order to meet	

the MDR requirements. This is because the device does not have its own packaging or leaflet. Finally, as notified to the Agency, the MAH took this opportunity to remove unnecessary details from the quality module currently registered for Onbrez/ Hirobriz/ Oslif Breezhaler." Request for Supplementary Information adopted on 07.11.2019.	
WS1712 **Blitzima-EMEA/H/C/004723/WS1712/0028** **Ritemvia-EMEA/H/C/004725/WS1712/0028** **Truxima-EMEA/H/C/004112/WS1712/0031** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz Opinion adopted on 05.12.2019.	Positive Opinion adopted by consensus on 05.12.2019. 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 Environmental Risk Assessment (ERA) report."	Request for supplementary information adopted with a specific timetable.
WS1739 **Fluenz Tetra-EMEA/H/C/002617/WS1739/0096** **Pandemic influenza vaccine H5N1 AstraZeneca-EMEA/H/C/003963/WS1739/0030** AstraZeneca AB, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 12.12.2019.	Positive Opinion adopted by consensus on 12.12.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

WS1757 **Silodosin Recordati-EMEA/H/C/004964/WS1757/0003** **Silodyx-EMEA/H/C/001209/WS1757/0038** **Urorec-EMEA/H/C/001092/WS1757/0041** Recordati Ireland Ltd, Lead Rapporteur: Daniela Melchiorri, "Update of section 5.1 of the SmPC with the cumulative data collected on the effects of silodosin 8 mg hard capsules when	The MAH withdrew the procedure on 05.12.2019.

administered once daily for the treatment of severe patients with Lower Urinary Tract Symptoms (LUTS). A rewording of the indication in section 4.1 of the SmPC is also proposed to better define the indication in line with the studies performed but it doesn't include an extension, modification or restriction of the indication." Withdrawal request submitted on 05.12.2019.	

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

WS1587/G **Abasaglar-EMEA/H/C/002835/WS1587/0028/G** **Humalog-EMEA/H/C/000088/WS1587/0178/G** Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder"Type II variation. B.IV.z. to introduce an additional prefilled pen presentation for Abasaglar, solution for injection (EU/1/14/944/007, EU/1/14/944/008, EU/1/14/944/012, EU/1/14/944/013), Humalog, solution for injection (EU/1/96/007/002, EU/1/96/007/004, EU/1/96/007/020, EU/1/96/007/021 EU/1/96/007/023), Humalog Kwikpen solution for injection (EU/1/96/007/031, EU/1/96/007/032, EU/1/96/007/039, EU/1/96/007/040, EU/1/96/007/041, EU/1/96/007/042) and Humalog Junior Kwikpen, solution for injection (EU/1/96/007/043, EU/1/96/007/044, EU/1/96/007/045). The pack contains 5 pre-filled pens. Type IAIN B. II.e.5.a.1 to request the 2x5 multipack. As a consequence, the following sections were updated 1, 4.2, 4.4, 6.2, 6.4, 6.5, 6.6, 8 of the SmPC in order to add new pre-filled pen presentation; the Package Leaflet and Labelling are updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to make an editorial change (removing comma in SK address in the PL)" Request for Supplementary Information adopted on 14.11.2019, 19.09.2019.	Request by the applicant for an extension of the clock stop to respond to the RSI adopted on 14.11.2019. The CHMP agreed to the clock stop extension.

IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0034, Orphan CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, "Submission of a variation to update the dosing regimen as follows: -21-day prophylaxis regimen with rIX-FP at a dose of 100 IU/kg body weight for patients ≥ 12 years who are well controlled on a 14-day prophylaxis regimen. -10- or 14-day prophylaxis regimen with rIX-FP at a dose of 75 IU/kg body weight for patients < 12 years who are well controlled on a 7-day prophylaxis regimen. This submission also updates the existing population PK model with additional intravenous and subcutaneous (SC) data from the PTPs in the PTP arm of study CSL654_3003 and re-evaluates the covariates that are possible determinants of PK variability." Request for Supplementary Information adopted on 14.11.2019.	Request by the applicant for an extension of the clock stop to respond to the RSI adopted on 14.11.2019. The CHMP agreed to the clock stop extension.
Tyverb - lapatinib - EMEA/H/C/000795/II/0059 Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to update Table 8 based on updated/corrected results from study EGF114299/LAP016A2307, an interventional study with progression free survival rate as primary objective, original report submitted during procedure EMEA/H/C/00795/II/0051." Request for Supplementary Information adopted on 14.11.2019, 26.04.2019.	Request by the applicant for an extension of the clock stop to respond to the RSI adopted on 14.11.2019. The CHMP agreed to the clock stop extension.

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

autologous cd34+ cell enriched population that contains hematopoietic stem and progenitor cells transduced ex vivo using a lentiviral vector encoding the human arylsulfatase a gene - EMEA/H/C/005321, Orphan, ATMP Orchard Therapeutics (Netherlands) BV, treatment of metachromatic leukodystrophy (MLD)	**Accelerated review**
Ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005343 is indicated for active immunization for	**Accelerated review**

prevention of disease caused by Ebola virus	
potassium - EMEA/H/C/005407, Orphan Advicenne Pharma S.A., treatment of distal renal tubular acidosis (dRTA) in patients aged 6 months and older.	
icosapent ethyl - EMEA/H/C/005398 indicated to reduce cardiovascular risk as an adjunct to statin therapy.	
baloxavir marboxil - EMEA/H/C/004974 Treatment of influenza in patients aged 12 and above, including patients at high risk of developing influenza-related complications and for post-exposure prophylaxis of influenza in individuals aged 12	
Ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005337 is indicated for active immunization for prevention of disease caused by Ebola virus (Zaire ebolavirus species)	**Accelerated review**
indacaterol / glycopyrronium / mometasone - EMEA/H/C/005518 treatment of asthma and to reduce asthma exacerbations	

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

Kalydeco - ivacaftor - EMEA/H/C/002494/X/0083/G, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, "Extension application to add a new strength of 75 mg film-coated tablets of ivacaftor to enable administration to patients aged 6 to less than 11 years C.II.6.a - To update sections 4.1, 4.2 and 6.5 the SmPC, and sections 1 and 2 of the PL for the 150 mg film-coated tablet presentations to extend the indication for use in children aged 6 to less than 11 years old in combination with tezacaftor/ivacaftor and to bring it in line with the new dosage form (75 mg film-coated tablets of ivacaftor). The RMP (version 8.6) is updated in accordance. In addition, the MAH took the opportunity to implement minor updates in the Product Information."	

Lacosamide Accord - lacosamide - EMEA/H/C/004443/X/0007

Accord Healthcare S.L.U., Generic, Generic of Vimpat, Rapporteur: John Joseph Borg, PRAC Rapporteur: Ulla Wändel Liminga, "Extension application to introduce a new pharmaceutical form (solution for infusion), a new strength (10mg/ml) and a new route of administration (intravenous use)."

Praluent - alirocumab - EMEA/H/C/003882/X/0054/G

sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege"Grouping of:
• Extension application to introduce a new strength of 300 mg solution for injection in pre-filled pen (in a pack of 1 and 3 pens, EU/1/15/1031/019-20)
• B.II.b.3.z
• B.II.d.2.a
• B.II.e.5.a.1
• B.II.e.5.a.1
• B.II.e.5.a.1
• B.II.e.5.a.1
• B.II.e.5.a.1
• B.II.e.6.b
• B.IV.1.c
Update of sections 1, 2, 4.2, 6.3, 6.5 and 8 of the SmPC; the Labelling and Package Leaflet are updated accordingly.
In addition, the applicant has taken the opportunity to update the contact details of the Maltese local representative in the Package Leaflet, to bring the PI in line with the latest QRD template (v. 10.1) and to introduce editorial changes to modules ."

Symkevi - tezacaftor / ivacaftor - EMEA/H/C/004682/X/0015/G, Orphan

Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, "Extension application to add a new strength of 50/75 mg film-coated tablets of tezacaftor/ivacaftor to enable administration to patients aged 6 to less than 11 years.
C.II.6.a - To update sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.1 of the SmPC, and sections 2, 3 and 6 of the PL for the 100/150 mg film-coated tablet presentations to extend the indication for use in children aged 6 to less than 11 years old in combination with ivacaftor and to bring it in

line with the new dosage form (50/75 mg film-coated tablets tezacaftor/ivacaftor).
The RMP (version 2.1) is updated in accordance.
In addition, the MAH took the opportunity to implement minor updates and formatting changes in the Product Information."

TEPADINA - thiotepa - EMEA/H/C/001046/X/0036, Orphan
ADIENNE S.r.l., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Extension application to introduce a new pharmaceutical form associated with new strength (400 mg powder and solvent for solution for infusion)."

Trimbow - beclometasone dipropionate / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004257/X/0008/G
Chiesi Farmaceutici S.p.A., Rapporteur: Janet Koenig, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Jan Neuhauser, "Extension application to introduce a new strength (172 µg / 5 µg / 9 µg) grouped with a type II variation (C.I.6.a) to add a new indication (asthma). The RMP (version 6.1) is updated in accordance."
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Trulicity - dulaglutide - EMEA/H/C/002825/X/0045
Eli Lilly Nederland B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Ilaria Baldelli, "Extension application to introduce two new strengths of 3 mg and 4.5 mg solution for injection."

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

indacaterol / mometasone furoate - EMEA/H/C/005067
treatment of asthma
List of Questions adopted on 19.09.2019.

budesonide / glycopyrronium / formoterol fumarate dihydrate - EMEA/H/C/004983
as a maintenance treatment in adult patients with moderate to very severe chronic obstructive pulmonary disease (COPD)
List of Questions adopted on 26.04.2019.

indacaterol / glycopyrronium / mometasone - EMEA/H/C/005061
treatment of asthma and to reduce asthma exacerbations
List of Questions adopted on 19.09.2019.

Halimatoz - adalimumab - EMEA/H/C/004866/X/0013
Sandoz GmbH, Duplicate, Duplicate of Hyrimoz, Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga, "Extension application to add a new strength of 20mg (20mg/0.4ml) for Halimatoz solution for injection in pre-filled syringe.
The RMP (version 2.0) is updated in accordance.
The MAH took also the opportunity to consolidate the RMP with changes approved in two other procedures (WS1565 and IB/11) and to align the PI with the latest QRD template (v.10.1)."
List of Questions adopted on 14.11.2019.

Hefiya - adalimumab - EMEA/H/C/004865/X/0013
Sandoz GmbH, Duplicate, Duplicate of Hyrimoz, Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga, "Extension application to add a new strength of 20mg (20mg/0.4ml) for Hefiya solution for injection in pre-filled syringe.
The RMP (version 2.0) is updated in accordance.
The MAH took also the opportunity to consolidate the RMP with changes approved in two other procedures (WS1565 and IB/10) and to align the PI with the latest QRD template (v.10.1)."
List of Questions adopted on 14.11.2019.

Hyrimoz - adalimumab - EMEA/H/C/004320/X/0013
Sandoz GmbH, Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga, "Extension application to add a new strength of 20mg (20mg/0.4ml) for Hyrimoz solution for injection in pre-filled syringe.
The RMP (version 2.0) is updated in accordance.
The MAH took also the opportunity to consolidate the RMP with changes approved in two other procedures (WS1565 and IB/11) and to align the PI with the latest QRD template (v.10.1)."
List of Questions adopted on 14.11.2019.

pretomanid - EMEA/H/C/005167, Orphan

FGK Representative Service GmbH, treatment of tuberculosis
List of Questions adopted on 25.07.2019.

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

Ceplene - histamine dihydrochloride - EMEA/H/C/000796/S/0039
Noventia Pharma Srl, Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald

Defitelio - defibrotide - EMEA/H/C/002393/S/0045, Orphan
Gentium S.r.l., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Obizur - susoctocog alfa - EMEA/H/C/002792/S/0028
Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski

Orphacol - cholic acid - EMEA/H/C/001250/S/0033, Orphan
Laboratoires CTRS, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Sofia Trantza

Vedrop - tocofersolan - EMEA/H/C/000920/S/0035
Recordati Rare Diseases, Rapporteur: Melinda Sobor, PRAC Rapporteur: Melinda Palfi

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

Deltyba - delamanid - EMEA/H/C/002552/R/0041, Orphan
Otsuka Novel Products GmbH, Rapporteur: Koenraad Norga, PRAC Rapporteur: Jean-Michel Dogné

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

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

Lorviqua - lorlatinib -

EMEA/H/C/004646/R/0004
Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Nikica Mirošević Skvrce

Ondexxya - andexanet alfa - EMEA/H/C/004108/R/0004
Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst

Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (H5N1) (live attenuated, nasal) - EMEA/H/C/003963/R/0031
AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sonja Hrabcik

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

Rubraca - rucaparib - EMEA/H/C/004272/R/0016
Clovis Oncology Ireland Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Annika Folin

WAYLIVRA - volanesorsen - EMEA/H/C/004538/R/0003, Orphan
Akcea Therapeutics Ireland Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Martin Huber

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

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: Paula Van Hennink

and Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski

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

Cosentyx - secukinumab - EMEA/H/C/003729/II/0057	Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, PRAC Rapporteur: Eva A. Segovia, "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."
Deltyba - delamanid - EMEA/H/C/002552/II/0040, Orphan	Otsuka Novel Products GmbH, Rapporteur: Koenraad Norga, PRAC Rapporteur: Jean-Michel Dogné, "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."
Imfinzi - durvalumab - EMEA/H/C/004771/II/0014/G	AstraZeneca AB, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: David Olsen, "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.”	
Sivextro - tedizolid phosphate - EMEA/H/C/002846/II/0035 Merck Sharp & Dohme B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maria del Pilar Rayon, “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”	
Xolair - omalizumab - EMEA/H/C/000606/II/0101 Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, “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."

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

Pfizer Ireland Pharmaceuticals, Rapporteur: Bjorg Bolstad, Co-Rapporteur: Romaldas Mačiulaitis, "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."

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

AstraZeneca AB, Lead Rapporteur: Kristina Dunder, Lead Co-Rapporteur: Martina Weise, Lead PRAC Rapporteur: Annika Folin, "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)

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Bemfola - follitropin alfa - EMEA/H/C/002615/II/0022

Gedeon Richter Plc., Rapporteur: Paula

Boudewina van Hennik

Brineura - cerliponase alfa - EMEA/H/C/004065/II/0019, Orphan
BioMarin International Limited, Rapporteur: Martina Weise

Bydureon - exenatide - EMEA/H/C/002020/II/0067
AstraZeneca AB, Rapporteur: Kristina Dunder

CooperSurgical Inc ART Media - human albumin solution - EMEA/H/D/002307/II/0006/G
BSI Group, Rapporteur: Kristina Dunder

Delstrigo - doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746/II/0012/G
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson

Delstrigo - doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746/II/0013/G
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson

Dupixent - dupilumab - EMEA/H/C/004390/II/0024/G
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus

Fasenra - benralizumab - EMEA/H/C/004433/II/0025/G
AstraZeneca AB, Rapporteur: Fátima Ventura

Fiasp - insulin aspart - EMEA/H/C/004046/II/0018/G
Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Amelia Cupelli

GONAL-f - follitropin alfa - EMEA/H/C/000071/II/0148
Merck Europe B.V., Rapporteur: Johann Lodewijk Hillege

Humalog - insulin lispro - EMEA/H/C/000088/II/0181
Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder

IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0037, Orphan
CSL Behring GmbH, Rapporteur: Jan Mueller-

Berghaus

IKERVIS - ciclosporin -
EMEA/H/C/002066/II/0018
Santen Oy, Rapporteur: Peter Kiely
Request for Supplementary Information adopted on 16.01.2020.

Kanuma - sebelipase alfa -
EMEA/H/C/004004/II/0023, Orphan
Alexion Europe SAS, Rapporteur: Bart Van der Schueren

Keytruda - pembrolizumab -
EMEA/H/C/003820/II/0084
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri

Kineret - anakinra -
EMEA/H/C/000363/II/0072
Swedish Orphan Biovitrum AB (publ), Rapporteur: Mark Ainsworth

Lemtrada - alemtuzumab -
EMEA/H/C/003718/II/0029/G
Sanofi Belgium, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth

Nimenrix - Meningococcal group A, C, W135 and Y conjugate vaccine -
EMEA/H/C/002226/II/0094/G
Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad

Nimenrix - Meningococcal group A, C, W135 and Y conjugate vaccine -
EMEA/H/C/002226/II/0095/G
Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad

Nivestim - filgrastim -
EMEA/H/C/001142/II/0059
Pfizer Europe MA EEIG, Rapporteur: Outi Mäki-Ikola

Nplate - romiplostim -
EMEA/H/C/000942/II/0074
Amgen Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro

Onpattro - patisiran -
EMEA/H/C/004699/II/0011/G, Orphan
Alnylam Netherlands B.V., Rapporteur: Kristina Dunder

Pifeltro - doravirine -

EMEA/H/C/004747/II/0010/G
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson

Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0155
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Rizmoic - naldemedine - EMEA/H/C/004256/II/0005/G
Shionogi B.V., Rapporteur: Mark Ainsworth

SonoVue - sulphur hexafluoride - EMEA/H/C/000303/II/0039/G
Bracco International B.V., Rapporteur: Alexandre Moreau

Spectrila - asparaginase - EMEA/H/C/002661/II/0015/G
medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Andrea Laslop

Starlix - nateglinide - EMEA/H/C/000335/II/0036/G
Novartis Europharm Limited, Rapporteur: Outi Mäki-Ikola

Stelara - ustekinumab - EMEA/H/C/000958/II/0075
Janssen-Cilag International NV, Rapporteur: Jayne Crowe

Trazimera - trastuzumab - EMEA/H/C/004463/II/0011
Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus

Ultomiris - ravulizumab - EMEA/H/C/004954/II/0003/G
Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez

Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0052/G
MCM Vaccine B.V., Rapporteur: Bart Van der Schueren

VIZAMYL - flutemetamol (18F) - EMEA/H/C/002557/II/0022/G
GE Healthcare AS, Rapporteur: Maria

Concepcion Prieto Yerro

Xadago - safinamide -
EMEA/H/C/002396/II/0034
Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege

Ziextenzo - pegfilgrastim -
EMEA/H/C/004802/II/0004
Sandoz GmbH, Rapporteur: Andrea Laslop

Ziextenzo - pegfilgrastim -
EMEA/H/C/004802/II/0005/G
Sandoz GmbH, Rapporteur: Andrea Laslop

WS1691/G
Infanrix hexa-EMEA/H/C/000296/
WS1691/0266/G
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

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

WS1740
ProQuad-EMEA/H/C/000622/WS1740/
0136
Zostavax-EMEA/H/C/000674/WS1740/
0126
MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus

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

Hexacima-EMEA/H/C/002702/WS1728/
0094/G
Hexaxim-EMEA/H/W/002495/WS1728/
0099/G
Hexyon-EMEA/H/C/002796/WS1728/

0098/G
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

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

Ambirix - hepatitis A (inactivated) and hepatitis B (rDNA) vaccine (adsorbed) - EMEA/H/C/000426/II/0105
GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of sections 4.2 and 5.1 of the Ambirix SmPC in order to reflect information on the long-term antibody persistence and immune memory up to 15 years after primary immunisation of adolescents, based on data from the Phase IV study HAB-084 EXT Y11-15 (An open, long-term follow-up study to evaluate long-term antibody persistence and immune memory between 11 and 15 years after the primary study HAB-084). The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1 and make some minor editorial changes. Furthermore, the MAH took the opportunity to update Annex II with regards to PSUR requirements."

Avamys - fluticasone furoate - EMEA/H/C/000770/II/0040
GlaxoSmithKline (Ireland) Limited, Rapporteur: 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."

BiResp Spiromax - budesonide / formoterol - EMEA/H/C/003890/II/0030
Teva Pharma B.V., Duplicate, Duplicate of DuoResp Spiromax, Rapporteur: John Joseph Borg, "Update of sections 4.2, 4.4 and 6.6 of the SmPC to add the use as reliever for allergen- and exercise-induced bronchoconstriction following assessment of the same change for the reference product Symbicort Turbohaler 160 mcg/4.5 mcg; the

Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to introduce some minor editorial amendments in the PI for the following languages: FR, NO and PT."

CABOMETYX - cabozantinib - EMEA/H/C/004163/II/0012

Ipsen Pharma, Rapporteur: Bjorg Bolstad, "Update of section 4.4 of the SmPC to include the risk of Osteonecrosis as a warning. Update of section 4.8 of the SmPC based on the Company Core Safety Information:
- to remove Anaemia, Oral pain and Dry mouth from the list of adverse reactions (ADRs), - to add Dysphagia and Hyperkeratosis to the existing ADR, - to replace Peripheral sensory neuropathy by Peripheral neuropathy in order to reflect the broader medical concept and to add DVT (Deep vein thrombosis) to the existing ADR venous thrombosis in order to alert prescribers to the most frequently reported type of venous thrombosis. Changes to the frequency categorisation of some ADRs are also proposed based on new pooled data. The Package Leaflet is updated accordingly. The MAH took the opportunity to align the product Information with the QRDv10.1 and update the local representative information of Hungary."

Cometriq - cabozantinib - EMEA/H/C/002640/II/0035, Orphan

Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.2 to introduce a clarification in alignment with Cabometyx; update of section 4.4 of the SmPC to include the addition of the risk of diarrhoea and additional test to the existing risks of thromboembolic events, haemorrhage, wound complications and RPLS (Reversible posterior leukoencephalopathy syndrome). Update of section 4.8 of the SmPC, based on the Company Core Safety Information, to remove oropharyngeal pain from the list of adverse reactions (ADRs) and to add DVT (Deep vein thrombosis) to the existing ADR venous thrombosis in order to alert prescribers to the most frequently reported type of venous thrombosis. Changes to the frequency categorisation of some ADRs are also proposed based on new pooled data. The Package Leaflet

is updated accordingly. The MAH took the opportunity to align the product Information with the QRDv10.1 and update the local representative information of Hungary.”
DuoResp Spiromax - budesonide / formoterol - EMEA/H/C/002348/II/0030 Teva Pharma B.V., Rapporteur: John Joseph Borg, “Update of sections 4.2, 4.4 and 6.6 of the SmPC to add the use as reliever for allergen- and exercise-induced bronchoconstriction following assessment of the same change for the reference product Symbicort Turbohaler 160 mcg/4.5 mcg; the Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to introduce some minor editorial amendments in the PI for the following languages: FR, NO and PT.”
Emgality - galcanezumab - EMEA/H/C/004648/II/0009 Eli Lilly Nederland B.V., Rapporteur: Daniela Melchiorri, “Update of sections 4.2 and 5.1 of the SmPC following final results from a CONQUER study (A Randomized, Double-Blind, Placebo-Controlled Study of Galcanezumab in Adults with Treatment-Resistant Migraine; the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity correct Slovakian contact information in the Package Leaflet.”
Evicel - human fibrinogen / human thrombin - EMEA/H/C/000898/II/0078 Omrix Biopharmaceuticals N. V., Rapporteur: Jan Mueller-Berghaus, “Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information following the final results from study 400-12-006 listed as in the paediatric investigation plan; this is a prospective, randomized, controlled study evaluating Evicel (fibrin sealant) as an adjunct to hemostasis during abdominal, retroperitoneal, pelvic or thoracic (non-Cardiac) surgery in pediatric patients. The Package Leaflet is updated accordingly.”
ILARIS - canakinumab - EMEA/H/C/001109/II/0067 Novartis Europharm Limited, Rapporteur: Jan

Mueller-Berghaus, "Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC and relevant sections of the PL with the results of study CACZ885GDE01T (a Multi-centre, phase II, randomized, placebo-controlled trial of Ilaris for the Treatment of adult-onset Still's Disease) and an updated pooled analyses of Systemic Juvenile Idiopathic Arthritis (SJIA) studies CACZ885A2203 (safety only), CACZ885G2305, CACZ885G2301, CACZ885G2301E1, CACZ885G2306 and CACZ885G1301."	
Lymphoseek - tilmanocept - EMEA/H/C/002085/II/0019 Norgine B.V., Rapporteur: Peter Kiely, "To update SmPC sections 4.2, 4.4 and 4.8 in order to correct the radiation dose for patients with hepatic and renal impairment, and section 12 in order to change the labelling-activity that can be added to the vial. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1."	
Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0029 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Jean-Michel Race, "Update of sections 4.2 and 5.1 of the Maviret SmPC to shorten the treatment duration in treatment-naïve subjects with compensated cirrhosis and HCV GT3 infection, from 12 to 8 weeks, based on second interim results from study M16-135: A Single Arm, Open-Label Study to Evaluate the Efficacy and Safety of Glecaprevir (GLE)/Pibrentasvir (PIB) in Treatment Naïve Adults with Chronic Hepatitis C Virus (HCV) Genotype 1 - 6 Infection and Compensated Cirrhosis (EXPEDITION-8)."	
Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0030 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Jean-Michel Race, "Update of section 4.2 of the Maviret SmPC to improve the clarity of the dosing instruction, based on post-marketing data and pharmacokinetic simulations."	
Menveo - Meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/001095/II/0093 GSK Vaccines S.r.l, Rapporteur: Johann	

Lodewijk Hillege, "Update of section 4.8 of the SmPC in order to include lymphadenopathy as a new expected adverse reaction after vaccination in Post-marketing experience based on final results from study V59_77 and substantiated by supportive clinical data only to establish frequency, following CHMP assessment of procedure P46/039.
Section 4 of the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1."

Nimenrix - Meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0096
Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad, "Update of section 5.1 of the SmPC based on final results from 3 extended follow-up paediatric studies (MenACWY-TT-099, MenACWY-TT-100 and MenACWY-TT-101) as well as paediatric study MenACWY-TT-102. Studies MenACWY-TT-099, MenACWY-TT-100 and MenACWY-TT-102 were previously submitted (P46 054, P46 053 and P46 052, respectively).
The Package Leaflet is updated accordingly. In addition, the opportunity is taken to bring the PI in line with the latest QRD template version 10.1."

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."

Olanzapine Apotex - olanzapine - EMEA/H/C/001178/II/0037
Apotex Europe BV, Generic, Generic of Zyprexa, Rapporteur: John Joseph Borg, "Update of sections 4.8 and 4.4 in order to add information regarding the risk of metabolic syndrome with the use of olanzapine, based on review of the available data."

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."	
Praluent - alirocumab - EMEA/H/C/003882/II/0053 sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Submission of the final report from study DFI14223, listed as a category 3 study in the RMP in order to fulfil MEA 029. The submission serves also to comply with article 46 of the regulation (EC) N° 1901/2206 (as amended) on medicinal products for paediatric use as study DFI14223 is also part of the PIP (MEA-001169-PIP01-11). This is an 8-week open label, sequential, repeated dose-finding study to evaluate the efficacy, safety and PK profile of alirocumab in children and adolescents with heterozygous familial hypercholesterolemia followed by an extension phase."	
Tafinlar - dabrafenib - EMEA/H/C/002604/II/0042 Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information on pulmonary embolism/deep vein thrombosis (PE/DVT) to be renamed to a broader term venous thromboembolism (VTE) based on cumulative analysis of data received from clinical trials and the post-marketing setting. The Package Leaflet is updated accordingly."	
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0032 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to update the safety information and include blood alkaline phosphatase increased, blood creatinine increased and alopecia as adverse drug reactions for atezolizumab given in combination with other medicinal products. The safety update is based on the review of safety data from a pooled population. In addition, instruction for treatment interruption for neutropenia and peripheral neuropathies	

when atezolizumab is used in combination with nab-paclitaxel in metastatic triple negative breast cancer are being revised in section 4.4 of the SmPC. The MAH also took the opportunity of this variation to introduce minor editorial comments. The Package Leaflet is updated accordingly."	
Twinrix Adult - hepatitis A (inactivated) and hepatitis B (rDNA) vaccine (adsorbed) - EMEA/H/C/000112/II/0140 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of sections 4.2 and 5.1 of the Twinrix Adult SmPC in order to reflect information on the long-term antibody persistence and immune memory up to 20 years after primary immunisation of adults, based on data from two phase IV long-term follow-up extension studies, HAB-028 EXT Y16-20 (An open, single centre study to evaluate the long-term antibody persistence and immune memory between 16 and 20 years after the primary study HAB-028) and HAB-032 EXT Y16-20 (An open single centre study to evaluate the long-term antibody persistence and immune memory between 16 and 20 years after the primary study HAB-032). 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."	
Twinrix Paediatric - hepatitis A (inactivated) and hepatitis B (rDNA) vaccine (adsorbed) - EMEA/H/C/000129/II/0141 GlaxoSmithkline Biologicals SA, Duplicate, Duplicate of Twinrix Adult, Rapporteur: Bart Van der Schueren, "Update of sections 4.2 and 5.1 of the Twinrix Paediatric SmPC in order to reflect information on the long-term antibody persistence and immune memory up to 15 years after primary immunisation of adolescents, based on data from Phase IV study HAB-084 EXT Y11-15 (An open, long-term follow-up study to evaluate long-term antibody persistence and immune memory between 11 and 15 years after the primary study HAB-084). 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 implement some minor editorial	

changes."

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 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."

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."

Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0020/G, Orphan

Ipsen Pharma, Rapporteur: Martina Weise, "To update sections 4.5 and 5.2 of the SmPC to update the information on the interaction with Carboxylesterases 2 inhibitors based on final results from the non-clinical study IPS000610; the Package Leaflet is updated accordingly. Additionally, the final study reports are submitted from studies XT173065, XT175092 and XT174037, with no subsequent changes to the PI. The MAH took the opportunity to update the PI to the latest QRD template v10.1."

Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0049

Pfizer Ireland Pharmaceuticals, Rapporteur: Alar Irs, "To add a warning pertaining to severe cutaneous adverse reactions (SCARs) and beta-lactam antibiotics in section 4.4 of the

ceftaroline fosamil/Zinforo SmPC, as a result of a summary safety review being published by Health Canada regarding beta-lactam antibiotics and the potential risk of severe skin side effects. The PL is proposed to be updated accordingly."	
WS1727 **Januvia-EMEA/H/C/000722/WS1727/0068** **Ristaben-EMEA/H/C/001234/WS1727/0060** **TESAVEL-EMEA/H/C/000910/WS1727/0068** **Xelevia-EMEA/H/C/000762/WS1727/0072** Merck Sharp & Dohme B.V., Lead Rapporteur: Johann Lodewijk Hillege, "Update of the SmPC sections 4.2, 4.8, 5.1 and 5.2, to include the data from paediatric study P083 (EMEA-000470-PIP01-08-M11)."	
WS1743 **Komboglyze-EMEA/H/C/002059/WS1743/0047** **Onglyza-EMEA/H/C/001039/WS1743/0049** **Qtern-EMEA/H/C/004057/WS1743/0026** AstraZeneca AB, Lead Rapporteur: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC in order to add a new warning about Bullous pemphigoid and section 4.8 of the SmPC to include Bullous pemphigoid as a new ADR with a frequency of 'Not known'. The Package Leaflet has been updated accordingly."	
WS1750 **Levitra-EMEA/H/C/000475/WS1750/0066** **Vivanza-EMEA/H/C/000488/WS1750/0062** Bayer AG, Lead Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 4.3 (contraindications) and section 4.5 (Interaction with other medicinal products and other forms of interaction) of the vardenafil SmPCs and relevant sections of the PILs to expand the information regarding vardenafil interactions with P-glycoprotein (P-gp) and cytochrome P450 (CYP) as a result of a general review of vardenafil pharmacokinetic properties."	
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."

B.6.10. CHMP-PRAC assessed procedures

Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0084/G

UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information following the final results from studies PS0002 (CIMPASI-2), PS0003 (CIMPACT) and PS0005 (CIMPASI-1) listed as category 3 studies in the RMP; these are results from the open label treatment periods assessing the safety and efficacy of long term use of certolizumab pergola in psoriasis. The RMP version 16.0 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."

Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0113

Genzyme Europe BV, PRAC Rapporteur: Liana Gross-Martirosyan, "Submission of the final report from study listed as a category 3 study in the RMP. This is a postauthorisation study (AGALSC08994) on Fabrazyme (agalsidase beta) home infusion educational materials

effectiveness evaluation: a survey of healthcare providers and patients / caregivers. The RMP version 2 has also been submitted accordingly and to comply with the Good Pharmacovigilance Practice (GVP) Module V Rev. 2 template and information on study (AGAL02603) and the Fabry Registry/Pregnancy Sub-registry (AGAL 19211)."

Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0043

GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jean-Michel Dogné, "Update of section 4.5 of the SmPC in order to add immunogenicity data following the interim results from study Malaria-073 listed as a category 3 study in the RMP; this is a phase 3 randomized, open, controlled study to evaluate the immunogenicity and safety of Mosquirix when administered as a primary vaccination schedule at 6, 7.5 and 9 months-of-age, with or without co-administration of measles and rubella and yellow fever vaccines, to children living in sub-Saharan Africa. The RMP version 5.1 has also been submitted. In addition, the Scientific opinion Holder (SOH) took the opportunity to bring the PI in line with the latest QRD template version 10.1."

Ogivri - trastuzumab - EMEA/H/C/004916/II/0009

Mylan S.A.S, Rapporteur: Koenraad Norga, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Submission of the final clinical study report (MYL-Her-3001) (a Multicenter, Double-blind, Randomized, Parallel-group, Phase III Study of the Efficacy and Safety of Hercules Plus Taxane Versus Herceptin Plus Taxane as First Line Therapy in Patients With HER2-Positive Metastatic Breast Cancer) with the final overall survival (OS). The RMP version 3 has also been submitted."

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."

VIZAMYL - flutemetamol (18F) - EMEA/H/C/002557/II/0021

GE Healthcare AS, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Martin Huber, "Update of sections 4.4 and 5.1 of the SmPC in order to include information on the possibility of quantitative assessment. The evidence based submitted consists of published studies.
Submission of an updated RMP version 2.1 to introduce a new educational programme as a consequence of the changes above and to align with the new RMP template."

Zometa - zoledronic acid - EMEA/H/C/000336/II/0091

Novartis Europharm Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, "Update of sections 4.4 and 5.1 of the SmPC in order to update the safety information on ONJ based on final results from study CZOL446EUS122 listed as a category 3 study in the RMP; this is a non-interventional, prospective, observational, multicenter cohort study to assess the incidence of ONJ in cancer patients with bone metastases starting zoledronic acid treatment.
The RMP version 12 has also been submitted."

WS1724
Blitzima-EMEA/H/C/004723/WS1724/0029
Ritemvia-EMEA/H/C/004725/WS1724/0029
Truxima-EMEA/H/C/004112/WS1724/0032

Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz, Lead PRAC Rapporteur: Hans Christian Siersted, "Submission of the final report from study CT-P10 3.3. This is a category

3 study, a Phase 1/3, randomised, parallel-group, active-controlled, double-blind study to demonstrate equivalence of pharmacokinetics and non-inferiority of efficacy for CT-P10 in comparison with Rituxan. Each Administered in Combination With Cyclophosphamide, Vincristine, and Prednisone (CVP) in Patients With Advanced Follicular Lymphoma. The RMP version 9.1 has also been submitted in order to align the safety concerns with those of MabThera and to incorporate the final results of Study CT-P10 3.3."

WS1756
Lixiana-EMEA/H/C/002629/WS1756/0025
Roteas-EMEA/H/C/004339/WS1756/0012
Daiichi Sankyo Europe GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Adrien Inoubli, "Update of section 4.2, 4.4 and 5.1 of the SmPC in order to update the safety information based on final results from the post-authorisation efficacy study DU176b-C-E314 (Evaluation of Edoxaban in Anticoagulant Naïve Patients with Non-Valvular Atrial Fibrillation [NVAF] and High Creatinine Clearance [protocol MEA004]). This is a study to compare the exposure of edoxaban 75 mg once daily dose to edoxaban 60 mg once daily dose in NVAF anticoagulant-naïve patients with CHADS2 score of ≥2 and CrCL >100 mL/min treated for up to 12 months. The RMP version 9.0 has also been submitted. In addition, the worksharing applicant 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 and to provide updates due to corrections of typos in several language versions of the Product Information."

B.6.11. PRAC assessed procedures

PRAC Led
BLINCYTO - blinatumomab -
EMEA/H/C/003731/II/0034/G, Orphan
Amgen Europe B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Eva Jirsová, PRAC-CHMP liaison: Ondřej Slanař, "Submission of the final reports from studies 20150163 and 20150228 assessed the effectiveness of Blincyto additional risk minimization measures for

healthcare professionals (study 20150163) and patients/caregivers (study 20150228) listed as a category 3 post-authorization safety studies (PASS) in the Risk Management Plan (RMP)."

PRAC Led

Docetaxel Zentiva - docetaxel - EMEA/H/C/000808/II/0061

Zentiva, k.s., Informed Consent of Taxotere, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 1.1 in order to revise the list of safety concerns in line with the GVP Module V Rev.2 and to complete Part II modules."

PRAC Led

GONAL-f - follitropin alfa - EMEA/H/C/000071/II/0147

Merck Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of RMP version 2.1 in order to:
- update as per GVP module V, rev 2.0.1 template;
- remove important identified risks of "Ovarian hyperstimulation syndrome (OHSS)", "Thromboembolic events usually with OHSS", "Hypersensitivity reactions, including anaphylactic reactions", "Asthma aggravated/exacerbation", "Multiple pregnancies" and "Gynecomastia in males";
- remove the important potential risks of "Breast cancer", "Other reproductive system cancers", "Ectopic pregnancy" and "Congenital abnormalities";
- increase the age from 40 to 42 years for the missing information of "Women older than 40 years"."

PRAC Led

Nulojix - belatacept - EMEA/H/C/002098/II/0063/G

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "Submission of the final report from studies IM103075 and IM103076 listed as category 3 studies in the RMP. Study IM103075 is a prospective cohort study to assess the

association between belatacept use and risk of post-transplant lymphoproliferative disorder (PTLD) in renal transplant recipients in the United States (US). IM103076 is a prospective patient registry study to estimate the incidence rates of confirmed PTLD, CNS PTLD and progressive multifocal leukoencephalopathy (PML) in adult renal transplant recipients treated with belatacept in the US. The RMP version 17.0 has also been submitted to reflect the completion of both studies and to make some administrative updates."

PRAC Led

Ozurdex - dexamethasone - EMEA/H/C/001140/II/0037

Allergan Pharmaceuticals Ireland, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of an updated RMP version 9.0 in order to reflect increased knowledge of the product and align to the new RMP template."

PRAC Led

Pergoveris - follitropin alfa / lutropin alfa - EMEA/H/C/000714/II/0066

Merck Europe B.V., Rapporteur: Mark Ainsworth, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Mark Ainsworth, "Submission of an updated RMP version 5.3 in order to:

• adapt to the RMP template as per Good Pharmacovigilance Practice (GVP) Module V, rev 2

• remove the important identified risks of "Ovarian Hyperstimulation Syndrome (OHSS)", "Thromboembolic events, usually with OHSS" and "Hypersensitivity reactions"

• remove the important potential risks of "Breast cancer", "Ovarian cancer", Endometrial cancer", "Congenital anomalies" and "Malignant melanoma""

PRAC Led

Revestive - teduglutide - EMEA/H/C/002345/II/0050, Orphan

Shire Pharmaceuticals Ireland Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 9 in order to update the list of safety

concers."

PRAC Led
Taxotere - docetaxel -
EMEA/H/C/000073/II/0134
Aventis Pharma S.A., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 1.1 in order to revise the list of safety concerns in line with the GVP Module V Rev.2 and to complete Part II modules."

PRAC Led
Torisel - temsirolimus -
EMEA/H/C/000799/II/0078
Pfizer Europe MA EEIG, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of an updated RMP version 4.0 in order to remove the safety concerns: "missing information", "risk of cardiovascular events in patients with coexisting cardiovascular conditions", "reproductive toxicity" from the RMP and to comply with the Module V, Risk Management Systems Rev 2 (as requested through EMEA/H/C/PSUSA/00002887/201803)."

PRAC Led
WS1653
Enbrel-EMEA/H/C/000262/WS1653/0230
LIFMIOR-EMEA/H/C/004167/WS1653/
0024
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 the second 5-year report from the British Society for Rheumatology Biologics Register (BSRBR, also referred as study B1801309) listed as a category 3 study in the RMP. This is a prospective observational cohort study which investigates the long-term outcomes of patients with rheumatoid arthritis treated with etanercept with particular reference to safety."

PRAC Led
WS1713
Kivexa-EMEA/H/C/000581/WS1713/0083
Triumeq-EMEA/H/C/002754/WS1713/
0075
Trizivir-EMEA/H/C/000338/WS1713/0115
Ziagen-EMEA/H/C/000252/WS1713/0109

ViiV Healthcare B.V., Lead PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Jean-Michel Race, "Submission of updated RMPs in order to remove the additional risk minimisation measure of provision of abacavir hypersensitivity education materials for healthcare professionals. Annex II is updated accordingly."

PRAC Led

WS1748

Lacosamide UCB-EMEA/H/C/005243/WS1748/0003

Vimpat-EMEA/H/C/000863/WS1748/0085

UCB Pharma S.A., Lead PRAC Rapporteur: Ulla Wändel Liminga, "To provide an updated RMP to propose changes of due dates for three category 3 studies as follows:
- SP848 due date change from 'Nov2021' to 'Dec2021';
- EP0012 due date change from 'Nov2022' to 'Dec2022';
- EP0034 due date change from 'May2024' to 'Aug2024';
Amended protocols for the studies SP848 and EP0034 in Annex 3 have also been provided."

PRAC Led

WS1755

Cymbalta-EMEA/H/C/000572/WS1755/0083

Duloxetine Lilly-EMEA/H/C/004000/WS1755/0020

Xeristar-EMEA/H/C/000573/WS1755/0086

Yentreve-EMEA/H/C/000545/WS1755/0068

Eli Lilly Nederland B.V., Duplicate, Duplicate of Ariclaim, Yentreve, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "As agreed in the procedure WS-1527G in order to address the foetal outcomes, submission of the final report from study FIJ-MC-B059 'Observational Study to Assess Fetal Outcomes Following Maternal Exposure to Duloxetine' and the revised final report from study Study F1J-MC-B057 'Observational Studies to Assess Maternal and Fetal Outcomes Following Exposure to Duloxetine'."

PRAC Led

WS1760

Lixiana-EMEA/H/C/002629/WS1760/0024

Roteas-EMEA/H/C/004339/WS1760/0011

Daiichi Sankyo Europe GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final study report from study ETNA-DUS: a retrospective drug utilisation chart review study listed as a category 3 study in the RMP. The Edoxaban Treatment in Routine Clinical Practice Drug Utilisation Study (ETNA-DUS) was designed to gain insight on how edoxaban is used in real practice. The ETNA-DUS intends to help identify prescription patterns and the effectiveness of the educational programs"

B.6.12. CHMP-CAT assessed procedures

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0017/G, Orphan, ATMP

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

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

WS1696/G

Glyxambi-EMEA/H/C/003833/WS1696/0025/G

Jentadueto-EMEA/H/C/002279/WS1696/0053/G

Trajenta-EMEA/H/C/002110/WS1696/0040/G

Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege

WS1698/G

Genvoya-EMEA/H/C/004042/WS1698/0066/G

Stribild-EMEA/H/C/002574/WS1698/0109/G

Tybost-EMEA/H/C/002572/WS1698/0052/G

Gilead Sciences Ireland UC, Lead Rapporteur: Bruno Sepodes

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

WS1703/G
Advagraf-EMEA/H/C/000712/WS1703/0055/G
Modigraf-EMEA/H/C/000954/WS1703/0034/G
Astellas Pharma Europe B.V., Lead Rapporteur: Jayne Crowe

WS1715/G
Ebymect-EMEA/H/C/004162/WS1715/0041/G
Xigduo-EMEA/H/C/002672/WS1715/0052/G
AstraZeneca AB, Lead Rapporteur: Kristina Dunder

WS1719
Zalviso-EMEA/H/C/002784/WS1719/0014
Grunenthal GmbH, Lead Rapporteur: Milena Stain, "To update section 4.4 of the SmPC in order to include new prescribing information on other side effects including central sleep apnea (CSA) and drug interactions following a Drug Safety Communication by FDA on 9 April 2019. Section 2 of the Package Leaflet has been updated accordingly."

WS1723
Advate-EMEA/H/C/000520/WS1723/0103
ADYNOVI-EMEA/H/C/004195/WS1723/0009
Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus

WS1725
Infanrix hexa-EMEA/H/C/000296/WS1725/0267
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1730/G
Filgrastim Hexal-EMEA/H/C/000918/WS1730/0053/G

Zarzio-
EMEA/H/C/000917/WS1730/0054/G
Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege

WS1741
Revatio-EMEA/H/C/000638/WS1741/0087
Viagra-EMEA/H/C/000202/WS1741/0103
Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege

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

WS1752
Nuwiq-EMEA/H/C/002813/WS1752/0034
Vihuma-EMEA/H/C/004459/WS1752/0016
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus

WS1753/G
Prezista-EMEA/H/C/000707/WS1753/0103/G
Rezolsta-EMEA/H/C/002819/WS1753/0036/G
Symtuza-EMEA/H/C/004391/WS1753/0022/G
Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege

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

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 - EMA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

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

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

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

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

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

G. ANNEX G

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

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

Qualification of Biomarkers:

HTA:

G.2. Ongoing procedures

G.3. PRIME

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

G.3.1. List of procedures concluding at 09-12 December 2019 CHMP plenary:

Haematology-haemostaseology		
1.	**CD34+enriched cells transduced ex vivo with lentiviral vector carrying the FANCA gene, PGK-FANCA-WPRE (RP-L102) -** ATMP; Treatment of Fanconi anaemia Type A	The CHMP granted eligibility to PRIME and adopted the critical summary report.
Oncology		
2.	Treatment of recurrent glioblastoma	The CHMP denied eligibility to PRIME and adopted the critical summary report.
3.	Treatment of patients with low or intermediate grade (G1 or G2) progressive, locally advanced or metastatic extra pancreatic NETs, which have been treated with at least 1 line of prior therapy	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Endocrinology-Gynaecology-Fertility-Metabolism		
4.	(SME); Treatment of patients with Arginase 1 Deficiency (hyperargininaemia)	The CHMP denied eligibility to PRIME and adopted the critical summary report.
5.	**Rebisufligene etisparvovec** (SME); ATMP; Treatment of Mucopolysaccharidosis Type IIIA, MPS IIIA (Sanfilippo A Syndrome)	The CHMP granted eligibility to PRIME and adopted the critical summary report.
Neurology		
6.	Treatment of mild to moderate Alzheimer's Disease	The CHMP denied eligibility to PRIME and adopted the critical summary report.

G.3.2. List of procedures starting in December 2019 for January 2020 CHMP adoption of outcomes

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