30 October 2018
EMA/CHMP/765541/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Minutes of the meeting on 17-20 September 2018

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

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

Note on access to documents

Some documents mentioned in the 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 that no restriction in the involvement of meeting participants in upcoming discussions was identified as included in the list of participants and restrictions. See (current) September 2018 CHMP minutes for the list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session held 17-20 September 2018 (to be published post October 2018 CHMP meeting).

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

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

1.2. Adoption of agenda

CHMP agenda for 17-20 September 2018

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 23-26 July 2018.

The CHMP adopted the CHMP minutes for 23-26 July 2018. The Minutes of the September 2018 CHMP ORGAM meeting held on 10 September 2018, together with all decisions taken at that meeting, were adopted.

CHMP minutes for August 2018 written procedure

The CHMP adopted the CHMP minutes for August 2018 written procedure.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. Apealea - paclitaxel - EMEA/H/C/004154

Oasmia Pharmaceutical AB; treatment of ovarian cancer

Scope: Oral explanation

Action: Oral explanation to be held on 18 September 2018 at time 14:30

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

List of Outstanding Issues adopted on 26.07.2018, 26.04.2018, 14.09.2017, 18.05.2017. List of Questions adopted on 23.06.2016.

The CHMP agreed that no oral explanation was needed at this time.

See 3.1

2.1.2. influenza vaccine surface antigen inactivated prepared in cell cultures - Article 28 - EMEA/H/C/004814

prophylaxis of influenza in adults and children from 9 years of age

Scope: Oral explanation

Action: Oral explanation to be held on 19 September 2018 at time 09:00

List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 22.03.2018.

The CHMP agreed that no oral explanation was needed at this time.

2.1.3. mexiletine hcl - Orphan - EMEA/H/C/004584

LUPIN (EUROPE) LIMITED; Treatment of myotonic disorders

Scope: Oral explanation, SAG report

Action: Oral explanation to be held on 18 September 2018 at time 11:00

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.12.2017.

The CHMP noted SAG report.

An oral explanation was held on 18 September 2018 at time 11:00.

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

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

Scope: Oral explanation

Action: Oral explanation to be held on 19 September 2018 at time 14:00

List of Outstanding Issues adopted on 28.06.2018, 26.04.2018. List of Questions adopted on 14.12.2017.

An oral explanation was held on 19 September 2018 at time 14:00.

See 3.2

2.2. Re-examination procedure oral explanations

2.2.1. Exondys - eteplirsen - Orphan - EMEA/H/C/004355

AVI Biopharma International Ltd; treatment of Duchenne muscular dystrophy

Scope: Oral Explanation, SAG report, Opinion

Action: Oral explanation to be held on 18 September 2018 at time 09:00

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

Opinion adopted on 31.05.2018.

Updated list of experts for SAG Neurology meeting to be held 7 September 2018 were adopted via written procedure on 4 September 2018.

An oral explanation was held on 18 September 2018 at time 09:00.

See 3.5

2.3. Post-authorisation procedure oral explanations

2.3.1. Xtandi - enzalutamide - EMEA/H/C/002639/II/0039/G

Astellas Pharma Europe B.V.

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Eva A. Segovia

Scope: "C.I.4: Update of sections 4.4, 4.7, 4.8 and 5.2 of the SmPC in order to amend the warning on possible association with seizure, to amend the effects on driving or operating machines, to amend the identified adverse reactions and to amend the 'Race' subsection regarding pharmacokinetic properties based on the results from the completed studies PROSPER, a Phase 3 Randomized Controlled Study, designed to investigate the Safety and Efficacy of Enzalutamide in Patients with Non-Metastatic Castration-Resistant Prostate

Cancer; and Asian PREVAIL, a Multinational Phase 3, Randomized, Double-blind, Placebo-controlled Efficacy and Safety Study of Oral Enzalutamide in Chemotherapy-naive Subjects with Progressive Metastatic Prostate Cancer Who Have Failed Androgen Deprivation Therapy; and the updated integrated clinical safety database.
The Package Leaflet is updated in accordance.
C.I.6.a: Extension of Indication to include patients with non-metastatic castration-resistant prostate cancer (CRPC) for Xtandi;
as a consequence, sections 4.1 and 5.1 of the SmPC are updated, based on the supportive clinical study results of MDV3100-14 (PROSPER), a Phase 3 Randomized Controlled Study, designed to investigate the Safety and Efficacy of Enzalutamide in Patients with Non-Metastatic Castration-Resistant Prostate Cancer; MDV3100-09 (STRIVE), a Multicenter Phase 2 Study to investigate the Safety and Efficacy of Enzalutamide Versus Bicalutamide in Men With Non-Mtastatic or Metastatic Castration-Resistant Prostate Cancer; and based on supportive non-clinical data from 7 new reports.
The Package Leaflet is updated in accordance.
An update RMP version 12.1 was submitted in order to include the changes related to the extension of indication."

Action: Oral explanation to be held on 18 September 2018 at time 16:30, SAG-Oncology report

The final list of experts for the SAG-Oncology meeting held on 6 September was adopted via written procedure on 4 September 2018.

Request for Supplementary Information adopted on 26.07.2018, 31.05.2018.

The CHMP agreed that no oral explanation was needed at this time.

See 5.1.

2.4. Referral procedure oral explanations

2.4.1. Diclofenac Sodium Spray Gel 4% cutaneous spray, solution and associated names– EMEA/H/A-29(4)/1467

MAHs: various

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Harald Enzmann

Scope: Oral explanation

Action: Oral explanation to be held on 19 September 2018 at time 12:00

An oral explanation was held on 19 September 2018 at time 12:00.

See 10.4

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Alunbrig - brigatinib - EMEA/H/C/004248

Takeda Pharma A/S; treatment of anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC)

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 25.01.2018, 12.10.2017. List of Questions adopted on 22.06.2017.

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

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

Furthermore, the CHMP considered that brigatinib 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.

3.1.2. Apealea - paclitaxel - EMEA/H/C/004154

Oasmia Pharmaceutical AB; treatment of ovarian cancer

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 26.07.2018, 26.04.2018, 14.09.2017, 18.05.2017. List of Questions adopted on 23.06.2016.

See 2.1

The CHMP agreed that no oral explanation was needed at 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 majority (29 positive out of 31 votes) together with the CHMP assessment report and translation timetable.

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

The divergent position (Jayne Crowe, Johann Lodewijk Hillege) was appended to the opinion.

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

The CHMP noted the letter of recommendation dated 20 September 2018.

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report

3.1.3. Buvidal - buprenorphine - EMEA/H/C/004651

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

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 25.01.2018.

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

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

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

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

The summary of opinion was circulated for information.

The CHMP noted the letter of recommendation dated 18 September 2018.

3.1.4. Pifeltro - doravirine - EMEA/H/C/004747

Merck Sharp & Dohme Limited; treatment, in combination with other antiretroviral medicinal products, of adults infected with HIV-1 without past or present evidence of resistance to the NNRTI class

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 28.06.2018. List of Questions adopted on 22.03.2018.

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

addressed.

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

Furthermore, the CHMP considered that doravirine 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.

3.1.5. Delstrigo - doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746

Merck Sharp & Dohme B.V.; treatment of adults infected with HIV-1 without past or present evidence of resistance to the NNRTI class, lamivudine, or tenofovir

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 28.06.2018. List of Questions adopted on 22.03.2018.

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

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

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

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

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

The summary of opinion was circulated for information.

3.1.6. Emgality - galcanezumab - EMEA/H/C/004648

Eli Lilly Nederland B.V.; prophylaxis of migraine

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 22.03.2018.

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

addressed.

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

Furthermore, the CHMP considers that galcanezumab 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.

3.1.7. Fulphila - pegfilgrastim - EMEA/H/C/004915

MYLAN S.A.S; treatment of neutropenia

Scope: Opinion

Action: For adoption

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

List of Questions adopted on 22.03.2018.

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

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

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

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

The summary of opinion was circulated for information.

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

Bayer AG; Treatment and prophylaxis of haemophilia A

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 28.06.2018. List of Questions adopted on 25.01.2018.

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

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

timetable.

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

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

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

The summary of opinion was circulated for information.

The CHMP noted the letter of recommendation dated 20 September 2018.

3.1.9. Luxturna - voretigene neparvovec - Orphan - ATMP - EMEA/H/C/004451

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

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 20.07.2018, 25.05.2018. List of Questions adopted on 08.12.2017.

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

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

Furthermore, the CHMP considered that voretigene neparvovec 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.

3.1.10. Pelmeg - pegfilgrastim - EMEA/H/C/004700

Cinfa Biotech S.L.; treatment of neutropenia

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 28.06.2018. List of Questions adopted on 25.01.2018.

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

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

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

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

The summary of opinion was circulated for information.

3.1.11. Poteligeo - mogamulizumab - Orphan - EMEA/H/C/004232

Kyowa Kirin Limited; for the treatment of adult patients with mycosis fungoides (MF) or Sézary syndrome (SS) who have received at least one prior systemic therapy

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 26.07.2018, List of Questions adopted on 22.02.2018.

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

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

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

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

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

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report.

3.1.12. Vabomere - meropenem / vaborbactam - EMEA/H/C/004669

Rempex London Ltd; treatment of urinary tract infection (cUTI), including pyelonephritis, intra-abdominal infection (cIAI), hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP), bacteraemia, infections due to bacterial organisms

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 09.11.2017.

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

addressed.

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

Furthermore, the CHMP considered that vaborbactam 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 18 September 2018.

The summary of opinion was circulated for information.

3.1.13. Ziextenzo - pegfilgrastim - EMEA/H/C/004802

Sandoz GmbH; treatment of neutropenia

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 22.02.2018.

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

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

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

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

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

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

Scope: List of Outstanding Issues

Action: For adoption

List of Questions adopted on 08.09.2017.

The Committee was reminded of the status of this application and its remaining outstanding issues and was updated on discussions at the CAT during their September meeting.

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

3.2.2. dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171

indicated for the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4

Scope: List of Outstanding Issues

Action: For adoption

List of Outstanding Issues adopted on 26.04.2018, 23.03.2017. List of Questions adopted on 21.07.2016.

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

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

3.2.3. apalutamide - EMEA/H/C/004452

treatment of non-metastatic castration resistant prostate cancer (NM CRPC)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.06.2018.

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.

3.2.4. romosozumab - EMEA/H/C/004465

Treatment of osteoporosis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 26.04.2018.

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.

3.2.5. fexinidazole - Article 58 - EMEA/H/W/002320

treatment of human African trypanosomiasis (HAT)

Scope: List of outstanding issues

List of experts and questions for SAG meeting to be held on 25 September 2018 were

adopted via written procedure on 13.09.2018.

Action: For adoption

List of Outstanding Issues adopted on 26.06.2018. List of Questions adopted on 24.04.2018.

The Committee was reminded of the status of this application and its remaining outstanding issues. The CHMP noted involvement of WHO experts and TC held.

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

The CHMP noted a SAG meeting (including WHO experts) to be held on 25 September 2018 and adopted questions to SAG.

3.2.6. macimorelin - EMEA/H/C/004660

Diagnosis of Adult growth hormone deficiency (AGHD)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.03.2018.

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.

3.2.7. trastuzumab - EMEA/H/C/004916

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.03.2018.

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.

3.2.8. lanadelumab - Orphan - EMEA/H/C/004806

Accelerated assessment

Shire Pharmaceuticals Ireland Limited; prevention of angioedema attacks, treatment of angioedema attacks

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 26.06.2018.

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.

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

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

Scope: Oral explanation/List of outstanding issues

Action: Oral explanation to be held on 19 September 2018 at time 14:00

List of Outstanding Issues adopted on 28.06.2018, 26.04.2018. List of Questions adopted on 14.12.2017.

An oral explanation was held on 19 September 2018 at time 14:00.

See 2.1

The Committee adopted a 3rd 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. ambrisentan - EMEA/H/C/004985

treatment of pulmonary arterial hypertension (PAH)

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. ambrisentan - EMEA/H/C/004955

treatment of pulmonary arterial hypertension (PAH)

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.3. cabazitaxel - EMEA/H/C/004951

treatment of prostate cancer

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. avatrombopag - EMEA/H/C/004722

treatment of thrombocytopenia

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. etanercept - EMEA/H/C/004711

Rheumatoid arthritis, Juvenile idiopathic arthritis, Psoriatic arthritis, Axial spondyloarthritis, Ankylosing spondylitis, Non-radiographic axial spondyloarthritis, Plaque psoriasis, Paediatric plaque psoriasis

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. febuxostat - EMEA/H/C/004773

treatment of hyperuricaemia

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. levodopa - EMEA/H/C/004786

treatment of symptoms of OFF periods in Parkinson's disease

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application

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

3.3.8. posaconazole - EMEA/H/C/005005

treatment of fungal infections

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.9. delafloxacin - EMEA/H/C/004860

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

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application,

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

3.3.10. edaravone - EMEA/H/C/004938

treatment of amyotrophic lateral sclerosis (ALS)

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.11. risankizumab - EMEA/H/C/004759

treatment of psoriasis in adults

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application

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

3.3.12. crisaborole - EMEA/H/C/004863

treatment of mild to moderate atopic dermatitis

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.13. ioflupane (123i) - EMEA/H/C/004745

indicated for detecting loss of functional dopaminergic neuron terminals in the striatum

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

3.3.14. talazoparib - EMEA/H/C/004674

for the treatment of adult patients with germline breast cancer susceptibility gene (BRCA) mutated human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer.

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

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

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

Post meeting note: The final list of questions to the SAG was adopted via written procedure on 1 October 2018.

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

3.4.1. andexanet alfa - EMEA/H/C/004108

treatment of direct or indirect factor Xa(FXa) inhibitor when reversal of anticoagulation is needed

Scope: Request for an extension of clock-stop to respond to the 2nd List of Outstanding Issues adopted in February 2018.

Action: For adoption

List of Outstanding Issues adopted on 09.11.2017, 22.02.2018. List of Questions adopted on 15.12.2016

The CHMP agreed to the request by the applicant for an extension of clock-stop to respond to the 2nd List of Outstanding Issues adopted in February 2018

3.4.2. glutamine - Orphan - EMEA/H/C/004734

Emmaus Medical Europe Ltd; treatment of sickle cell disease

Scope: Request by the applicant dated 16.08.2018 for an extension to the clock stop to respond to the List of Questions adopted on 28.06.2018.

Action: For adoption

List of Questions adopted on 28.06.2018.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Questions adopted on 28.06.2018.

3.4.3. trientine dihydrochloride - Orphan - EMEA/H/C/004111

Univar BV; Treatment of Wilson's disease.

Scope: Request by the applicant dated 06.09.2018 for an extension to the clock stop to respond to the List of Questions adopted on 28.06.2018.

Action: For adoption

List of Questions adopted on 28.06.2018.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Questions adopted on 28.06.2018.

3.4.4. cemiplimab - EMEA/H/C/004844

as monotherapy, indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma

Scope: Request by the applicant dated 05.09.2018 for an extension to the clock stop to

respond to the List of Questions adopted on 26.07.2018.

Action: For adoption

List of Questions adopted on 26.07.2018.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Questions adopted on 26.07.2018.

3.4.5. ciprofloxacin - EMEA/H/C/004394

treatment of non-cystic fibrosis bronchiectasis (NCFBE) patients with chronic lung infection with Pseudomonas aeruginosa (P. aeruginosa)

Scope: Request by the applicant dated 14.09.2018 for an extension to the clock stop to respond to the List of Questions adopted on 26.07.2018.

Action: For adoption

List of Questions adopted on 26.07.2018.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Questions adopted on 26.07.2018.

3.4.6. paclitaxel - EMEA/H/C/004441

treatment of metastatic breast cancer

Scope: Letter from third party ; Request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted on 26.07.2018

Action: For adoption

List of Outstanding Issues adopted on 26.07.2018, 31.05.2018. List of Questions adopted on 14.12.2017.

The CHMP noted the letter from the third party.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted on 26.07.2018

3.4.7. pegfilgrastim - EMEA/H/C/005008

treatment of neutropenia

Scope: Request by the applicant for an extension to the clock stop to respond to the List of Questions adopted on 28.06.2018

Action: For adoption

List of Questions adopted on 28.06.2018.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Questions adopted on 28.06.2018

3.4.8. pegfilgrastim - EMEA/H/C/004789

treatment of neutropenia

Scope: Request by the applicant for an extension to the clock stop to respond to the List of Questions adopted on 28.06.2018

Action: For adoption

List of Questions adopted on 28.06.2018.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Questions adopted on 28.06.2018

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

3.5.1. Exondys - eteplirsen - Orphan - EMEA/H/C/004355

AVI Biopharma International Ltd; treatment of Duchenne muscular dystrophy

Scope: Oral explanation to be held on 18 September 2018 at time 09:00

SAG report, Opinion

Action: For adoption

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

Opinion adopted on 31.05.2018.

An updated list of experts for SAG Neurology meeting held 7 September 2018 was adopted via written procedure on 04.09.2018. The CHMP noted SAG report.

An oral explanation was held on 18 September 2018 at time 09:00.

Participation of patients' representatives

The CHMP was concerned that the main study, which involved just 12 patients, did not compare Exondys with placebo beyond 24 weeks, during which there was no meaningful difference between Exondys and placebo in the 6-minute walking distance. The methods for comparing results of the main studies with historical data were not satisfactory for showing that the medicine was effective.

The Committee considered further data were needed to show that the very low amounts of shortened dystrophin produced as a result of Exondys treatment bring lasting benefits relevant to the patient.

Therefore, the CHMP was of the opinion that the balance of benefits and risks of Exondys in the treatment of DMD could not be established and recommended that the marketing authorisation be refused.

The CHMP adopted a negative opinion by consensus, recommending the refusal of the granting of the conditional marketing authorisation. The CHMP adopted the assessment report.

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

The refusal question and answers document was circulated for information.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. Treprostinil SciPharm Sàrl - treprostinil – Orphan - EMEA/H/C/004847

SciPharm Sarl, Treatment of chronic thromboembolic pulmonary hypertension

Scope: Letter dated 05.09.2018 informing EMA about the withdrawal of MAA

Action: For information

The CHMP noted the withdrawal of the marketing authorisation application.

3.7.2. Entolimod TMC – entolimod – Orphan – EMEA/H/C/004656

TMC Pharma Services Ltd, treatment of acute radiation syndrome

Scope: Letter dated 31.07.2018 informing EMA about the withdrawal of MAA

Action: For information

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. Elocta - efmoroctocog alfa - EMEA/H/C/003964/X/0021

Swedish Orphan Biovitrum AB (publ)

Rapporteur: Jan Mueller-Berghaus

Scope: “Extension application to introduce new strength of 4000 IU, 5000 IU and 6000 IU primarily enabling prophylactic dosing in adult patients.”

Action: For adoption

List of Questions adopted on 31.05.2018.

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. Gilenya - fingolimod - EMEA/H/C/002202/X/0044/G

Novartis Europharm Limited

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension application to introduce a new strength of hard capsules (0.25 mg) to the currently approved presentations of Gilenya, grouped with a type II variation (extension of indication) to add a new indication for the treatment of paediatric patients of 10 years of age and above with relapsing multiple sclerosis (RMS). As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 5.3, 6 and 8 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. In addition, Annex II is updated to be brought in line with the latest QRD template version 10."

Action: For adoption

List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 22.03.2018.

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 agreed by consensus on an additional 1 year of market protection for a new indication.

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. Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/X/0034/G

Vertex Pharmaceuticals (Europe) Ltd.

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Rhea Fitzgerald

Scope: "1. Extension application to introduce a new pharmaceutical form (granules) in 2 strengths (100/125 mg and 150/188 mg) for paediatric use (2 to 5 years). An updated RMP (v 4.0) has been submitted.
2. Type II (C.I.4): Update of sections 4.1, 4.2, 4.5, 4.8 and 5.3 of the SmPC of the tablets formulation to bring it in line with the proposed paediatric 2-5 years old extension application."

Action: For adoption

List of Questions adopted on 28.06.2018.

The Committee discussed the issues identified in this application, mainly relating to the extrapolation to 2 – 5 year old patients and required longer term post-authorisation data.

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. Simponi - golimumab - EMEA/H/C/000992/X/0083/G

Janssen Biologics B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add a new strength of 100 mg/ml solution for injection for paediatric use.
C.I.6.a - Extension of indication to include paediatric patients from the age of 2 years and older for the treatment of polyarticular juvenile idiopathic arthritis (pJIA) with Simponi 100 mg/ml solution for injection. As a consequence, sections 4.1, 4.2, 5.1 and section 4.1 of the 50mg strength have been updated accordingly.
C.I.11.z - To update the RMP to version 18.0 to delete the following safety concerns: vasculitis, psoriasis (new onset or worsening of pre-existing), and sarcoidosis/sarcoid like reaction. This change has been agreed by the CHMP in the outcome of variation Type II/068.
C.I.11.z - To update the RMP to version 18.0 to change the due date of the category 3 study MK-8259-050. This change has been agreed by the CHMP in the outcome of MEA033.
In addition, the marketing authorisation holder took the opportunity to:
- update the Product Information in line with the latest QRD template (version 10);
- implement the recommendations stated in the revised Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' with regards to the excipient Sorbitol (E420);
- add a statement in Section 4.4 of the SmPC to record the name and the batch number of the administered product, in line with Good Pharmacovigilance Practice (GVP) Module PII: Biological medicinal products."

Action: For adoption

The Committee noted the issues identified in this application.

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

4.3.2. Trisenox - arsenic trioxide - EMEA/H/C/000388/X/0068

Teva B.V.

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension application to add a new strength of 2 mg/ml (concentrate for solution for solution for infusion) in vials.
The RMP (version 2.0) is updated accordingly."

Action: For adoption

The Committee discussed the issues identified in this application, which related to quality and safety data.

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

4.3.3. Zykadia - ceritinib - EMEA/H/C/003819/X/0025

Novartis Europharm Limited

Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Annika Folin

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

Action: For adoption

The Committee discussed the issues identified in this application.

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

4.4. 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. Adcetris - brentuximab vedotin - Orphan - EMEA/H/C/002455/II/0055

Takeda Pharma A/S

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of the existing Hodgkin lymphoma (HL) indication to include the frontline treatment of adult patients with CD30+ advanced HL in combination with chemotherapy, based on data from ECHELON-1 (C25003), a phase 3 multi-centre, randomised, open-label study comparing the modified progression-free survival (mPFS) obtained with brentuximab vedotin, doxorubicin, vinblastine and dacarbazine versus the mPFS obtained with doxorubicin, bleomycin, vinblastine and dacarbazine. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Furthermore, the PI is brought in line with the latest QRD template version 10. The MAH also submitted an updated RMP version 13."

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018.

The Committee noted the issues identified in this application.

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

5.1.2. Cabometyx - cabozantinib - EMEA/H/C/004163/II/0005

Ipsen Pharma

Rapporteur: Robert James Hemmings, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to add Cabometyx as monotherapy for the treatment of hepatocellular carcinoma in adults who have previously been treated with sorafenib; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated with safety and efficacy information. The package leaflet and the risk management plan (version 4.2) are updated accordingly."

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018.

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

addressed.

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

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

The summary of opinion was circulated for information.

5.1.3. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/II/0069

Vertex Pharmaceuticals (Europe) Ltd.

Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Maria del Pilar Rayon

Scope: "Extension of Indication to include treatment of cystic fibrosis in children age 12 to less than 24 months who have one of the currently approved gating mutations in the CFTR gene for Kalydeco 50 mg & 75 mg Granules; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. Relevant consequential changes are made to the Kalydeco 150 mg film-coated tablet Product Information. The Package Leaflet is updated in accordance.
The RMP version 7.2 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018.

The Committee noted the issues identified in this application.

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

5.1.4. Kisqali - ribociclib - EMEA/H/C/004213/II/0004

Novartis Europharm Limited

Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver

Scope: "Extension of Indication to include treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant. In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist for Kisqali. The proposed extension to the indication is based upon data from study CLEE011E2301 (A Phase III randomized, double-blind, placebo-controlled study of LEE011 or placebo in combination with tamoxifen and goserelin or a non-steroidal aromatase inhibitor (NSAI) and goserelin for the treatment of premenopausal women with hormone receptor positive, HER2- negative, advanced breast cancer) and study CLEE011F2301 (A randomized double-blind, placebo-controlled study of ribociclib in combination with fulvestrant for the treatment of men and postmenopausal women with hormone receptor positive, HER2 negative, advanced breast cancer who have received no or only one line of prior endocrine treatment).
As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC have been updated and the Package Leaflet has been updated accordingly.

In addition, the MAH took the opportunity to make some editorial changes in the SmPC and to make an administrative update to the Estonian and Latvian local representatives addresses in the Package Leaflet.
An updated RMP version 2.0 was submitted as part of the application."

Action: For adoption

The Committee discussed the issues identified in this application, related to SmPC wording.

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

5.1.5. Lynparza - olaparib - EMEA/H/C/003726/II/0020

AstraZeneca AB

Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to include the use of Lynparza tablets as a monotherapy for the treatment of adult patients with BRCA1/2-mutated HER2 negative metastatic breast cancer who have previously been treated with chemotherapy. These patients could have received chemotherapy in the neoadjuvant, adjuvant or metastatic setting.
As a consequence, section 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC for Lynparza tablets have been updated. Section 4.8 of Lynparza capsules and relevant sections of the package leaflet have been updated accordingly. Furthermore, RMP version 16 has also been provided."

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018.

The Committee discussed the issues identified in this application, which related to therapeutic indication.

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

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

Post meeting note: The final list of questions to the SAG were adopted via written procedure on 1 October 2018.

5.1.6. Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0012

AbbVie Deutschland GmbH & Co. KG

Rapporteur: Joseph Emmerich, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "Extension of indication to extend the Maviret indication to adolescents (from 12 to 18 years of age) with chronic hepatitis C infection, based on new clinical data from study M16-123, an open-label, multi-centre study to evaluate the pharmacokinetics, safety, and efficacy of glecaprevir/pibrentasvir in paediatric subjects with genotypes 1 - 6 chronic hepatitis C virus infection (DORA), using the adult co-formulated tablets in adolescents. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package

Leaflet is updated in accordance.
In addition, the marketing authorisation holder (MAH) submitted a revised RMP version 4, updated in accordance with the second revision of the RMP template."

Action: For adoption

The Committee discussed the issues identified in this application related to the lack of weight criterion in the SmPC and to further discuss the exclusion of 3 patients from the PK analysis.

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

5.1.7. Ravicti - glycerol phenylbutyrate - Orphan - EMEA/H/C/003822/II/0019

Horizon Pharma Ireland Limited

Rapporteur: Greg Markey, Co-Rapporteur: Jayne Crowe

Scope: "C.I.6 - Extension of indication to include in the authorised indication the new paediatric population from 0 to 2 months for RAVICTI based on the final results from study HPN-100-009, an Open Label Study of the Safety, Efficacy and Pharmacokinetics of Glycerol Phenylbutyrate in Pediatric Subjects under Two Years of Age with Urea Cycle Disorders (UCDs); as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.
This submission covers as well the requirement to submit clinical studies in the paediatric population in accordance with Article 46 of Regulation (EC) No 1901/2006 (the 'Paediatric Regulation') for study HPN-100-009."

Action: For adoption

The Committee discussed the issues identified in this application.

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

5.1.8. Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0050

Novartis Europharm Limited

Rapporteur: Concepcion Prieto Yerro

Scope: "Change of the Revolade indication of immune thrombocytopaenic purpura to specify the duration of the disease. As a result the SmPC sections 4.1, 4.2, 4.4, 4.8 and 5.1 are being revised. The Package leaflet is being updated accordingly."

Action: For adoption

The Committee discussed the issues identified in this application.

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

5.1.9. RoActemra - tocilizumab - EMEA/H/C/000955/II/0076

Roche Registration GmbH

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "To add the paediatric indication 'treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 1 year of age and older, who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids' to the RoActemra 162 mg solution for injection in pre-filled syringe formulation, based on data from the Phase Ib pharmacokinetic/pharmacodynamic bridging study WA28118 (JIGSAW 118), designed to confirm the RoActemra subcutaneous dosing regimens in patients aged 1 to 17 years old with sJIA, as well as assess the safety of the RoActemra subcutaneous formulation. 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 accordingly.
In addition, sections 4.2, 4.8 and 5.2 of the SmPC of the RoActemra 20 mg/mL concentrate for solution for infusion formulation are updated to reflect data from the pivotal RoActemra intravenous study WA18221 (TENDER), a randomised, placebo-controlled study to evaluate the effect of tocilizumab on disease response in patients with active sJIA."

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018.

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

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

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

The summary of opinion was circulated for information.

5.1.10. Rubraca - rucaparib - Orphan - EMEA/H/C/004272/II/0001

Clovis Oncology UK Limited

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Annika Folin

Scope: "Extension of Indication to include new indication for Rubraca "Rubraca is indicated as monotherapy for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy". As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated with the expanded clinical eficacy and safety data. The Package Leaflet is also updated in accordance.
The updated RMP version 2.0 has also been submitted.
In addition, the applicant took the opportunity to propose the move of one paragraph from section 4.4 to 5.1 in the SmPC for consistency with other SmPC agents in this class with this indication."

Action: For adoption

The Committee discussed the issues identified in this application, which related to the wording of indication.

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

The CHMP adopted the similarity assessment report.

5.1.11. Sprycel - dasatinib - EMEA/H/C/000709/II/0059

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Fátima Ventura, PRAC Rapporteur: Doris Stenver

Scope: "Extension of Indication to include a paediatric indication for Philadelphia chromosome positive acute lymphoblastic leukaemia for Sprycel; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 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 to the product information.
The RMP version 16.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018.

The Committee noted the issues identified in this application.

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

5.1.12. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0007/G

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of indication to include in combination with bevacizumab, paclitaxel and carboplatin the first-line treatment of adult patients with metastatic non-squamous non small cell lung cancer (NSCLC), based on the interim results of study GO29436 (IMpower 150). As a consequence sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated.
In addition update of section 4.8 of the SmPC in order to update the monotherapy safety data and reflect the largest pooled monotherapy population available (now including also data from IMvigor211 and PCD4989g studies).
The Package Leaflet and the RMP (version 4.0) are updated in accordance. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to make small corrections and formatting changes throughout the SmPC."

Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018.

The Committee discussed the issues identified in this application, which related to

therapeutic indication and significant clinical benefit.

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

5.1.13. Trimbow - beclometasone dipropionate / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004257/II/0002

Chiesi Farmaceutici S.p.A.

Rapporteur: Harald Enzmann, PRAC Rapporteur: Jan Neuhauser

Scope: "Extension of Indication for Trimbow to all adult patients with moderate or severe chronic obstructive pulmonary disease (COPD).
As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated in order to add the results of two Phase III studies (Triple 7 and Triple 8);
Triple 7 (CCD-05993AA1-07) is a multinational, multicentre, randomised, open-label, active-controlled, 26-week, 2-arm, parallel group study to evaluate the non-inferiority of fixed combination of beclomethasone dipropionate plus formoterol fumarate plus glycopyrronium bromide administered via pressurised metered dose inhaler (pMDI) (CHF 5993) versus (vs.) fixed combination of fluticasone furoate plus vilanterol administered via dry powder inhaler (DPI) (Relvar®) plus tiotropium bromide (Spiriva®) for the treatment of patients with Chronic Obstructive Pulmonary Disease (COPD).
Triple 8 (CCD-05993AA1-08) is a 52-week, double blind, double dummy, randomized, multinational, multicentre, 2-arm parallel group, active controlled clinical trial of fixed combination of beclomethasone dipropionate plus formoterol fumarate plus glycopyrronium bromide administered via pMDI (CHF 5993) versus indacaterol/glycopyrronium (Ultibro®) via DPI in patients with Chronic Obstructive Pulmonary Disease (TRIBUTE).
The Package Leaflet and the Risk Management Plan are updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018.

The Committee discussed the issues identified in this application. The applicant was asked to further discuss the benefit/risk balance.

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

5.1.14. Venclyxto - venetoclax - Orphan - EMEA/H/C/004106/II/0008

AbbVie Deutschland GmbH & Co. KG

Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty

Scope: "Extension of Indication to include Venclyxto in combination with rituximab for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the SmPC are updated.
The Package Leaflet is updated in accordance.

This submission also fulfils the Annex II condition to submit the results of the MURANO study comparing venetoclax plus rituximab to bendamustine plus rituximab in patients with relapsed/refractory CLL.
In addition, RMP version 3.3 (in version 2 of the RMP template) is being approved."

Action: For adoption

Request for Supplementary Information adopted on 26.04.2018.

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.

The CHMP adopted the similarity assessment report

5.1.15. Xtandi - enzalutamide - EMEA/H/C/002639/II/0039/G

Astellas Pharma Europe B.V.

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Eva A. Segovia

Scope: "C.I.4: Update of sections 4.4, 4.7, 4.8 and 5.2 of the SmPC in order to amend the warning on possible association with seizure, to amend the effects on driving or operating machines, to amend the identified adverse reactions and to amend the 'Race' subsection regarding pharmacokinetic properties based on the results from the completed studies PROSPER, a Phase 3 Randomized Controlled Study, designed to investigate the Safety and Efficacy of Enzalutamide in Patients with Non-Metastatic Castration-Resistant Prostate Cancer; and Asian PREVAIL, a Multinational Phase 3, Randomized, Double-blind, Placebo-controlled Efficacy and Safety Study of Oral Enzalutamide in Chemotherapy-naive Subjects with Progressive Metastatic Prostate Cancer Who Have Failed Androgen Deprivation Therapy; and the updated integrated clinical safety database.
The Package Leaflet is updated in accordance.
C.I.6.a: Extension of Indication to include patients with non-metastatic castration-resistant prostate cancer (CRPC) for Xtandi;
as a consequence, sections 4.1 and 5.1 of the SmPC are updated, based on the supportive clinical study results of MDV3100-14 (PROSPER), a Phase 3 Randomized Controlled Study, designed to investigate the Safety and Efficacy of Enzalutamide in Patients with Non-Metastatic Castration-Resistant Prostate Cancer; MDV3100-09 (STRIVE), a Multicenter Phase 2 Study to investigate the Safety and Efficacy of Enzalutamide Versus Bicalutamide in Men With Non-Mtastatic or Metastatic Castration-Resistant Prostate Cancer; and based on supportive non-clinical data from 7 new reports.
The Package Leaflet is updated in accordance.
An update RMP version 12.1 was submitted in order to include the changes related to the extension of indication."

Oral explanation to be held on 18 September 2018 at time 16:00, SAG-Oncology report

Action: For adoption

Request for Supplementary Information adopted on 26.07.2018, 31.05.2018.

See also 2.3

The CHMP noted the SAG-Oncology report.

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

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

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

The summary of opinion was circulated for information.

5.1.16. WS1369
Elebrato Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004781/WS1369/0001
Trelegy Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004363/WS1369/0001

GlaxoSmithKline Trading Services Limited

Lead Rapporteur: Peter Kiely, Lead Co-Rapporteur: Harald Enzmann, PRAC Rapporteur: Annika Folin

Scope: “To modify the approved current COPD therapeutic indication to "maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD)".
As a consequence, the indication section (4.1), Undesirable effects section (4.8) and Pharmacodynamic Properties section (5.1), Pharmacokinetic properties section (5.2), Preclinical Safety data section (5.3) of the EU SmPC, and the Possible side effects section (4) of the package leaflet are updated accordingly. This is based on the result of study CTT116855 and study 200812 and the population PK report 208059.
The updated RMP (version 02) has also been submitted.”

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018.

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

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

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

The summary of opinion was circulated for information.

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

5.2.1. Hemlibra - emicizumab - EMEA/H/C/004406/II/0002

Roche Registration GmbH

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of Indication to include routine prophylaxis of bleeding episodes in patients with hemophilia A without factor VIII inhibitors, for Hemlibra. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated with efficacy and safety information of the pivotal trials:
- Study BH30071 (HAVEN 3) - an ongoing, multicenter, open-label, randomized Phase III clinical study evaluating the efficacy, safety and PK of emicizumab prophylaxis at doses of 1.5 mg/kg/week (QW) and 3 mg/kg/every 2 weeks (Q2W) versus no prophylaxis in adults and adolescent patients (age of 12 or above) with haemophilia A without inhibitors against factor VIII (FVIII).
- Study BO39182 (HAVEN 4) - an ongoing multicenter, open-label, non-randomized Phase III study evaluating the efficacy, safety and PK of emicizumab given as the dose of 6 mg/kg/every 4 weeks (Q4W) in adults and adolescent patients (age of 12 or above) with hemophilia A with or without FVIII inhibitors.
- Study BH29992 (HAVEN 2) - a multicenter, open-label, non-randomized Phase III study evaluating the efficacy, safety and PK of emicizumab at the QW dose in pediatric patients (<12 years old or 12-17 years old and <40kg) with hemophilia A with FVIII inhibitors.
The Package Leaflet and the Risk Management Plan (v.2.0) is updated in accordance.
In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor corrections and clarity to sections 4.4, 4.5 and 4.6 of the SmPC."

Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For discussion

Letter from third party

The CHMP noted the letter from the third party.

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

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

Amgen Europe B.V.

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

Labelling is updated in accordance.
RMP version 4.0 is included in this submission."

Re-examination timetable.

Action: For adoption

Opinion adopted on 26.07.2018. An oral explanation was held on 24.07.2018.

Request for Supplementary Information adopted on 26.04.2018, 14.12.2017, 22.06.2017.

The CHMP adopted the re-examination timetable.

5.3.2. WS1278
OPDIVO - nivolumab - EMEA/H/C/003985/WS1278/0042
Yervoy - ipilimumab - EMEA/H/C/002213/WS1278/0053

Bristol-Myers Squibb Pharma EEIG

Scope: "Extension of indication to include the combination treatment with nivolumab and ipilimumab of adult patients with intermediate/poor-risk advanced renal cell carcinoma. As a consequence sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the Opdivo and Yervoy SmPCs are updated. The Package Leaflet and the Risk Management Plan (version 19.0 for Yervoy and version 13.0 for Opdivo) are updated in accordance. In addition, the Worksharing applicant (WSA) took the opportunity to correct some typos throughout the Yervoy and Opdivo product information."

Re-examination timetable.

Action: For adoption

Opinion adopted on 26.07.2018. An oral Explanation was held on 25.07.2018.

Request for Supplementary Information adopted on 31.05.2018, 22.02.2018.

The CHMP adopted the re-examination timetable.

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

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

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

Scope: Request by the applicant dated 10 September 2018 requesting an extension of clock stop to respond to the List of Questions adopted on 22 March 2018.

Action: For adoption

List of Questions adopted on 22.03.2018.

The CHMP agreed to the request for an extension of clock stop to respond to the List of Questions adopted on 22 March 2018.

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. quizartinib –Orphan - H0004468

Daiichi Sankyo Europe GmbH, Treatment of adults with relapsed or refractory acute myeloid leukemia (AML) which is FLT3-ITD positive

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

Action: For adoption

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

8.2. Priority Medicines (PRIME)

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

8.2.1. List of applications received

Action: For information

The CHMP noted the applications received.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 4 recommendations for eligibility to PRIME: 1 was granted and 3 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. Onivyde - irinotecan hydrochloride trihydrate – Orphan - EMEA/H/C/004125/II/0008

Baxalta Innovations GmbH

Rapporteur: Filip Josephson, PRAC Rapporteur: David Olsen,

Scope: "Update of sections 1, 2, 4.2, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC in order to reflect the expression of strength based on irinotecan anhydrous free-base. The Labelling and Package Leaflet are updated accordingly. In addition the MAH took the opportunity to introduce minor editorial changes. The updated RMP version 2.1 has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application.

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

9.1.2. Orgalutran - ganirelix - EMEA/H/C/000274/II/0041

Merck Sharp & Dohme B.V.

Rapporteur: Outi Mäki-Ikola,

Scope: "Update of section 4.3 of the SmPC to expand the existing contraindication regarding hypersensitivity to include also wording regarding dry natural rubber/latex and sections 4.4 and 6.5 of the SmPC to clarify that this product is in contact with dry natural rubber/latex. The labelling and Package Leaflet have been updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representative in Belgium in the Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 26.07.2018.

The Committee discussed the issues identified in this application, which related to the SmPC section 4.4.

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

10. Referral procedures

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

No items

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

No items

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

No items

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

10.4.1. Diclofenac Sodium Spray Gel 4% cutaneous spray, solution and associated names– EMEA/H/A-29(4)/1467

MAHs: various

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Harald Enzmann

Scope: Oral explanation

Action: For adoption

An oral explanation was held on 19 September 2018 at time 12:00. It was noted that the applicant should provide further evidence and justifications for bridging with other products used in the studies submitted by means of literature to establish safety and efficacy.

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

Post-meeting note: final timetable was adopted via written procedure on 2 October 2018:

Submission of responses: 11.10.2018

Re-start of the procedure: 18.10.2018

Rapporteur/co-rapporteur assessment report(s) circulated to CHMP: 31.10.2018

Comments: 05.11.2018

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 08.11.2018

CHMP Opinion: November 2018 CHMP

10.4.2. Syner-KINASE 10 000 IU - EMEA/H/A-29(4)/1472

Syner-Medica Ltd

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Sol Ruiz

Scope: Request for an extension to the clock stop to respond to the list of questions adopted in July 2018.

Action: For adoption

RMS: UK; CMS: DE, ES, FR, NL; Mutual Recognition Procedure number: UK/H/6520/01-05/MR, Disagreements regarding benefit/risk balance, safety and manufacturing.

The CHMP agreed to the request for an extension to the clock stop to respond to the list of questions adopted in July 2018.

List of questions adopted: 26.07.2018

Submission of responses: 31.10.2018

Re-start of the procedure: 15.11.2018

Rapporteur/co-rapporteur assessment report circulated to CHMP: 28.11.2018

Comments: 03.12.2018

Updated rapporteur/co-rapporteur assessment report circulated to CHMP: 06.12.2018

LoOI/CHMP opinion: December 2018 CHMP

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. Metamizole containing medicinal products – metamizole sodium - EMEA/H/A-31/1469

MAH various

Rapporteur: Ewa Balkowiec, Co-rapporteur: Harald Enzmann

Scope: List of outstanding issues

Action: For adoption

The Polish 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 whether the scientific data regarding the maximum daily dose and contraindications concerning pregnancy and breastfeeding are adequately presented in the product information of metamizole containing medicinal products.

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

Submission of responses: 31.10.2018

Re-start of the procedure: 15.11.2018

Joint assessment report circulated to CHMP: 28.11.2018

Comments: 03.12.2018

Updated joint assessment report circulated to CHMP: 06.12.2018

CHMP 2nd RSI or CHMP opinion: December 2018 CHMP

10.6.2. Angiotensin-II-receptor antagonists (sartans) containing a tetrazole group - EMEA/H/A-31/1471

MAHs: various

Rapporteur: Martina Weise

Scope: List of outstanding issues

Action: For adoption

Referral notification from European Commission regarding an API manufacturer (Zhejiang Huahai Pharmaceutical, China), who has detected the presence of a previously undetected impurity, N-nitrosodimethylamine (NDMA, also known as dimethylnitrosamine) in the valsartan API manufactured at its site in Chuannan. Zhejiang Huahai is one of the API manufacturers that are supplying valsartan for medicinal products authorised in the EU.

The CHMP was updated on the situation and the actions taken. Furthermore they were informed about the latest exchange of information between international partners.

The CHMP agreed to consult the QWP and SWP and adopted lists of questions to these groups.

The CHMP adopted a list of questions to the MAHs and active substance manufacturers with a specific timetable.

Submission of responses: 31.10.2018

Re-start of the procedure: 15.11.2018

Joint assessment report circulated to CHMP: 28.11.2018

Comments: 03.12.2018

Updated joint assessment report circulated to CHMP: 06.12.2018

CHMP 2nd RSI or CHMP opinion: December 2018 CHMP

Furthermore it was agreed to extend the review to other sartans containing a tetrazole group (candesartan, irbesartan, losartan and olmesartan).

The CHMP agreed to appoint one Rapporteur for each active substance in addition to a procedure coordinator.

10.6.3. Omega-3-acid-ethyl esters- containing medicinal products for oral use – EMEA/H/A-31/1464

MAHs: various

Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise

Scope: List of experts for SAG Cardiovascular meeting to be held on 10 October 2018

Action: For adoption

Review of the benefit-risk balance following notification by the MPA in Sweden on 15 March 2018 of a referral under Article 31 of Directive 2001/83/EC.

The CHMP adopted list of experts for SAG Cardiovascular meeting to be held on 10 October 2018.

Post-meeting note: Updated list of experts was adopted via written procedure on 8 October 2018

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

September 2018 Early Notification System on envisaged CHMP/CMDh outcome accompanied

by communication to the general public.

Action: For information

The CHMP noted the ENS.

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

Minutes of ITF Briefing meeting held on 19th July 2018

Action: For information

The CHMP noted the minutes.

13.2. Innovation Task Force briefing meetings

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

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Election of new CHMP chairperson

Action: For adoption

The mandate of the CHMP Chairperson, Tomas Salmonson, ended on 20 September 2018 having served the maximum of two 3-year mandates. The EMA Secretariat thanked Tomas Salmonson for his enormous achievements during his chairmanship, his leadership as chair to the CHMP as well as his contributions to the EU network.

The election of the new chairperson took place in accordance to the CHMP rules of procedure. The CHMP elected Harald Enzmann as new CHMP chair, for a three-year mandate, starting on 21 September 2018.

The CHMP and the Agency congratulated Harald Enzmann on his election and wished him all the best in his new role as Chair of the Committee.

14.1.2. Telematics strategy 2020-2025: Concept Paper

Action: For discussion

The CHMP noted the call for contributors.

14.1.3. Concepts of significant benefit (follow-up to CHMP Work Plan 2017)

Action: For discussion

The CHMP noted the analysis on Concepts of significant benefit (follow-up to CHMP Work Plan 2017).

14.1.4. Joint CHMP-PDCO Strategic Review and Learning meeting under EU Austrian Presidency

Final Agenda for 26-28 September 2018 in Vienna, Austria

Action: For adoption

The CHMP adopted the final agenda.

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 03-06 September 2018

Action: For information

The CHMP noted the Summary of recommendations and advice.

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for September 2018

Action: For adoption

The CHMP noted the EURD list.

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 12-14 September 2018
Action: For information

The CHMP noted the draft minutes.

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Agenda of the HMPC meeting to be held on 23-24 September 2018

Action: For information

The CHMP noted the agenda.

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at September 2018 PDCO

Action: For information

The CHMP noted the information.

Report from the PDCO meeting held on 25–27 July 2018

Action: For information

The CHMP noted the report.

FINAL Reflection paper on the use of extrapolation in the development of medicines for paediatrics

Action: For discussion/adoption

Postponed to October ORGAM

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 11-13 September 2018

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 17-19 September 2018

Action: For information

The CHMP noted the report.

CMDh questions to BWP on leeches (EMA/CMDh/270304/2018)

Action: For information

Follow up from May 2018 CHMP. Following clarification from EMA, the CMDh questions have been forwarded to BWP for response.

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 3-6 September 2018. Table of conclusions

Action: For information

Scientific advice letters: Information related to scientific advice letters cannot be released at present time as these contain commercially confidential content.

The CHMP noted the report.

Information on upcoming elections for SAWP

Action: For information

The CHMP noted the information about the upcoming elections regarding SAWP Detailed timelines for the launch of the call for nomination and the deadlines for nominations will be communicated shortly.

14.3.2. Name Review Group (NRG)

No items

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP September 2018 meeting to CHMP for adoption:

- 10 reports on products in scientific advice and protocol assistance
- 15 reports on products in pre-authorisation procedures
- 1 report on products in plasma master file

Action: For adoption

The CHMP adopted the BWP reports.

14.3.4. Guideline Consistency Group (GCG)

Chair: Aranzazu Sancho-Lopez,

Feedback from Barbara van Zwieten-Boot as previous GCG chair

Action: For information

The CHMP noted the feedback and thanked the previous Chair for her contribution.

14.3.5. Excipients Drafting Group

Chair: Dominique Masset

Information for the package leaflet regarding ethanol used as an excipient in medicinal products for human use (EMA/CHMP/43486/2018)
Action: For adoption

Information for the package leaflet regarding dextrans used as excipients in medicinal products for human use (EMA/CHMP/187129/2016)
Action: For adoption for 6-month public consultation

Information for the package leaflet regarding proline used as an excipient in medicinal products for human use (EMA/CHMP/108086/2016)
Action: For adoption for 6-month public consultation

Information for the package leaflet regarding lactose used as an excipient in medicinal products for human use (EMA/CHMP/186428/2016)
Action: For adoption for 6-month public consultation

Information for the package leaflet regarding polysorbates used as excipients in medicinal products for human use (EMA/CHMP/190743/2016)

Action: For adoption for 6-month public consultation

The CHMP is asked to provide comments in writing by Thursday 27 September . If no comments received all the documents are considered adopted.

Post meeting note: No comments were received and therefore the document on ethanol was considered as adopted and the other documents were considered adopted for 6-month public consultation on 27.09.2018

14.3.6. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus/Romaldas Mačiulaitis

Response from RIWP and PKWP to CMDh questions on Classification as Narrow Therapeutic Index (NTI) drug and advice on requirements for bioequivalence studies – colchicine

Action: For adoption

The CHMP adopted the response.

14.3.7. Safety Working Party (SWP)

Chair: Jan Willem Van der Laan

Response from SWP to PRAC regarding prenatal exposure to paracetamol and impact on the urogenital apparatus or impact on neurodevelopment

SWP Lead: Mikael Andersson (SE),

Action: For adoption

The CHMP adopted the response.

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

14.5.1. International Council on Harmonisation (ICH)

Clinical electronic Structured Harmonized Protocol (CeSHarP): Call for expression of interest of one expert

Action: For information

The CHMP noted the call for expression of interest of one expert.

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. New marketing authorisation applications for 2018 with and without appointed rapporteurs

Action: For information

The CHMP noted the report.

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Recommendations of HMA-EMA Joint Big Data taskforce

Action: For information

The CHMP noted the information.

15.1.2. Regulatory Science Engagement Plan to 2025

Scope: presentation of EMA's regulatory science engagement plan

Action: For discussion

The CHMP noted the information.

15.1.3. Preparedness of the system and capacity increase

Action: For information

The CHMP noted the information

16. List of participants

List of participants including any restrictions with respect to involvement of members/alternates/experts following evaluation of declared interests for the 17 – 20 September 2018 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Tomas Salmonson	Chair	Sweden	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Milena Stain	Alternate	Austria	No interests declared	
Christophe Focke	Alternate	Belgium	No restrictions applicable to this meeting	
Mila Vlaskovska	Member	Bulgaria	No interests declared	
Katarina Vučić	Member	Croatia	No interests declared	
Emilia Mavrokordatou	Member	Cyprus	No interests declared	
Ondřej Slanař	Member	Czech Republic	No interests declared	
Tomas Boran	Alternate	Czech Republic	No interests declared	
Sinan B. Sarac	Member	Denmark	No interests declared	
Mark Ainsworth	Alternate	Denmark	No restrictions applicable to this meeting	
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	
Harald Enzmann	Member (Vice-Chair)	Germany	No interests declared	
Martina Weise	Alternate	Germany	No restrictions applicable to this meeting	
Eleftheria Nikolaidi	Member	Greece	No interests declared	
Agnes Gyurasics	Member	Hungary	No interests declared	
Hrefna Gudmundsdottir	Alternate	Iceland	No interests declared	
Jayne Crowe	Member	Ireland	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Peter Kiely	Alternate	Ireland	No interests declared	
Daniela Melchiorri	Member	Italy	No restrictions applicable to this meeting	
Juris Pokrotnieks	Member	Latvia	No restrictions applicable to this meeting	
Natalja Karpova	Alternate	Latvia	No interests declared	
Romaldas Mačiulaitis	Member	Lithuania	No participation in final deliberations and voting on	5.1.9. RoActemra - tocilizumab - EMEA/H/C/000955/II/0076 5.1.12. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0007/G 5.2.1. Hemlibra - emicizumab - EMEA/H/C/004406/II/0002
John Joseph Borg	Member	Malta	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	
Svein Rune Andersen	Member	Norway	No interests declared	
Bjorg Bolstad	Alternate	Norway	No restrictions applicable to this meeting	
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Vacant	Alternate	Poland		
Bruno Sepodes	Member	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No restrictions applicable to this meeting	
Simona Badoi	Member	Romania	No interests declared	
Francisek Drafi	Member	Slovakia	No interests declared	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Concepcion Prieto Yerro	Member	Spain	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Jorge Camarero Jiménez	Alternate	Spain	No participation in final deliberations and voting on	5.1.9. RoActemra - tocilizumab - EMEA/H/C/000955/II/0076 5.1.12. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0007/G 5.2.1. Hemlibra - emicizumab - EMEA/H/C/004406/II/0002
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Greg Markey	Member	United Kingdom	No interests declared	
Nithyanandan Nagercoil	Alternate	United Kingdom	No restrictions applicable to this meeting	
Robert James Hemmings	Co-opted member	United Kingdom	No interests declared	
Koenraad Norga	Co-opted member	Belgium	No participation in final deliberations and voting on:	5.1.16. WS1369 Elebrato Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004781/WS1369/0001 Trelegy Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004363/WS1369/0001
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	
Sabine Mayrhofer	Expert - in person*	Germany	No interests declared	
Barbara van Zwieten-Boot	Expert - in person*	Netherlands	No interests declared	
Pierre Demolis	Expert - in person*	France	No interests declared	
Theis Moeslund Jensen	Expert - in person*	Denmark	No restrictions applicable to this meeting	
Patricia Diaz Ramos	Expert - in person*	Spain	No interests declared	
Aaron Emmanuel Sosa Mejia	Expert - in person*	Denmark	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Linda Trauffler	Expert - in person*	Austria	No interests declared	
Julie Williams	Expert - in person*	United Kingdom	No interests declared	
Koenraad Brusselmans	Expert - via telephone*	Belgium	No restrictions applicable to this meeting	
Serge Bakchine	Expert - via telephone*	France	No interests declared	
Jonas Bergh	Expert - via telephone*	Sweden	No restrictions applicable to this meeting	
Olga Kholmanskikh	Expert - via Adobe*	Belgium	No interests declared	
Cecilia Chisholm	Expert - via telephone*	United Kingdom	No interests declared	
Michael Page	Expert - in person*	United Kingdom	No restrictions applicable to this meeting	
Marie Louise Schougaard Christiansen	Expert - via telephone*	Denmark	No interests declared	
Martina Schussler-Lenz	Expert - via telephone*	Germany	No interests declared	
Nikolai Constantin Brun	Expert - via telephone*	Denmark	No restrictions applicable to this meeting	
Gary Inwards	Expert - via telephone*	United Kingdom	No interests declared	
Joseph Emmerich	Alternate	France	No interests declared	
Nele Steens	Expert - in person*	Belgium	No interests declared	
Mario Miguel Coelho da Silva Rosa	Expert - via telephone*	Portugal	No interests declared	
Georgios Aislaitner	Expert - via Adobe*	Germany	No interests declared	
Andreas Wilhelm Grummel	Expert - via Adobe*	Germany	No interests declared	
Ellen Pantke	Expert - via Adobe speaking*	Germany	No restrictions applicable to this meeting	
Joerg Zinserling	Expert - via Adobe*	Germany	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Janet Koenig	Expert - via Adobe*	Germany	No interests declared	
Maria Chamorro Somoza Diaz-Sarmiento	Expert - via Adobe*	Spain	No interests declared	
Irmgard Resch	Expert - via Adobe*	Austria	No interests declared	
Leena Luukkanen	Expert - via Adobe*	Finland	No interests declared	
Patients' representative	Patient observer		No interests declared	
Patients' representative	Patient observer		No interests declared	
Representative from the European Commission attended the meeting Meeting run with the help of EMA staff				

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

17. Explanatory notes

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

Oral explanations *(section 2)*

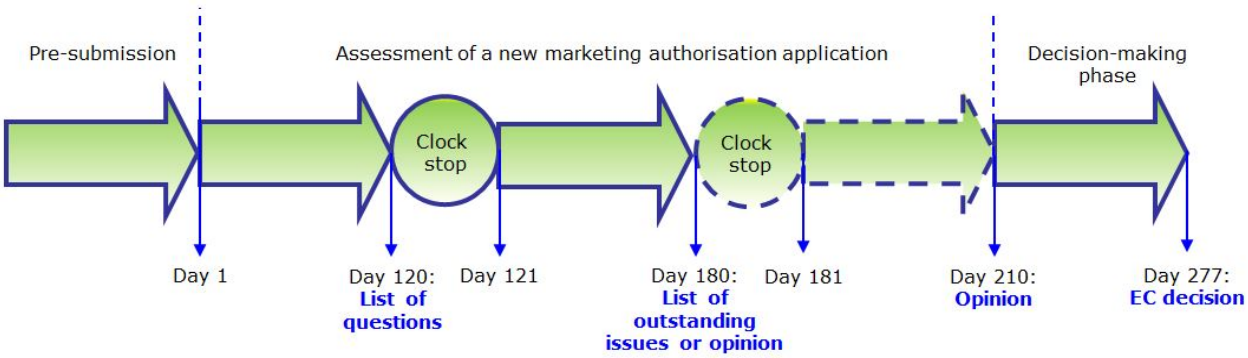
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

Initial applications *(section 3)*

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

Re-examination procedures *(section5.3)*

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

Withdrawal of application *(section 3.7)*

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

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

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

Pre-submission issues *(section 8)*

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

Post-authorisation issues *(section 9)*

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

Referral procedures *(section 10)*

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

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

Pharmacovigilance issues *(section 11)*

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

Inspections Issues *(section 12)*

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

Innovation task force *(section 13)*

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

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

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

Satellite groups / other committees *(section 14.2)*

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

Invented name issues *(section 14.3)*

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

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

30 October 2018
EMA/CHMP/768841/2018

Annex to 17-20 September 2018 CHMP Minutes

Pre submission and post authorisation issues

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

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

Final Outcome of Rapporteurship allocation for September 2018: **For adoption**	Adopted.

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

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

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

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

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/R/0079 AstraZeneca AB, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Jean-Michel Dogné Request for Supplementary Information adopted on 28.06.2018.	The CHMP, having considered the application as set out in the appended assessment report, is of the opinion that the risk-benefit balance of the above mentioned medicinal product remains favourable and therefore recommends by consensus, the renewal of the marketing authorisation for the above mentioned medicinal product. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. The summary of opinion was circulated for information.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Adempas - riociguat - EMEA/H/C/002737/R/0026, Orphan Bayer AG, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Julie Williams Request for Supplementary Information adopted on 20.09.2018.	Request for supplementary information adopted with a specific timetable.
Bemfola - follitropin alfa - EMEA/H/C/002615/R/0019 Gedeon Richter Plc., Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Menno van der Elst	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Brintellix - vortioxetine - EMEA/H/C/002717/R/0019 H. Lundbeck A/S, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Laurence de Fays Request for Supplementary Information adopted on 26.07.2018.	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.
Entyvio - vedolizumab - EMEA/H/C/002782/R/0032 Takeda Pharma A/S, Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Adam Przybylkowski Request for Supplementary Information adopted on 20.09.2018.	Request for supplementary adopted with a specific timetable.
Ixiaro - japanese encephalitis vaccine (inactivated, adsorbed) - EMEA/H/C/000963/R/0091 Valneva Austria GmbH, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Brigitte Keller-Stanislawski	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.
Izba - travoprost - EMEA/H/C/002738/R/0011	Positive Opinion adopted by consensus together with the CHMP assessment report and translation

Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Rhea Fitzgerald Request for Supplementary Information adopted on 26.07.2018.	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.
Latuda - lurasidone - EMEA/H/C/002713/R/0020 Aziende Chimiche Riunite Angelini Francesco S.p.A., Rapporteur: Filip Josephson, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Ulla Wändel Liminga	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Levetiracetam Hospira - levetiracetam - EMEA/H/C/002783/R/0018 Hospira UK Limited, Generic, Generic of Keppra, Rapporteur: Juris Pokrotnieks, PRAC Rapporteur: Laurence de Fays Request for Supplementary Information adopted on 26.07.2018.	Positive Opinion adopted by consensus together with the CHMP assessment report. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.
Mirvaso - brimonidine - EMEA/H/C/002642/R/0021 Galderma International, Rapporteur: Filip Josephson, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Julie Williams	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.
Neuraceq - florbetaben (18F) - EMEA/H/C/002553/R/0025 Life Radiopharma Berlin GmbH, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Patrick Batty Request for Supplementary Information adopted on 26.07.2018.	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.
Synflorix - pneumococcal polysaccharide	Positive Opinion adopted by consensus together

conjugate vaccine (adsorbed) - EMEA/H/C/000973/R/0128 GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ulla Wändel Liminga	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.
Thymanax - agomelatine - EMEA/H/C/000916/R/0040 Servier (Ireland) Industries Ltd., Duplicate, Duplicate of Valdoxan, Rapporteur: Svein Rune Andersen, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Karen Pernille Harg Request for Supplementary Information adopted on 20.09.2018.	Request for supplementary information adopted with a specific timetable.
Valdoxan - agomelatine - EMEA/H/C/000915/R/0042 Les Laboratoires Servier, Rapporteur: Svein Rune Andersen, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Karen Pernille Harg Request for Supplementary Information adopted on 20.09.2018.	Request for supplementary information adopted with a specific timetable.
Vimizim - elosulfase alfa - EMEA/H/C/002779/R/0024, Orphan BioMarin Europe Ltd, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Harald Enzmann, PRAC Rapporteur: Patrick Batty Request for Supplementary Information adopted on 20.09.2018.	Request for supplementary information adopted with a specific timetable.
Zoledronic Acid Accord - zoledronic acid - EMEA/H/C/002667/R/0006 Accord Healthcare Limited, Generic, Generic of Zometa, Rapporteur: Alar Irs, PRAC Rapporteur: Doris Stenver	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion.

B.2.3. Renewals of Conditional Marketing Authorisations

OCALIVA - obeticholic acid - EMEA/H/C/004093/R/0009, Orphan Intercept Pharma Ltd, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van	Request for supplementary information adopted with a specific timetable.

der Elst Request for Supplementary Information adopted on 20.09.2018.	

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection PRAC recommendations on signals adopted at the PRAC meeting held on 03-06 September 2018 PRAC:	
Signal of cytomegalovirus (CMV) infection: **LEMTRADA - Alemtuzumab – EMEA/H/C/003718** Sanofi Belgium, Rapporteur: Mark Ainsworth, Co-Rapporteur: Filip Josephson PRAC recommendation on a variation**: For adoption**	Adopted.
Signal of immune thrombocytopenic purpura, thrombocytopenia: **TECFIDERA - Dimethyl Fumarate – EMEA/H/C/002601** Biogen Idec Ltd, Rapporteur: Martina Weise, Co-Rapporteur: Robert James Hemmings PRAC recommendation on a variation**: For adoption**	Adopted.
Signal of interstitial lung disease: **- Duloxetine -** **ARICLAIM - EMEA/H/C/000552** Eli Lilly Nederland B.V., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Kristina Dunder **CYMBALTA - EMEA/H/C/000572** **XERISTAR - EMEA/H/C/000573** **YENTREVE - EMEA/H/C/000545** **DULOXETINE LILLY - EMEA/H/C/004000** Eli Lilly Nederland B.V., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Filip Josephson **DULOXETINE MYLAN - EMEA/H/C/003981**	Adopted.

Mylan S.A.S, Rapporteur: John Joseph Borg **DULOXETINE ZENTIVA -EMEA/H/C/003935** Zentiva k.s., Rapporteur: Kristina Dunder PRAC recommendation on a variation: **For adoption**	
Signal of aortic aneurysm and dissection: **QUINSAIR – Fluoroquinolones - EMEA/H/C/002789** Chiesi Farmaceutici S.p.A., Rapporteur: Robert James Hemmings, Co-Rapporteur: Ondrej Slanar PRAC recommendation on a variation/DHPC: **For adoption**	Adopted.
Signal of skin cancer: **- Hydrochlorothiazide –** **Actelsar HCT - telmisartan, hydrochlorothiazide – EMEA/H/C/002676** Actavis Group PTC ehf, Rapporteur: Alar Irs **Kinzalkomb - telmisartan, hydrochlorothiazide – EMEA/H/C/000415** **PritorPlus - telmisartan, hydrochlorothiazide – EMEA/H/C/000414** Bayer AG, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Harald Enzmann **MicardisPlus - telmisartan, hydrochlorothiazide – EMEA/H/C/000413** Boehringer Ingelheim International, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Harald Enzmann **Ifirmacombi - irbesartan, hydrochlorothiazide - EMEA/H/C/002302** Krka, d.d., Novo mesto, Rapporteur: Concepcion Prieto Yerro **Tolucombi – telmisartan, hydrochlorothiazide – EMEA/H/C/0002549** Krka, d.d., Novo mesto, Rapporteur: Alar Irs **Rasilez HCT - aliskiren, hydrochlorothiazide - EMEA/H/C/000964**	Adopted.

Noden Pharma DAC, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Agnes Gyurasics **Copalia HCT - amlodipine, valsartan, hydrochlorothiazide - EMEA/H/C/001159** **Dafiro HCT - amlodipine besylate, valsartan, hydrochlorothiazide - EMEA/H/C/0001160** Novartis Europharm Limited, Rapporteur: Mark Ainsworth, Co-Rapporteur: Alar Irs **Irbesartan Hydrochlorothiazide Zentiva - irbesartan, hydrochlorothiazide - EMEA/H/C/000783** **Karvezide - irbesartan, hydrochlorothiazide - EMEA/H/C/000221** Sanofi-aventis groupe Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Outi Maki-Ikola **CoAprovel - irbesartan, hydrochlorothiazide - EMEA/H/C/000222** Sanofi Clir SNC, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Outi Maki-Ikola **Irbesartan/Hydrochlorothiazide Teva - irbesartan, hydrochlorothiazide - EMEA/H/C/001112** Teva B.V., Rapporteur: Concepcion Prieto Yerro PRAC recommendation on a variation/DHPC: **For adoption**	
Signal of cytomegalovirus gastrointestinal infection: **YERVOY – Ipilimumab – EMEA/H/C/002213** Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jorge Camarero Jiménez PRAC recommendation on a variation: **For adoption**	Adopted.
Signal of pulmonary hypertension and fatal cases associated with use in an off-label indication, early-onset intrauterine growth restriction:	Adopted.

REVATIO - Sildenafil – EMEA/H/C/000638 **VIAGRA -Sildenafil – EMEA/H/C/000202** Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Concepcion Prieto Yerro PRAC recommendation on a DHPC: **For adoption**	
Signal of premature ending of the GALILEO5 study in patients who have received an artificial heart valve through a transcatheter aortic valve replacement (TAVR): **XARELTO – Rivaroxaban – EMEA/H/C/000944** Bayer AG, Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise PRAC recommendation on a DHPC: **For adoption**	Adopted.
PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its September 2018 meeting:	
EMEA/H/C/PSUSA/00000985/201801 (dexamethasone (centrally authorised product indicated in uveitis and macular oedema)) CAPS: **Ozurdex** (EMEA/H/C/001140) (dexamethasone), Allergan Pharmaceuticals Ireland, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, "28 Jan 2017 – 27 Jan 2018"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 to update the adverse reaction "Complication of device insertion" to "Complication of device insertion resulting in ocular tissue injury". The following changes to the product information of medicinal products containing dexamethasone are recommended (new text underlined and in bold, deleted text strike through): Summary of Product Characteristics • Section 4.8 Undesirable effects Complication of device insertion resulting in ocular tissue injury The PRAC considered that the RMP is acceptable. In addition, minor revisions were recommended to be taken into account at the next RMP update. The Icelandic and the Norwegian CHMP members

	agree with the above-mentioned recommendation of the CHMP. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00001393/201802 (fingolimod) CAPS: **Gilenya** (EMEA/H/C/002202) (fingolimod), Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "01-Mar-2017 - 28-Feb-2018"	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 include safety information on the effect of fingolimod on HPV infections; section 4.8 is also updated to include myalgia and arthralgia under common frequency and to further update information regarding cutaneous T-cell lymphoma (mycosis fungoides). The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00002169/201802 (nitisinone) CAPS: **Orfadin** (EMEA/H/C/000555) (nitisinone), Swedish Orphan Biovitrum International AB, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, "From 21 Feb 2017 - To 20 Feb 2018"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended together with the detailed explanation of the scientific grounds for the differences with the PRAC recommendation, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.4 of the SmPC to add a recommendation with regards to regular examination of the eyes after treatment initiation. 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/00002499/201802 (prasugrel) CAPS: **Efient** (EMEA/H/C/000984) (prasugrel), Daiichi Sankyo Europe GmbH, Rapporteur: Mark	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

Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, "26-Feb-2017 to 25-Feb-2018"	terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): "Update of sections 4.4 and 4.5 of the SmPC to add information on interaction with morphine. 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/00002611/201801 (ranolazine) CAPS: **Ranexa** (EMEA/H/C/000805) (ranolazine), Menarini International Operations Luxembourg S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "27 Jan 2015 - 26 Jan 2018"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.4 of the SmPC to add a warning to specify that the observed QT prolongation is dose dependent and update of Annex II to remove the additional risk minimisation measures. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010022/201801 (axitinib) CAPS: **Inlyta** (EMEA/H/C/002406) (axitinib), Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: David Olsen, "27 January 2017 to 26 January 2018"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of sections 4.4 and 4.8 of the SmPC to add a warning on the risk of aneurysm rupture and to add the new ADR 'aneurysm rupture' as an example of bleeding in a footnote under the table of adverse 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/00010043/201801 (meningococcal group-B vaccine (rDNA, component, adsorbed)) CAPS: **Bexsero** (EMEA/H/C/002333) (meningococcal group B vaccine (recombinant, component,	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following changes:

adsorbed)), GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “14/07/2017 - 13/01/2018”	Update of section 4.8 of the SmPC to add meningeal irritation with a frequency unknown and to add a short description to the term stating that symptoms such as photophobia and neck stiffness have been sporadically reported and that these events have been of mild and transient nature. The Package leaflet is updated accordingly. In addition, the risk management plan is revised (version 7.0) to update the list of important identified risks, the list of important potential risks and the list of missing information. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010120/201802 (nalmefene) CAPS: **Selincro** (EMEA/H/C/002583) (nalmefene), H. Lundbeck A/S, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, “25 Feb 2017 - 24 Feb 2018”	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 of the SmPC to add priapism, angioedema, urticaria, pruritus, rash, and erythema with a frequency unknown. The Package leaflet should be updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00000090/201801 (alitretinoin) CAPS: **Panretin** (EMEA/H/C/000279) (alitretinoin), Eisai Limited, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams “19 January 2017 – 18 January 2018”	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) with systemic absorption, concerning the following change(s): Update of section 4.8 of the SmPC to add ‘Hair texture Changes’ with a frequency rare. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010140/201801 (vismodegib)	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation

CAPS: **Erivedge** (EMEA/H/C/002602) (vismodegib), Roche Registration GmbH, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "30 January 2017 to 29 January 2018"	and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 of the SmPC to add the adverse reaction drug induced liver injury with a frequency not known. The Package leaflet is updated accordingly. The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP.
EMEA/H/C/PSUSA/00010363/201801 (dasabuvir) CAPS: **Exviera** (EMEA/H/C/003837) (dasabuvir), AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, PRAC Rapporteur: Dolores Montero Corominas, "15 January 2017 to 14 January 2018"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 of the SmPC to add diarrhoea with a frequency very common, vomiting with a frequency common and dehydratation with a frequency uncommon as adverse reactions identified with Exviera in combination with ombitasvir/paritaprevir/ritonavir and ribavirin. 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/00010367/201801 (ombitasvir / paritaprevir / ritonavir) CAPS: **Viekirax** (EMEA/H/C/003839) (ombitasvir / paritaprevir / ritonavir), AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, PRAC Rapporteur: Maria del Pilar Rayon, "15 January 2017 – 14 January 2018"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 of the SmPC to add diarrhoea with a frequency very common, vomiting with a frequency common and dehydratation with a frequency uncommon as adverse reactions identified with Viekirax in combination with dasabuvir and ribavirin. 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

Treprostinil SciPharm Sarl - treprostinil - EMEA/H/C/004847, Orphan SciPharm Sarl, Treatment of chronic	For information only. Comments can be sent to the EPL in case necessary.

thromboembolic pulmonary hypertension **WPAR**

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

Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0056/G, Orphan Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 05.07.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Alprolix - eftrenonacog alfa - EMEA/H/C/004142/II/0020, Orphan Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 20.09.2018.	Request for supplementary information adopted with a specific timetable.
Armisarte - pemetrexed - EMEA/H/C/004109/II/0017/G Actavis Group PTC ehf, Rapporteur: Alar Irs Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 21.06.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Bortezomib Accord - bortezomib - EMEA/H/C/003984/II/0014 Accord Healthcare Limited, Generic, Generic of VELCADE, Rapporteur: Milena Stain Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
Bortezomib Hospira - bortezomib - EMEA/H/C/004207/II/0008 Pfizer Europe MA EEIG, Generic, Generic of VELCADE, Rapporteur: Milena Stain Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
Cuprior - trientine - EMEA/H/C/004005/II/0001/G GMP-Orphan SA, Rapporteur: Jayne Crowe Opinion adopted on 13.09.2018. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 26.07.2018.	
Cyramza - ramucirumab - EMEA/H/C/002829/II/0024/G Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik Opinion adopted on 20.09.2018. Request for Supplementary Information adopted on 26.07.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cyramza - ramucirumab - EMEA/H/C/002829/II/0025 Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 19.07.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Daptomycin Hospira - daptomycin - EMEA/H/C/004310/II/0006/G Hospira UK Limited, Generic, Generic of Cubicin, Rapporteur: Kolbeinn Gudmundsson Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 22.02.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Dupixent - dupilumab - EMEA/H/C/004390/II/0009/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
EXJADE - deferasirox - EMEA/H/C/000670/II/0061 Novartis Europharm Limited, Rapporteur: Alexandre Moreau Opinion adopted on 20.09.2018. Request for Supplementary Information adopted on 26.07.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0106 Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Gliolan - aminolevulinic acid - EMEA/H/C/000744/II/0015 medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Bruno Sepodes Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 20.09.2018, 28.06.2018.	
Herzuma - trastuzumab - EMEA/H/C/002575/II/0005 Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 26.07.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kentera - oxybutynin - EMEA/H/C/000532/II/0047 Nicobrand Limited, Rapporteur: Bart Van der Schueren Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0051/G Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 19.07.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kineret - anakinra - EMEA/H/C/000363/II/0060 Swedish Orphan Biovitrum AB (publ), Rapporteur: Mark Ainsworth Opinion adopted on 20.09.2018. Request for Supplementary Information adopted on 26.07.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kyntheum - brodalumab - EMEA/H/C/003959/II/0004/G LEO Pharma A/S, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Lemtrada - alemtuzumab - EMEA/H/C/003718/II/0025/G Sanofi Belgium, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
Lonquex - lipegfilgrastim - EMEA/H/C/002556/II/0041/G Sicor Biotech UAB, Rapporteur: Greg Markey Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
MULTAQ - dronedarone - EMEA/H/C/001043/II/0041 sanofi-aventis groupe, Rapporteur: Johann	Request for supplementary information adopted with a specific timetable.

Lodewijk Hillege Request for Supplementary Information adopted on 13.09.2018.	
Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0082 Pfizer Europe MA EEIG, Rapporteur: Greg Markey Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
NovoSeven - eptacog alfa (activated) - EMEA/H/C/000074/II/0106 Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 20.09.2018.	Request for supplementary information adopted with a specific timetable.
Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0004 Roche Registration GmbH, Rapporteur: Mark Ainsworth Opinion adopted on 20.09.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ongentys - opicapone - EMEA/H/C/002790/II/0009 Bial - Portela & Cª, S.A., Rapporteur: Greg Markey Request for Supplementary Information adopted on 20.09.2018, 26.04.2018.	Request for supplementary information adopted with a specific timetable.
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0136/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
Reagila - cariprazine - EMEA/H/C/002770/II/0008 Gedeon Richter Plc., Rapporteur: Kristina Dunder Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Rekovelle - follitropin delta - EMEA/H/C/003994/II/0008/G Ferring Pharmaceuticals A/S, Rapporteur: Joseph Emmerich Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 28.06.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0052/G Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 20.09.2018.	
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0007 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Somavert - pegvisomant - EMEA/H/C/000409/II/0086/G Pfizer Europe MA EEIG, Rapporteur: Joseph Emmerich Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0125 GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 14.06.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0127/G GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 19.07.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tamiflu - oseltamivir - EMEA/H/C/000402/II/0135 Roche Registration GmbH, Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
Yervoy - ipilimumab - EMEA/H/C/002213/II/0058/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 12.07.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1404 **Nuwiq-EMEA/H/C/002813/WS1404/0022** **Vihuma-EMEA/H/C/004459/WS1404/0004**	Request for supplementary information adopted with a specific timetable.

Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 13.09.2018, 05.07.2018.	
WS1415 **Blitzima-EMEA/H/C/004723/WS1415/0015** **Ritemvia-EMEA/H/C/004725/WS1415/0015** **Rituzena-EMEA/H/C/004724/WS1415/0016** **Truxima-EMEA/H/C/004112/WS1415/0016** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz Opinion adopted on 20.09.2018. Request for Supplementary Information adopted on 26.07.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1427 **Nuwiq-EMEA/H/C/002813/WS1427/0024** **Vihuma-EMEA/H/C/004459/WS1427/0007** Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 20.09.2018.	Request for supplementary information adopted with a specific timetable.
WS1452 **Rixathon-EMEA/H/C/003903/WS1452/0013** **Riximyo-EMEA/H/C/004729/WS1452/0013** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Afinitor - everolimus - EMEA/H/C/001038/II/0058 Novartis Europharm Limited, Rapporteur: Harald Enzmann, “Submission of the final report from study CRAD001Y2201, listed as a category 1 study in the RMP. This is a three arm randomised study investigating the combination of everolimus with exemestane versus everolimus alone versus capecitabine in patients with oestrogen receptor positive metastatic breast	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

cancer after recurrence or progression on letrozole or anastrozole. Consequently, Annex II of the Product Information was updated to remove this study." Opinion adopted on 20.09.2018. Request for Supplementary Information adopted on 31.05.2018.	
Alecensa - alectinib - EMEA/H/C/004164/II/0016 Roche Registration GmbH, Rapporteur: Filip Josephson, "Submission of the final study analysis on secondary ALK-mutation positive/negative samples and correlation with clinical outcome in fulfilment of a CHMP recommendation for alectinib, adopted during the initial Marketing Authorisation. The application is based on an additional analysis generated from two studies (NP28673 and NP28761)." Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Atripla - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/000797/II/0130 Bristol-Myers Squibb and Gilead Sciences Ltd., Rapporteur: Martina Weise, "Update of sections 4.3 and 4.5 of the SmPC in order to include drug-drug interaction data between efavirenz (EFV) and grazoprevir/elbasvir based on a review of the antiviral product Zepatier. The Marketing authorisation holder (MAH) has taken the opportunity to introduce changes to the sodium wording in Section 4.4 of the SmPC and to align the text in Section 4.6 (Fertility, pregnancy and lactation) for Atripla with the currently approved wording in the Eviplera SmPC. The Package Leaflet (PIL) has been updated accordingly. In addition, the MAH has also taken the opportunity to implement some minor linguistic amendments (MLAs) to the translations of the product information annexes for the following languages: DE, FI, FR, IT, NL and NO." Opinion adopted on 20.09.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Baraclude - entecavir - EMEA/H/C/000623/II/0059 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, "Update of section 5.1 of the	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

SmPC in order to include information regarding the newly detected resistance information showing reduced susceptibility to entecavir for the rtA 181C substitution in combination with LVDr substitutions, rtL 180M + rtM204V. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10. The MAH also took the opportunity to add the sodium concentration for Baraclude 0.05 mg/ml oral solution in section 2 of the SmPC and section 2 of the PL according to the guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'." Opinion adopted on 13.09.2018.	
Brilique - ticagrelor - EMEA/H/C/001241/II/0041 AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 4.4 of the SmPC in order to clarify the posology in patients having an acute coronary syndromes (ACS) event, to update the warning related to bradyarrhythmia based on already assessed studies and post-marketed use (clinical trials PLATO (D5130C05262), PEGASUS (D5132C00001), SOCRATES (D5134C00001) and EUCLID (D5135C00001)) and to introduce "stroke" as a possible even in case of premature discontinuation. Furthermore the MAH took the opportunity to update the PI in relation to sodium content in line with QRD and to update the list of local representatives in the Package Leaflet."	Request for supplementary information adopted with a specific timetable.
Ceprotin - human protein C - EMEA/H/C/000334/II/0104 Baxter AG, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information of Ceprotin based on an update of the Company Core Safety Information. The Package Leaflet has been further updated." Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 21.06.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Coagadex - human coagulation factor X - EMEA/H/C/003855/II/0009, Orphan	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP

Bio Products Laboratory Limited, Rapporteur: Andrea Laslop, “Update of section section 5.2 of the SmPC in order to reflect data on long-term use based on final results from the study Ten05, a multicentre, retrospective data collection study on the use of BPL’s high purity factor X in the treatment of patients with hereditary factor X deficiency on a compassionate use basis. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the number of patients treated with Coagadex in section 4.8 of the SmPC based on studies Ten01, Ten02 and Ten03 as well as to include some editorial changes in section 4.2 of the SmPC. Furthermore, the information on perioperative management in the Package Leaflet has been aligned with information in the SmPC.” Opinion adopted on 20.09.2018.	Members were in agreement with the CHMP recommendation.
Cyramza - ramucirumab - EMEA/H/C/002829/II/0023/G Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik, “Submission of the final report from study Study I4T-MC-JVCZ Randomized Phase 2 Trial Evaluating Alternative Ramucirumab Doses in Combination with Paclitaxel in Second-Line Metastatic or Locally Advanced, Unresectable Gastric or Gastroesophageal Junction Adenocarcinoma and Study I4T-MC-JVDB Randomized Phase 2 Trial Evaluating Pharmacokinetics and Safety of Four Ramucirumab Dosing Regimens in Second Line Gastric or Gastroesophageal Junction Adenocarcinoma in fulfilment with Annex II condition linked to Cyramza Marketing Authorisation. Annex II of the product information has been updated accordingly.” Request for Supplementary Information adopted on 13.09.2018, 14.06.2018.	Request for supplementary information adopted with a specific timetable.
Dacogen - decitabine - EMEA/H/C/002221/II/0035, Orphan Janssen-Cilag International N.V., Rapporteur: Alexandre Moreau, “Update of section 4.4, and 4.8 of the SmPC in order to add the adverse events "Hepatic Function abnormal" and "Hyperbilirubinaemia" with the frequency common and to include clinical recommendations in patients developing signs or symptoms of hepatic impairment based on a cumulative review of post-marketing data; the Package Leaflet is updated accordingly.	Request for supplementary information adopted with a specific timetable.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of the local representative in Portugal in the Package Leaflet. Furthermore, the term "(for pH adjustment)" has been removed from the Annex IIIA in accordance with the revision 2 of the European Commission guideline on Excipients in the labelling and package leaflet of medicinal products for human use." Request for Supplementary Information adopted on 20.09.2018, 26.07.2018.	
ILARIS - canakinumab - EMEA/H/C/001109/II/0060 Novartis Europharm Limited, Rapporteur: Jan Mueller-Berghaus, "Update of section 5.1 of the SmPC based on the final clinical study report (CSR) from Study ACZ885G2306 (β-SPECIFIC 4 Patients: Study of Paediatric efficacy and safety with first-line use of canakinumab: An open-label canakinumab (ACZ885) dose reduction or dose interval prolongation efficacy and safety study in patients with Systemic Juvenile Idiopathic Arthritis (SJIA)). The submission of the final CSR addresses the post-authorisation measure MEA 036.3 (PAES) and the requirements of article 46 of the paediatric regulation." Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Isentress - raltegravir - EMEA/H/C/000860/II/0078/G Merck Sharp & Dohme B.V., Rapporteur: Greg Markey, "Submission of the final reports from 3 in vitro studies evaluating the inhibitory effect of raltegravir at higher concentrations on OATP1B3, OCT1, OCT2, MATE1 and MATE2-K transporters and CYP2B6, CYP2D6, UGT2B7 enzyme activities, and a final CSR to assess the drug-drug interaction (DDI) potential of raltegravir at a 1,200 mg once daily clinical dose, according to the request from the CHMP following the assessment of X/59." Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
Jinarc - tolvaptan - EMEA/H/C/002788/II/0015 Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information on acute liver failure	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

requiring liver transplantation, based post-marketing experience with tolvaptan in autosomal dominant polycystic kidney disease (ADPKD). The Package Leaflet is updated accordingly." Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 21.06.2018.	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0054 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Update of section 5.1 of the SmPC based on the final clinical study report (CSR) for KEYNOTE-045 (KN045); a phase III randomized clinical trial of pembrolizumab (MK-3475) versus paclitaxel, docetaxel or vinflunine in subjects with recurrent or progressive metastatic urothelial cancer. The submission addresses the post-authorisation measure 'ANX 020' and Annex IID has been updated accordingly." Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
Kyprolis - carfilzomib - EMEA/H/C/003790/II/0030, Orphan Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of section 4.4 of the SmPC in order to include a warning of the increased risk of cardiac failure in Asian patients treated with carfilzomib based on postmarketing experience and 3 phase 3, randomized-controlled studies (CLARION-Study 2011-003; ENDEAVOR-Study 20130398 and A.R.R.O.W.- Study 20140355). In addition, the Marketing authorisation holder (MAH) took the opportunity to propose few minor typographical changes to SmPC." Opinion adopted on 20.09.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Latuda - lurasidone - EMEA/H/C/002713/II/0021 Aziende Chimiche Riunite Angelini Francesco S.p.A., Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC to add new paediatric data available in children and adolescent patients (10-17 years of age) with bipolar I disorder, upon request by CHMP following the assessment of the paediatric study D1050326 submitted according to Art. 46 procedure (no. EMEA/H/C/002713/P46/008)."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 20.09.2018.	
Lemtrada - alemtuzumab - EMEA/H/C/003718/II/0023 Sanofi Belgium, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth, "Update of section 4.8 of the SmPC in order to update the table of frequencies of adverse reactions in accordance with the SmPC guideline following request from PRAC in procedure EMEA/H/C/PSUSA/00010055/201703. This procedure also included an update in section 4.4 to add warning on acute acalculous cholecystit following a cumulative review of the cases. The Package Leaflet is updated accordingly." Opinion adopted on 20.09.2018. Request for Supplementary Information adopted on 12.07.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
LUTATHERA - lutetium (177Lu) oxodotreotide - EMEA/H/C/004123/II/0005, Orphan Advanced Accelerator Applications, Rapporteur: Robert James Hemmings, "Update of the SmPC section 5.1 to include information on the quality of life based on analysis of Netter-I Quality of Life data." Request for Supplementary Information adopted on 20.09.2018.	Request for supplementary information adopted with a specific timetable.
Mircera - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/II/0067 Roche Registration GmbH, Rapporteur: Concepcion Prieto Yerro, "Update of sections 4.2., 5.1. and 5.2. of the SmPC in order to update the paediatric information based on results from phase II dose finding study NH 19707 (Dolphin): An Open-Label, Multi-Center, Multiple Dose Study to Determine the Optimum Starting Dose of Intravenous MIRCERA for Maintenance Treatment of Anemia in Pediatric Patients with Chronic Kidney Disease on Hemodialysis; listed as a category 3 study in the RMP. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 20.09.2018.	Request for supplementary information adopted with a specific timetable.
Orgalutran - ganirelix - EMEA/H/C/000274/II/0041	Request for supplementary information adopted with a specific timetable.

Merck Sharp & Dohme B.V., Rapporteur: Outi Mäki-Ikola, “Update of section 4.3 of the SmPC to expand the existing contraindication regarding hypersensitivity to include also wording regarding dry natural rubber/latex and sections 4.4 and 6.5 of the SmPC to clarify that this product is in contact with dry natural rubber/latex. The labelling and Package Leaflet have been updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representative in Belgium in the Package Leaflet.” Request for Supplementary Information adopted on 20.09.2018, 26.07.2018.	
Otezla - apremilast - EMEA/H/C/003746/II/0021 Celgene Europe BV, Rapporteur: Peter Kiely, “Update of sections 4.2 and 5.1 of Otezla SmPC to include data (up to 5 years of treatment) from the following studies (CC-10004-PSA-002, -003, -004, -005 and CC-10004-PSOR-008, - 009)) listed as a category 3 study in the RMP (MEA 002).” Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
Ozempic - semaglutide - EMEA/H/C/004174/II/0001 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, “Update of section 5.1 of the SmPC in order to reflect final results from the SUSTAIN 7 trial (NN9535-4216), a 40-week open-label trial comparing the safety and efficacy of 0.5 mg of Ozempic to 0.75 mg of dulaglutide and 1 mg of Ozempic to 1.5 mg of dulaglutide in patients on metformin with type-2 diabetes.” Request for Supplementary Information adopted on 13.09.2018, 26.07.2018, 25.05.2018.	Request for supplementary information adopted with a specific timetable.
Praluent - alirocumab - EMEA/H/C/003882/II/0040 sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, “Submission of the final clinical study report of study R727-CL-1018 (study title: A Phase 2 Pilot Study with a Randomized Double-Blind Treatment Phase to Evaluate the Pharmacodynamics and Safety of Alirocumab in Patients with Autosomal Dominant Hypercholesterolemia and Gain-of-Function Mutations in 1 or Both Alleles of the PCSK9 Gene or Loss-of-Function Mutations in 1 or More Alleles	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

of the Apolipoprotein B Gene), as per MEA012." Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 19.07.2018.	
Praluent - alirocumab - EMEA/H/C/003882/II/0041 sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Submission of the final clinical study report of study R727-CL-1119 (study title: A Randomized, Double-Blind, Double-Dummy, Active-Controlled Study to Evaluate the Efficacy and Safety of REGN727/SAR236553 in Patients with Primary Hypercholesterolemia Who Are Intolerant to Statins), as per MEA011." Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
Revestive - teduglutide - EMEA/H/C/002345/II/0043, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Mark Ainsworth, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC based on the final CSR of study TED-C14-006 ("a 24-Week Double-blind, Safety, Efficacy, and Pharmacodynamic Study Investigating Two Doses of Teduglutide in Pediatric Subjects Aged 1 Year Through 17 Years With Short Bowel Syndrome who are Dependent on Parenteral Support"; a category 3 study in the RMP). The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 20.09.2018, 26.07.2018, 31.05.2018.	Request for supplementary information adopted with a specific timetable.
Skilarence - dimethyl fumarate - EMEA/H/C/002157/II/0008/G Almirall S.A, Rapporteur: Robert James Hemmings, "Submission of the final report from study AML/27. This is an in vitro study aimed to assess the potential of dimethyl fumarate to inhibit human hepatic cytochrome P450 (CYP) enzymes. Submission of the final report from study AML/28. This is an in vitro study aimed to assess the potential interaction of dimethyl fumarate with p-glycoprotein (P-gp). Submission of the final report from study Almirall-15-05May2017. This is an in vitro study aimed to assess the interaction of dimethyl fumarate with human BCRP efflux (ABC)	Request for supplementary information adopted with a specific timetable.

transporters." Request for Supplementary Information adopted on 13.09.2018.	
Soliris - eculizumab - EMEA/H/C/000791/II/0103, Orphan Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez, "To update SmPC section 4.4 describing reports of serious infections with Neisseria species (other than Neisseria meningitidis), including disseminated gonococcal infections, SmPC section 4.5 describing the theoretical potential for drug-drug interaction between eculizumab and intravenous human immunoglobulin (IVIg), and SmPC section 4.8, clarifying sepsis as the most common presentation of Neisseria meningococcal infections. The annex II and the package leaflet are updated accordingly. The MAH took the opportunity to align the Product information with the QRD template." Opinion adopted on 20.09.2018. Request for Supplementary Information adopted on 28.06.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Somavert - pegvisomant - EMEA/H/C/000409/II/0084 Pfizer Europe MA EEIG, Rapporteur: Joseph Emmerich, "Update of sections 4.2 and 4.4 of the SmPC to introduce posology recommendations to recommend an assessment of baseline levels of liver tests (LTs) [serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum total bilirubin (TBIL), and alkaline phosphatase (ALP)] prior initiation of treatment with Somavert following analysis of the interim result for study "A6291010 (ACROSTUDY) - A multicenter, post marketing surveillance study of pegvisomant therapy in patients with acromegaly – extension" as requested in procedure EMEA/H/C/000409/MEA 061.1. The PL has been updated accordingly." Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 12.07.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Strensiq - asfotase alfa - EMEA/H/C/003794/II/0029, Orphan Alexion Europe SAS, Rapporteur: Greg Markey, "Update of annex II after submission of the final report from study AA-HPP-208 listed as a category 1 study in the RMP (ANX001.2). This is a	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

multicentre, randomised, open-label, phase 2a study of Strensiq in patients with hypophosphatasia. The MAH took also the occasion to update the PI to QRD version 10.0." Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 28.06.2018.	
Sustiva - efavirenz - EMEA/H/C/000249/II/0145/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, "Update of sections 4.3 and 4.5 of the SmPC in order to add contraindication with elbasvir/grazoprevir due to the potential for significant decreases in plasma concentrations of elbasvir and grazoprevir, based on the post-approval and literature data, the Package Leaflet is updated accordingly. Update of sections 4.4 and 4.5 to include warnings in relation to the co-administration of efavirenz and sofosbuvir/velpatasvir; efavirenz and vepatasvir/sofosbuvir/voxilaprevir and efavirenz and glecaprevir/pibrentasvir; based on the post-approval and literature data, the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet." Opinion adopted on 20.09.2018. Request for Supplementary Information adopted on 26.07.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Translarna - ataluren - EMEA/H/C/002720/II/0045, Orphan PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 4.5 of the SmPC in order to include information on Drug-Drug Interaction with sensitive probe substrate of organic anion transporting polypeptide 1B3 (OATP1B3) based on study PTC124-GD-042-HV (MEA016). The package leaflet is updated accordingly." Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
Translarna - ataluren - EMEA/H/C/002720/II/0046, Orphan PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update information on patients with moderate to	Request for supplementary information adopted with a specific timetable.

severe renal impairment based on results from study PTC124-GD-032-HV (MEA010). In addition the MAH took the opportunity to amend section 5.2 to propose correction of the biotransformation statement. The Package leaflet is updated accordingly." Request for Supplementary Information adopted on 20.09.2018.	
VELCADE - bortezomib - EMEA/H/C/000539/II/0090 Janssen-Cilag International NV, Rapporteur: Daniela Melchiorri, "Update of section 5.1 of the SmPC to update the information based on final long-term follow-up and overall survival data for LYM-3002, a Randomized, Open-label, Multicenter Phase 3 Study of the Combination of Rituximab, Cyclophosphamide, Doxorubicin, VELCADE, and Prednisone (VcR-CAP) or Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (R-CHOP) in Patients With Newly Diagnosed Mantle Cell Lymphoma who are not Eligible for a Bone Marrow Transplant. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of Local representatives in the Package Leaflet." Opinion adopted on 20.09.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Venclyxto - venetoclax - EMEA/H/C/004106/II/0011, Orphan AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "The Annex II is being updated following the fulfilment of Specific Obligation, which was requested to confirm the efficacy and safety of venetoclax in monotherapy, based on the assessment of interim study report of M14-032. In addition, section 5.1 of SmPC is being updated to reflect the updated results of Study M14-032. The Package Leaflet is updated accordingly. Study M14-032 is: a phase II open-label study investigating efficacy and safety of venetoclax in patients with CLL with relapse or refractory to B-cell receptor signalling pathway inhibitor therapy, listed as a category 2 study in the RMP. The CHMP recommends granting of a marketing authorisation no longer subject to specific obligations." Opinion adopted on 20.09.2018. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 28.06.2018.	
Venclyxto - venetoclax - EMEA/H/C/004106/II/0016, Orphan AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Submission of the report from study M13-982 listed as a category 3 study in the RMP. This is a Phase 2 Open-Label Study of the Efficacy of ABT199 (GDC-0199) in Subjects with Relapsed/Refractory or Previously Untreated Chronic Lymphocytic Leukemia Harboring the 17p Deletion." Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
Xadago - safinamide - EMEA/H/C/002396/II/0027 Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 4.5 of the SmPC in order to implement information regarding interaction of safinamide and rosuvastatin, following results from study CRO-PK-17-318. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Ireland in the Package Leaflet and to include editorial changes in the English, German and Spanish product information." Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
XALKORI - crizotinib - EMEA/H/C/002489/II/0055 Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, "Update of section 4.2 of the SmPC in order to provide greater clarity in the crizotinib dosing regimen modification recommendations for patients who receive a reduced dose of crizotinib, either because of pre-existing moderate or severe hepatic impairment or severe renal impairment or because of a previous dose reduction while on treatment with crizotinib. The Package Leaflet has been updated accordingly." Opinion adopted on 20.09.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
XALKORI - crizotinib - EMEA/H/C/002489/II/0057 Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, "Submission of a number of analysis pertaining to the mechanisms of tumor resistance to crizotinib due to secondary ROS1 kinase domain mutations in patients with ROS1-positive	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

non-small cell lung cancer (NSCLC)." Opinion adopted on 13.09.2018.	
XALKORI - crizotinib - EMEA/H/C/002489/II/0058 Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, "Submission of the final study report for study A8081038, a multinational active safety surveillance study of crizotinib in Europe and the United States." Opinion adopted on 06.09.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xultophy - insulin degludec / liraglutide - EMEA/H/C/002647/II/0026 Novo Nordisk A/S, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to reflect data for use of Xulthopy in combination with sodium glucose co-transporter 2 inhibitors (SGLT2i) in patients inadequately controlled on SGLT2i ±other oral anti-diabetic drug. The update is based on data from the clinical trial: NN9068-4229: "A Clinical Trial Comparing Glycaemic Control and Safety of Insulin Degludec/Liraglutide (IDegLira) versus Insulin Glargine (IGlar) as Add-on Therapy to SGLT2i in Subjects with Type 2 Diabetes Mellitus"." Opinion adopted on 20.09.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0038 Pfizer Ireland Pharmaceuticals, Rapporteur: Greg Markey, "Update of section 4.2 of the SmPC to amend the recommended duration of ceftaroline fosamil intravenous (IV) infusion for standard dose regimens in adults and paediatrics to a range of 5 to 60 minutes from the currently recommended infusion duration of 1 hour. The PIL is updated accordingly. In addition the MAH has also taken the opportunity to reformat section 4.2 of the SmPC Posology and method of administration and to incorporate minor editorial updates to sections 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC." Request for Supplementary Information adopted on 20.09.2018.	Request for supplementary information adopted with a specific timetable.
Zostavax - shingles (herpes zoster) vaccine (live) - EMEA/H/C/000674/II/0117 MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.5 and 5.1 of the SmPC to include that Zostavax can be given concomitantly with pneumococcal vaccine and to reflect the	Request for supplementary information adopted with a specific timetable.

results of an observational post-marketing study comparing the effectiveness of Zostavax when co-administrated with a 23-valent pneumococcal polysaccharide vaccine (Bruxvoort K et al. 2018). The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet." Request for Supplementary Information adopted on 20.09.2018.	
WS1371 **Rasilez-EMEA/H/C/000780/WS1371/0119** **Rasilez** **HCT-EMEA/H/C/000964/WS1371/0086** Noden Pharma DAC, Lead Rapporteur: Daniela Melchiorri, "Update of section 4.8 and 5.1 of the Rasilez SmPC and section 4.8 of the Rasilez/HCTZ SmPC in order to reflect the results from paediatric study CSPP100A2365E2 (a multicenter, 52 to 104 week extension study to evaluate the long term growth and development of pediatric hypertensive patients 6–17 years of age treated previously with aliskiren) provided as per the requirement of article 46." Request for Supplementary Information adopted on 20.09.2018, 31.05.2018.	Request for supplementary information adopted with a specific timetable.
WS1380 **Ebymect-EMEA/H/C/004162/WS1380/0033** **Edistride-EMEA/H/C/004161/WS1380/0027** **Forxiga-EMEA/H/C/002322/WS1380/0046** **Xigduo-EMEA/H/C/002672/WS1380/0045** AstraZeneca AB, Lead Rapporteur: Kristina Dunder, "Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to reflect the final study results from study D1690C00024 (DERIVE); A Multicentre, Double-Blind, Placebo-Controlled, Parallel Group, Randomized, Phase III Study to Evaluate the Glycaemic Efficacy and Renal Safety of Dapagliflozin in Patients with Type 2 Diabetes Mellitus and Moderate Renal Impairment (CKD 3A) Who Have Inadequate Glycaemic Control. In addition, the Worksharing applicant took the opportunity to implement minor editorial changes in Edistride, Ebymect and Xigduo PI and to update the list of local representatives in the Package Leaflets for Edistride and Ebymect." Opinion adopted on 20.09.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Request for Supplementary Information adopted on 26.07.2018.	
WS1392 **ProQuad-EMEA/H/C/000622/WS1392/0125** MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC in order to add the adverse reaction (ADR) meningitis with a frequency "not known" and to add a clarifying foot note for immunocompromised or immunocompetent individuals applicable to the ADR meningitis, herpes zoster and encephalitis. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to make some editorial changes in the product information and to update the list of local representatives in the package leaflet." Request for Supplementary Information adopted on 13.09.2018, 05.07.2018.	Request for supplementary information adopted with a specific timetable.
WS1411/G **Aluvia-EMEA/H/W/000764/WS1411/0105/G** **Kaletra-EMEA/H/C/000368/WS1411/0171/G** **Norvir-EMEA/H/C/000127/WS1411/0150/G** AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Joseph Emmerich, "Update of section 4.5 of the SmPC in order to update the safety information on the interaction with ibrutinib based on the company core data sheets. The Package Leaflet is updated accordingly. Update of section 4.5 of the SmPC in order to update the safety information of ritonavir, lopinavir/ritonavir on the interaction with levothyroxine based on the PRAC signal final assessment report EMA/101535/2018 leading to decreased levothyroxine efficacy and hypothyroidis." Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1417/G **Invega-EMEA/H/C/000746/WS1417/0060/G** **Trevicta-EMEA/H/C/004066/WS1417/0013/G** **Xeplion-EMEA/H/C/002105/WS1417/0039/G** Janssen-Cilag International NV, Lead	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Rapporteur: Kristina Dunder, “Update of sections 4.4 and 4.5 of the SmPC in order to add information regarding concomitant use of paliperidone and risperidone with psychostimulants (in line with the CMDh recommendations for risperidone) and of section 4.8 of the SmPC to add catatonia as a new side-effect categorised as ‘Rare’. The Package Leaflet is updated accordingly. The MAH took also the occasion to include editorial changes in the PI and to update the local representative for Ireland in the Package leaflet for Trevicta, Invega and Xeplion and Bulgaria for Risperidal Consta. The MAH also implemented the weekdays in section 5 of the annex IIIA for invega OPA blister according to the QRD guidance.” Opinion adopted on 13.09.2018.	
WS1422 **CONTROLOC** **Control-EMEA/H/C/001097/WS1422/0030** **PANTOLOC** **Control-EMEA/H/C/001100/WS1422/0034** **PANTOZOL** **Control-EMEA/H/C/001013/WS1422/0032** **SOMAC** **Control-EMEA/H/C/001098/WS1422/0031** Takeda GmbH, Lead Rapporteur: Greg Markey, “Update of section 5.3 of the SmPC in order to update the safety information based on the final results of study 14GR325 “A pre- and postnatal developmental toxicity study of pantoprazole sodium (PF-05208751) by oral gavage in rats focused on postnatal evaluation of bone development” as required by the PRAC Recommendation of EMEA/H/C/PSUSA/00002285/201708.” Request for Supplementary Information adopted on 20.09.2018.	Request for supplementary information adopted with a specific timetable.
WS1429 **Descovy-EMEA/H/C/004094/WS1429/0032** **Genvoya-EMEA/H/C/004042/WS1429/0048** **Odefsey-EMEA/H/C/004156/WS1429/0033** Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings, “Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC with data in patients on chronic haemodialysis from the Study GS-US-292-1825; this is a Phase 3b Open-Label	Request for supplementary information adopted with a specific timetable.

Study toEvaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of E/C/F/TAF Fixed Dose Combination (FDC) in HIV-1 Infected Subjects on Chronic Hemodialysis. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to introduce changes to the lactose wording for Genvoya and Odefsey and an administrative correction to the Genvoya Patient information leaflet (PIL) in order to add "lurasidone" to the second list of contra-indicated drugs appearing in the PIL. The WSA has also taken the opportunity to introduce some minor administrative amendments throughout the product information for all three products as well as to implement some minor linguistic amendments (MLAs) to the translations of the respective product information annexes: - Genvoya: DE, ES, FI, HR, HU, IS, IT, NO, SL and SV languages - Descovy: DA, DE, ES, FR, HR, NL, NO, PT and SL languages - Odefsey: CS, DE, LV, MT, NL, PL, SL and SV languages." Request for Supplementary Information adopted on 20.09.2018.	
WS1433 **Clopidogrel** **Zentiva-EMEA/H/C/000975/WS1433/0061** **Clopidogrel/Acetylsalicylic acid** **Zentiva-EMEA/H/C/001144/WS1433/0051** **DuoPlavin-EMEA/H/C/001143/WS1433/0050** **Iscover-EMEA/H/C/000175/WS1433/0133** **Plavix-EMEA/H/C/000174/WS1433/0130** Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, "In response to PRAC recommendation for the signal of insulin autoimmune syndrome (EPITT ref 19155), update of section 4.8 of the SmPC to the new adverse reaction 'insulin autoimmune syndrome'. The Package Leaflet are updated accordingly. In addition, at the request of the Agency, MA numbers of Plavix and Iscover were reviewed and updated as per the current format. The Plavix	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

and Iscover Annex A and PI were updated accordingly." Opinion adopted on 13.09.2018.	
WS1444 **Kisplyx-EMEA/H/C/004224/WS1444/0012** **Lenvima-EMEA/H/C/003727/WS1444/0016** Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren, "Update of Sections 4.4 and 4.8 of the SmPC to add pneumothorax and nephrotic syndrome. The PIL is updated accordingly." Request for Supplementary Information adopted on 13.09.2018.	Request for supplementary information adopted with a specific timetable.
WS1449 **Relvar Ellipta-EMEA/H/C/002673/WS1449/0038** **Revinty Ellipta-EMEA/H/C/002745/WS1449/0035** Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, "Update of section 4.8 of the SmPC in order to add hyperglycaemia as an adverse reaction based on a cumulative review of hyperglycaemia/new onset diabetes associated with fluticasone/vilanterol (FF/VI); the Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to update the Package Leaflet with a clarification on the adverse event "blurred vision" already included in the SmPC (WS-1224)."	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation
WS1459 **Clopidogrel Zentiva-EMEA/H/C/000975/WS1459/0062** **Clopidogrel/Acetylsalicylic acid Zentiva-EMEA/H/C/001144/WS1459/0052** **DuoPlavin-EMEA/H/C/001143/WS1459/0051** **Iscover-EMEA/H/C/000175/WS1459/0134** **Plavix-EMEA/H/C/000174/WS1459/0131** Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, "Update of section 5.1 of the SmPC in order to reflect the clinical outcome data of 2 randomised investigator-sponsored studies regarding de-escalation of P2Y12 receptor inhibitor to clopidogrel in ACS." Opinion adopted on 20.09.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.3. CHMP-PRAC assessed procedures

Advate - octocog alfa - EMEA/H/C/000520/II/0092 Baxter AG, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 5.1 of the SmPC in order to add new data on immune tolerance induction (ITI). This update follows final results from study PASS-INT-004; this was a prospective, multi-centre, uncontrolled, open-label, non-interventional postauthorization safety surveillance study conducted to evaluate Advate in ITI therapy in subjects with moderate or severe hemophilia A (baseline factor VIII ≤ 2%) and a high titer (> 5 BU) inhibitor to FVIII. The RMP version 16.0 has also been submitted." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Aflunov - prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - EMEA/H/C/002094/II/0044/G Seqirus S.r.l, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, "Update of sections 4.4, 4.6, 4.8 and 5.1 of the SmPC following clinical study reports of studies V87_25 and V87_26 listed as post approval commitments; these are Phase 3, stratified, randomized, controlled, observer-blind, multicenter studies; the Package Leaflet and Labelling are updated accordingly. The updated RMP version 3.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement some amendments to the PI and make some additional minor editorial corrections." Request for Supplementary Information adopted on 20.09.2018.	Request for supplementary information adopted with a specific timetable.
Brilique - ticagrelor - EMEA/H/C/001241/II/0042 AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.9 and 5.2 of the SmPC in order to update the safety information in relation to renal impairment based on the final	Request for supplementary information adopted with a specific timetable.

results from study D5130L00067; this is a single dose, randomized, open label, parallel group study conducted to compare the pharmacokinetics (PK), pharmacodynamics (PD), safety and tolerability of ticagrelor in haemodialysis patients to subjects with normal renal function. The RMP version 11 has also been submitted." Request for Supplementary Information adopted on 20.09.2018.	
Bydureon - exenatide - EMEA/H/C/002020/II/0050 AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of sections 4.1, 4.2, 4.4 and 5.1 of the SmPC based on the final CSR of study EXSCEL (EXenatide Study of Cardiovascular Event Lowering; 'A randomized, placebo controlled clinical trial to evaluate cardiovascular outcomes after treatment with exenatide once weekly in patients with type 2 diabetes mellitus ') in fulfilment of LEG 009. In addition, RMP version 31 has been submitted as part of this application." Opinion adopted on 20.09.2018. Request for Supplementary Information adopted on 28.06.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cosentyx - secukinumab - EMEA/H/C/003729/II/0033/G Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, PRAC Rapporteur: Eva A. Segovia, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to include information on dose up-titration for Psoriatic Arthritis (PsA) and update of the radiographic sub-section for Psoriatic Arthritis (PsA) based on results from the 24-week data from study CAIN457F2342, the pooled data from PsA Phase 3 studies, the pooled data from patients who up-titrated their secukinumab dose in studies CAIN457F2306E1, CAIN457F2312 and CAIN457F2318, and long-term study observations which demonstrate higher rates of discontinuation for patients on secukinumab 150 mg compared to patients on secukinumab 300 mg. The Package leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Bulgaria, Estonia, Lithuania, Latvia and Hungary in the Package Leaflet and to bring the Package leaflet in line with the latest approved SmPC as	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

per procedure (EMEA/H/C/003729/IB/0028). The RMP (v.3.1) has also been updated including suicidal ideation and behaviour as an important potential risk in the RMP and including minor administrative/editorial changes (LEG 005.2)." Opinion adopted on 20.09.2018. Request for Supplementary Information adopted on 31.05.2018.	
CYLTEZO - adalimumab - EMEA/H/C/004319/II/0004 Boehringer Ingelheim International GmbH, Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from study 1297.3 listed as a category 3 study in the RMP. This is an interventional trial to generate long-term safety, efficacy, and immunogenicity data for the administration of the proposed biosimilar Cyltezo in patients with moderate to severe rheumatoid arthritis." Request for Supplementary Information adopted on 06.09.2018.	Request for supplementary information adopted with a specific timetable.
Herzuma - trastuzumab - EMEA/H/C/002575/II/0006 Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski Opinion adopted on 20.09.2018. Request for Supplementary Information adopted on 26.07.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kisqali - ribociclib - EMEA/H/C/004213/II/0003/G Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver, "C.I.4: Update of section 5.2 of the SmPC in order to reflect on results from study CLEE011A2109: A Phase I, open label, multi-centre, parallel cohort, single dose study to evaluate the pharmacokinetics of LEE011 in healthy subjects with normal hepatic function and subjects with impaired hepatic function; C.I.4: Update of section 4.2 and 5.2 of the SmPC in order to reflect on results from study CLEE011A2116-Part I: A phase I, open label, multicentre, parallel-group, single dose two-staged study to evaluate the pharmacokinetics and safety of a single 400 mg oral dose of LEE011 in subjects with varying degrees of impaired renal function compared to	Request for supplementary information adopted with a specific timetable.

matched healthy volunteers with normal renal function. The RMP version 2.0 has also been submitted." Request for Supplementary Information adopted on 06.09.2018.	
NovoMix - insulin aspart - EMEA/H/C/000308/II/0095 Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of sections 4.2, 4.5 and 5.1 of the SmPC to include data on the use of NovoMix® 30 combination use with GLP-1 receptor agonists. The PIL is updated accordingly. The RMP is laso updated (version 3)" Request for Supplementary Information adopted on 20.09.2018.	Request for supplementary information adopted with a specific timetable.
Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0002 Roche Registration GmbH, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Julie Williams, "Update of sections 4.4 and 4.5 of the SmPC in order to include information on vaccination based on interim results from study BN29739 listed as a category 3 study in the RMP; this is a phase IIIb, multicentre, randomised, parallel-group, open-label study to evaluate the effects of ocrelizumab on immune response in patients with relapsing forms of multiple sclerosis. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted." Request for Supplementary Information adopted on 06.09.2018, 12.07.2018, 17.05.2018.	Request for supplementary information adopted with a specific timetable.
OFEV - nintedanib - EMEA/H/C/003821/II/0021, Orphan Boehringer Ingelheim International GmbH, Rapporteur: Jayne Crowe, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of section 4.8 of the SmPC in order to include 'myocardial infarction' as a new adverse drug reaction with a frequency 'uncommon' in order to fulfil LEG 004.1, following the assessment of PSUSA/00010319/201704. The Package Leaflet is updated accordingly. The RMP version 6.0 (in revision 2 of the template) has also been submitted." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 06.09.2018.	
Oncaspar - pegaspargase - EMEA/H/C/003789/II/0016/G Baxalta Innovations GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Patrick Batty, "Update of sections 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1 5.2 and 5.3 of the SmPC with the final results from studies DFCI 11-001 and AALL07P4 listed as category 3 studies in the RMP; Study DFCI 11-001 is a Phase 2, open-label, randomized, multicenter study to determine the safety and feasibility of administering an investigational asparaginase product (asparaginase formulation) compared with Oncaspar in subjects aged 1 to <22 years with newly diagnosed ALL and lymphoblastic lymphoma. Study AALL07P4 is a multicenter, open label, randomized, active-controlled, parallel design clinical pilot study conducted to evaluate the PK, pharmacodynamics, safety, immunogenicity and efficacy of an investigational asparaginase product in comparison with Oncaspar in patients aged 1 to <31 years newly diagnosed with high risk B-precursor ALL. The Package Leaflet is proposed to be updated accordingly. The RMP version 3.0 has also been submitted." Request for Supplementary Information adopted on 06.09.2018, 17.05.2018.	Request for supplementary information adopted with a specific timetable.
Onivyde - irinotecan hydrochloride trihydrate - EMEA/H/C/004125/II/0008, Orphan Baxalta Innovations GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: David Olsen, "Update of sections 1, 2, 4.2, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC in order to reflect the expression of strength based on irinotecan anhydrous free-base. The Labelling and Package Leaflet are updated accordingly. In addition the MAH took the opportunity to introduce minor editorial changes. The updated RMP version 2.1 has also been submitted." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 20.09.2018.	
Ovitrelle - choriogonadotropin alfa - EMEA/H/C/000320/II/0073/G Merck Europe B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of section 4.8 of the SmPC in order to indicate that thromboembolism can also occur without the presence of ovarian hyperstimulation syndrome (OHSS). The package leaflet and risk management plan (RMP) version 6.0 are updated accordingly. The RMP is also updated to extend the important potential risk of 'misuse' to 'weight loss and anabolic growth promoting effect'. In addition, the marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the package leaflet, to make editorial changes in the product information and in the Annex A (list of authorised presentations). The MAH also took the opportunity to make some revisions in the RMP." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Plegridy - peginterferon beta-1a - EMEA/H/C/002827/II/0046 Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Julie Williams, "Update of sections 4.4 and 4.8 of the SmPC in order to add new warning and safety information about anaphylaxis. The RMP version 3.2 has also been submitted." Request for Supplementary Information adopted on 06.09.2018.	Request for supplementary information adopted with a specific timetable.
Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0161 Pfizer Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final study report from study B1851041, a phase 4 post marketing study to determine 'National trends in Ambulatory Care Visits for Otitis Media in Children Under the Age of Five in the United States.' Consequently, the RMP version 12 has been updated." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 12.04.2018.	
Remicade - infliximab - EMEA/H/C/000240/II/0214 Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the RMP (v 17.0) and Annex II-D of the Product Information to remove the Educational material for health care professionals. In addition, the MAH is taking the opportunity to update the package leaflet with some missing warnings and ADRs already reflected in the SmPC, as requested by CHMP, and to introduce some minor QRD related changes." Request for Supplementary Information adopted on 20.09.2018, 26.07.2018.	Request for supplementary information adopted with a specific timetable.
Ryzodeg - insulin aspart / insulin degludec - EMEA/H/C/002499/II/0028 Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 5.1 of the SmPC based on new clinical data from a cardiovascular outcome trial EX1250-4080 (DEVOTE) conducted for insulin degludec. DEVOTE was a randomised, double-blind and event-driven clinical trial with a median duration of 2 years comparing the cardiovascular safety of insulin degludec versus insulin glargine (100 units/mL) in patients with type 2 diabetes mellitus at high risk of cardiovascular events. Based on the long-term exposure and safety data from DEVOTE which are also relevant for insulin degludec/insulin aspart, the Ryzodeg SmPC is updated with data from the trial in alignment with a recent update of the SmPC for insulin degludec. Section 6.5 of the SmPC is also being amended for an editorial improvement to more precisely describe the nature of the plunger stopper. The RMP version 7 has also been submitted, with updates consequent to the data in support of the application." Opinion adopted on 06.09.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tamiflu - oseltamivir - EMEA/H/C/000402/II/0136 Roche Registration GmbH, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka,	Request for supplementary information adopted with a specific timetable.

"Update of sections 4.2, 4.8, 5.1 and 5.2 to guide prescribers on the use of Tamiflu for treatment in immunocompromised (IC) patients based on studyt NV20234, a Phase III, double-blind, randomized, stratified, multicenter study of conventional and double dose oseltamivir for the treatment of influenza in IC patients. The PL and RMP (v15) have been updated accordingly. In addition, the MAH took the opportunity to correct some minor errors." Request for Supplementary Information adopted on 20.09.2018.	
Toujeo - insulin glargine - EMEA/H/C/000309/II/0105/G Sanofi-Aventis Deutschland GmbH, Duplicate, Duplicate of Lantus, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 20.09.2018.	Request for supplementary information adopted with a specific timetable.
Truberzi - eluxadoline - EMEA/H/C/004098/II/0005/G Allergan Pharmaceuticals International Ltd, Rapporteur: Harald Enzmann, PRAC Rapporteur: Adam Przybylkowski, "Update of sections 4.5 and 5.2 of the SmPC in order to update the drug interaction information based on the final report from study 3030-102-002: a single-center, non-randomized, open-label, single-sequence study to evaluate the effect of eluxadoline on the single-dose pharmacokinetics of midazolam in healthy subjects, listed as a category 3 study in the RMP. The package leaflet was updated accordingly. Submission of the final report from study ELX-PH-08: in vitro evaluation of eluxadoline as an inducer of cytochrome P450 (CYP) 1A2 and 3A4 expression in cultured human hepatocytes, listed as a category 3 study in the RMP. Following the assessment of EMEA/H/C/PSUSA/00010528/201703, the RMP was updated to version 2.1 to update the existing important identified risk "SO spasm" to "SO spasm (Sphincter of Oddi dysfunction, SOD)" and include pancreatitis as a new important identified risk." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 12.07.2018, 17.05.2018, 08.03.2018.	
Varuby - rolapitant - EMEA/H/C/004196/II/0007/G Tesaro UK Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adam Przybylkowski, "- Update of SmPC section 4.5 regarding interaction with OCT1 substrates following the submission of the non-clinical study: in vitro evaluation of the substrate and inhibitor potential of rolapitant for efflux and update of transporters (17TESAP2R1). - Update of SmPC section 4.5 regarding interaction with UGT substrates following the submission of the 2 non-clinical studies: evaluation of potential UGT inhibition by rolapitant in cryopreserved human hepatocytes (170594) and evaluation of potential rolapitant metabolism by recombinantly expressed human UGT enzymes (TSRP/REP/07CRD75486/2017) - Update of SmPC section 4.5 following the submission of the open-label, single-d0se study to assess the effects of rolapitant (oral) on the pharmacokinetics of caffeine (CYP1A2) in healthy subjects (1000-01-001) The RMP version 1.2 has also been submitted." Request for Supplementary Information adopted on 06.09.2018, 12.07.2018.	Request for supplementary information adopted with a specific timetable.
WS1390 **Levitra-EMEA/H/C/000475/WS1390/0062** **Vivanza-EMEA/H/C/000488/WS1390/0058** Bayer AG, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Maria del Pilar Rayon, "Update of sections 4.4 and 4.8 of the SmPC to reflect data from two post-marketing observational studies indicating an increased risk of Non-arteritic Anterior Ischaemic Optic Neuropathy (NAION) when using phosphodiesterase 5 (PDE5) inhibitors. The MAH is also terminating the Bayer NAION study 12912 and the RMP is updated accordingly to version 5.0. In addition, the PI is brought in line with version 10.0 of the QRD template and the contact details of the Bulgarian local representative are updated in the Package Leaflets. The Package Leaflets for the 5 mg, 10 mg and 20 mg film-coated tablets strengths are combined into a single Package Leaflet and the PI for the 10 mg orodispersible tablet is updated for aspartame and sorbitol,	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

according to the annex to the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. Some editorial amendments are also made to the PI." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018.	
WS1396 **Kisplyx-EMEA/H/C/004224/WS1396/0011** **Lenvima-EMEA/H/C/003727/WS1396/0015** Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren, Lead PRAC Rapporteur: Annika Folin, "Update of section 4.5 of the SmPC to include that there is no significant drug-drug interaction risk with midazolam, based on the results of study E7080-A001-109 (A Phase 1 Study to determine DDI of lenvatinib and midazolam, a cytochrome P450 3A4 (CYP3A4) substrate, in subjects with advanced solid tumors). The RMP is updated (version 10.4)." Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 12.07.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.4. PRAC assessed procedures

PRAC Led **Deltyba - delamanid - EMEA/H/C/002552/II/0030, Orphan** Otsuka Novel Products GmbH, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "Update of the RMP (finally approved version 2.11), as requested by PRAC following the assessment of the Annual renewal to revise the risk re-categorisation justifications and lay language wording, as well as to add clarifications to the described additional pharmacovigilance activities to assess the effectiveness of risk minimisation measures and the set up date of an EU network of laboratories." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Humira - adalimumab - EMEA/H/C/000481/II/0182**	Request for supplementary information adopted with a specific timetable.

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, “Submission of an updated RMP version 14.0 in order to include a thorough review of the currently specified safety concerns in the Humira RMP, to updated in regards of previously assessed safety concerns and to make associated updates in line with GVP Module V.” Request for Supplementary Information adopted on 06.09.2018.	
PRAC Led **Kengrexal - cangrelor - EMEA/H/C/003773/II/0015** Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, “Submission of an updated RMP version 2.0 in order to update the requirements for a study listed as category 3 in the RMP. In addition, the MAH took the opportunity to revise the RMP in line with the RMP template version 2.0.” Request for Supplementary Information adopted on 06.09.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **MabThera - rituximab - EMEA/H/C/000165/II/0152** Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, “Submission of the final study report of the non-interventional drug utilisation study (DUS) BA28478 (MabThera drug utilisation study and patient alert card evaluation in non-oncology patients in Europe: an infusion centre-based approach). Consequently, update of sections 4.2 and 4.4 of the SmPC and Annex II.E to remove the patient alert card as an additional risk minimisation measure for the risks of PML and infections, for the non-oncology indications. The Package leaflet is updated in accordance. The RMP is laso updated (version 18). This submission is done in fulfilment of FUM-68.1 and FUM-71.” Request for Supplementary Information adopted on 06.09.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Mycamine - micafungin - EMEA/H/C/000734/II/0038** Astellas Pharma Europe B.V., Rapporteur: Harald	Request for supplementary information adopted with a specific timetable.

Enzmann, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "Submission of an updated RMP version 20.0 in order to streamline and improve the educational programme and communication to physicians prescribing Mycamine as requested in variation II/0035." Request for Supplementary Information adopted on 06.09.2018.	
PRAC Led **Neofordex - dexamethasone - EMEA/H/C/004071/II/0008** Laboratoires CTRS, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 4.0 in order to propose the removal a category 3 activity 'removal of the score line for subdivision of the 40mg tablet and consequent deletion of the 20mg posology'. In addition, the MAH updated the other category 3 activity 'Development of a 20mg oral dosage form'. The MAH implemented the RMP revision 2 format." Request for Supplementary Information adopted on 06.09.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Pegasys - peginterferon alfa-2a - EMEA/H/C/000395/II/0101** Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "Submission of an updated RMP version 9.0 in order to remove the NV25361 study (category 3 study); in addition, the YV25718 (study to establish the efficacy and safety of PEG-IFN monotherapy in children from 3 to less than 18 years of age with CHB) long term follow up milestone is amended from Q3 2020 to Q4 2021. The classification of some risks is also amended as per revision 2 of Module V of GVP including updates in the epidemiology section." Opinion adopted on 06.09.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Resolor - prucalopride - EMEA/H/C/001012/II/0042** Shire Pharmaceuticals Ireland Limited, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "Submission of the final clinical study report for	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

the post-authorization drug utilization study SHP555-804 in fulfilment of MEA 006.11 A drug utilisation study to examine characteristics of patients prescribed prucalopride (Resolor) and a pharmacoepidemiological study of the occurrence of major cardiovascular events, pregnancy, and pregnancy outcomes in the UK CPRD Database. The RMP (v 14.0) has also been updated to reflect the study results." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018, 12.04.2018.	
PRAC Led **Revestive - teduglutide - EMEA/H/C/002345/II/0045, Orphan** Shire Pharmaceuticals Ireland Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 8 in order to include the safety information from the final CSR of study TED-C14-006 ("a 24-Week Double-blind, Safety, Efficacy, and Pharmacodynamic Study Investigating Two Doses of Teduglutide in Pediatric Subjects Aged 1 Year Through 17 Years With Short Bowel Syndrome who are Dependent on Parenteral Support"; a category 3 study in the RMP) that was submitted within variation EMEA/H/C/002345/II/0043." Opinion adopted on 20.09.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Simponi - golimumab - EMEA/H/C/000992/II/0084** Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Update of the RMP to version 18.0, based upon the conclusion of the PSUR Assessment report (PSUSA/00001560/201704), in order to remove the Educational programme for prescribing healthcare professionals (HCPs) as an additional risk minimisation measure. The Patient Alert Card is maintained and renamed Patient Reminder Card across the SmPC, Annex II, Labelling and Package Leaflet. In addition, the Marketing authorisation holder took the opportunity to update the list of local representatives in the Package Leaflet."	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 06.09.2018.	
PRAC Led **Thymanax - agomelatine - EMEA/H/C/000916/II/0038** Servier (Ireland) Industries Ltd., Duplicate, Duplicate of Valdoxan, Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Karen Pernille Harg, PRAC-CHMP liaison: Svein Rune Andersen, "Submission of the final report from study CLE-20098-096 listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study: drug utilisation study (DUS) to assess effectiveness of risk-minimisation measures." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Valdoxan - agomelatine - EMEA/H/C/000915/II/0039** Les Laboratoires Servier, Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Karen Pernille Harg, PRAC-CHMP liaison: Svein Rune Andersen, "Submission of the final report from study CLE-20098-096 listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study: drug utilisation study (DUS) to assess effectiveness of risk-minimisation measures." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0186** Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Joseph Emmerich, "Submission of the final report from study GS-EU-174-1846, listed as a category 3 study in the RMP, in fulfilment of MEA 273. This is a 'Multicenter, Non-Interventional, Retrospective, Matched Cohort Study of Patients Monoinfected with Chronic Hepatitis B and with Moderate or Severe Renal Impairment Treated with Viread or Baraclude'." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 14.06.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Led **Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0188** Gilead Sciences Ireland UC, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Joseph Emmerich, "Submission of the final report from study GS-EU-174-0224 listed as a category 3 study in the RMP. This is a cross-sectional drug utilisation study in children and adolescents with Chronic Hepatitis B to assess whether physicians prescribing Viread to paediatric patients with Chronic Hepatitis B in the EU were following the relevant recommendations in the Viread SmPC and educational brochures." Opinion adopted on 06.09.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0190** Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Joseph Emmerich, "Submission of an updated RMP version 22.1 (in accordance with the revised guidance in the Guideline on good pharmacovigilance practices Module V) to propose removing the additional risk minimization activities for HIV and HBV adults associated with the renal safety concern from the RMP." Opinion adopted on 06.09.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Votubia - everolimus - EMEA/H/C/002311/II/0055, Orphan** Novartis Europharm Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "Submission of the final report from the non-interventional study CRAD001MIC03, listed as a category 3 study in the RMP. This is an international disease registry collecting data on manifestations, interventions and outcomes in patients with tuberous sclerosis complex." Opinion adopted on 06.09.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Xeloda - capecitabine - EMEA/H/C/000316/II/0077** Roche Registration GmbH, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "To update the Xeloda RMP (version 9.1) in line with the product information changes	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

recently approved within variation EMEA/H/C/000163/II/0074. The following updates are included: post-authorisation exposure updated, presentation of important identified risk dihydropyrimidine dehydrogenase deficiency (DPD) updated and inclusion of additional updates related to section 4.4 of the SmPC for DPD, revised as part of procedure EMEA/H/C/316/II/0074. In addition MAH took the opportunity to introduce the new EU RMP template." Opinion adopted on 06.09.2018.	
PRAC Led **WS1270** **Enbrel-EMEA/H/C/000262/WS1270/0216** **LIFMIOR-EMEA/H/C/004167/WS1270/0013** Pfizer Europe MA EEIG, Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Robert James Hemmings, "Submission of the final report from study B1801396, a non-interventional PASS listed as a category 3 study in the RMP. This is a non-interventional, population-based, multi-country, observational cohort register study to evaluate the risk of adverse pregnancy outcomes in patients with rheumatoid arthritis and related inflammatory diseases, who were treated with etanercept compared to patients with the same diseases of interest who were treated with non-biologic systemic drugs, but without etanercept or other biologics during pregnancy, using merged data from Sweden, Denmark and Finland." Request for Supplementary Information adopted on 06.09.2018, 17.05.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **WS1357** **Efficib-EMEA/H/C/000896/WS1357/0089** **Janumet-EMEA/H/C/000861/WS1357/0089** **Januvia-EMEA/H/C/000722/WS1357/0063** **Ristaben-EMEA/H/C/001234/WS1357/0055** **Ristfor-EMEA/H/C/001235/WS1357/0076** **TESAVEL-EMEA/H/C/000910/WS1357/0063** **Velmetia-EMEA/H/C/000862/WS1357/0092**	Request for supplementary information adopted with a specific timetable.

Xelevia-EMEA/H/C/000762/WS1357/0067 Merck Sharp & Dohme B.V., Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 10 in order to remove "theoretic carcinogenic potential" form the list of safety concerns, currently classified as "missing information"." Request for Supplementary Information adopted on 06.09.2018, 12.04.2018.	
PRAC Led **WS1370** **Zoledronic acid** **Mylan-EMEA/H/C/002482/WS1370/0015** Mylan S.A.S, Generic, Generic of Zometa, Lead PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "The RMP has been updated to the latest template. In addition the MAH has included "and other anatomical sites" in addition to "Osteonecrosis of the jaw" as an important identified risk, to be in line with CHMP assessment report for zoledronic acid, procedure number EMEA/H/C/PSUSA/00003149/201608, dated 21 April 2017." Opinion adopted on 06.09.2018. Request for Supplementary Information adopted on 10.07.2018.	Positive Opinion adopted by consensus on 06.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1402** **Bretaris Genuair-EMEA/H/C/002706/WS1402/0038** **Eklira Genuair-EMEA/H/C/002211/WS1402/0038** AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, Lead PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Robert James Hemmings, "Submission of an updated RMP version 7.0 in order to proposed changes in categorisation of safety concerns and missing information in the RMP as per the guidance provide for the revision 2 of the RMP and to provide the RMP under the revision 2 template." Request for Supplementary Information adopted on 06.09.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **WS1403**	Request for supplementary information adopted with a specific timetable.

Brimica Genuair-EMEA/H/C/003969/WS1403/0023 **Duaklir Genuair-EMEA/H/C/003745/WS1403/0023** AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, Lead PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Robert James Hemmings, "Submission of an updated RMP version 4.0 in order to proposed changes in categorisation of safety concerns and missing information in the RMP as per the guidance provide for the revision 2 of the RMP and to provide the RMP under the revision 2 template." Request for Supplementary Information adopted on 06.09.2018.	

B.5.5. CHMP-CAT assessed procedures

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0024, ATMP Amgen Europe B.V., Rapporteur: Olli Tenhunen, Opinion adopted on 20.09.2018, 14.09.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

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

WS1324/G Afinitor-EMEA/H/C/001038/WS1324/0056/G Votubia-EMEA/H/C/002311/WS1324/0050/G Novartis Europharm Limited, Lead Rapporteur: Harald Enzmann Opinion adopted on 13.09.2018. Request for Supplementary Information adopted on 03.05.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1353/G Hexacima-EMEA/H/C/002702/WS1353/0079/G Hexaxim-EMEA/H/W/002495/WS1353/0084/G	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Hexyon-EMEA/H/C/002796/WS1353/0083/G Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 20.09.2018. Request for Supplementary Information adopted on 19.07.2018, 17.05.2018.	
WS1407 **HyQvia-EMEA/H/C/002491/WS1407/0042** **Kiovig-EMEA/H/C/000628/WS1407/0083** Baxalta Innovations GmbH, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1409 **Keppra-EMEA/H/C/000277/WS1409/0172** UCB Pharma S.A., Lead Rapporteur: Koenraad Norga,	Request for supplementary information adopted with a specific timetable.
WS1410 **Infanrix hexa-EMEA/H/C/000296/WS1410/0243** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1412 **Blitzima-EMEA/H/C/004723/WS1412/0016** **Ritemvia-EMEA/H/C/004725/WS1412/0016** **Rituzena-EMEA/H/C/004724/WS1412/0017** **Truxima-EMEA/H/C/004112/WS1412/0017** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz Opinion adopted on 20.09.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1416 **Kisplyx-EMEA/H/C/004224/WS1416/0014** **Lenvima-EMEA/H/C/003727/WS1416/0018** Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1419 **Abseamed-EMEA/H/C/000727/WS1419/0073** **Binocrit-EMEA/H/C/000725/WS1419/0073**	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Epoetin alfa **Hexal-EMEA/H/C/000726/WS1419/0072** Sandoz GmbH, Lead Rapporteur: Alexandre Moreau Opinion adopted on 13.09.2018.	
WS1424 **Eviplera-EMEA/H/C/002312/WS1424/0092** **Odefsey-EMEA/H/C/004156/WS1424/0032** Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1425 **Nuwiq-EMEA/H/C/002813/WS1425/0023** **Vihuma-EMEA/H/C/004459/WS1425/0005** Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1431 **Ceprotin-EMEA/H/C/000334/WS1431/0105** Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1437/G **Anoro Ellipta-EMEA/H/C/002751/WS1437/0020/G** **Elebrato Ellipta-EMEA/H/C/004781/WS1437/0004/G** **Incruse Ellipta-EMEA/H/C/002809/WS1437/0019/G** **Laventair Ellipta-EMEA/H/C/003754/WS1437/0023/G** **Rolufta Ellipta-EMEA/H/C/004654/WS1437/0006/G** **Trelegy Ellipta-EMEA/H/C/004363/WS1437/0003/G** Glaxo Group Ltd, Lead Rapporteur: Peter Kiely Opinion adopted on 20.09.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1440/G	Positive Opinion adopted by consensus on

Hirobriz **Breezhaler-EMEA/H/C/001211/WS1440/0050/G** **Onbrez** **Breezhaler-EMEA/H/C/001114/WS1440/0048/G** **Oslif** **Breezhaler-EMEA/H/C/001210/WS1440/0048/G** Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth Opinion adopted on 13.09.2018.	13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1443 **Actos-EMEA/H/C/000285/WS1443/0080** **Competact-EMEA/H/C/000655/WS1443/0071** **Glustin-EMEA/H/C/000286/WS1443/0079** **Tandemact-EMEA/H/C/000680/WS1443/0058** Takeda Pharma A/S, Lead Rapporteur: Peter Kiely, “To bring the annexes in line with QRD version 10 and the EC guideline of excipients on lactose. In addition the MAH took the opportunity to update the local representative in Estonia and Slovakia along with some editorial changes throughout the annexes.”	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1448/G **Ultibro** **Breezhaler-EMEA/H/C/002679/WS1448/0027/G** **Ulunar** **Breezhaler-EMEA/H/C/003875/WS1448/0026/G** **Xoterna** **Breezhaler-EMEA/H/C/003755/WS1448/0030/G** Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth Opinion adopted on 13.09.2018.	Positive Opinion adopted by consensus on 13.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1463 **Abseamed-EMEA/H/C/000727/WS1463/0074** **Binocrit-EMEA/H/C/000725/WS1463/0074** **Epoetin alfa** **Hexal-EMEA/H/C/000726/WS1463/0073** Sandoz GmbH, Lead Rapporteur: Alexandre Moreau Opinion adopted on 20.09.2018.	Positive Opinion adopted by consensus on 20.09.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

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

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

ibalizumab - EMEA/H/C/004961 , treatment of adults infected with HIV-1 resistant to at least 1 agent in 3 different classes	**Accelerated review**
larotrectinib - EMEA/H/C/004919, Orphan Bayer AG, treatment of adult and paediatric patients with locally advanced or metastatic solid tumours	**Accelerated review**

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

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

fremanezumab - EMEA/H/C/004833
, prevention of episodic and chronic migraine
List of Questions adopted on 31.05.2018.

atazanavir - EMEA/H/C/004859
, treatment of HIV-1 infection, Generic, Generic of Reyataz
List of Questions adopted on 26.07.2018.

bevacizumab - EMEA/H/C/004697
, Treatment of adult patients with metastatic carcinoma of the colon or rectum, metastatic breast cancer, unresectable advanced, metastatic or recurrent non-small cell lung cancer, advanced and/or metastatic renal cell cancer, persistent, recurrent, or metastatic carcinoma of the cervix
List of Questions adopted on 28.06.2018.

Dupixent - dupilumab - EMEA/H/C/004390/X/0004/G
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Peter Kiely,

PRAC Rapporteur: Kimmo Jaakkola, “Extension application to add a new strength of 200 mg solution for injection in pre-filled syringe with safety system (PFS-S) and pre-filled pen (PFP), grouped with a type II variation (C.I.6.a) to add the following indications:
- Add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older, who are inadequately controlled with medium-to-high dose inhaled corticosteroids (ICS) plus another medicinal product for maintenance treatment, including those with or without an eosinophilic phenotype;
- Maintenance therapy to improve lung function;
- Maintenance therapy to reduce oral steroid use and improve lung function in steroid-dependent asthma patients;
Based on the pivotal studies DRI12544, QUEST and VENTURE.
As a consequence, SmPC sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 have been updated and the Package Leaflet has been updated accordingly.
The RMP (version 2.0) is uppdated accordingly.
In addition, the MAH proposed to merge the SmPCs for the 200 mg and 300 mg strengths.”
List of Questions adopted on 26.07.2018.

cannabidiol - EMEA/H/C/004675, Orphan
GW Research Ltd, Adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS)
List of Questions adopted on 31.05.2018.

hydroxycarbamide - EMEA/H/C/004837
, prevention of complications of Sickle Cell disease
List of Questions adopted on 28.06.2018.

adalimumab - EMEA/H/C/004475
, treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis
List of Questions adopted on 22.03.2018.

miglustat - EMEA/H/C/004904
, treatment of adult patients with mild to moderate type 1 Gaucher disease and only in the treatment of patients for whom enzyme replacement therapy is unsuitable, Generic, Generic of Zavesca
List of Questions adopted on 26.07.2018.

buprenorphine - EMEA/H/C/004743
, Substitution treatment for opioid drug

dependence
List of Questions adopted on 22.03.2018.

silodosin - EMEA/H/C/004964
, treatment of prostatic hyperplasia (BPH),
Generic, Generic of Urorec
List of Questions adopted on 28.06.2018.

dacomitinib - EMEA/H/C/004779
, first-line treatment of adults with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR)-activating mutations.
List of Questions adopted on 28.06.2018.

canakinumab - EMEA/H/C/004754
, prevention of major cardiovascular events
List of Questions adopted on 31.05.2018.

sotagliflozin - EMEA/H/C/004889
, indicated as an adjunct to insulin therapy to improve glycaemic control in adults with type 1 diabetes mellitus.
List of Questions adopted on 26.07.2018.

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

antithrombin alfa - EMEA/H/C/000587/S/0035

asfotase alfa - EMEA/H/C/003794/S/0032, Orphan
Alexion Europe SAS

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

Cometriq - cabozantinib - EMEA/H/C/002640/R/0029, Orphan
Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Menno van der Elst

CRYSVITA - burosumab - EMEA/H/C/004275/R/0002, Orphan
Kyowa Kirin Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Brigitte Keller-Stanislawski

Ebilfumin - oseltamivir - EMEA/H/C/003717/R/0012
Actavis Group PTC ehf, Generic, Generic of

Tamiflu, Rapporteur: Milena Stain, PRAC Rapporteur: Kirsti Villikka
Mekinist - trametinib - EMEA/H/C/002643/R/0029 Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty
SIMBRINZA - brinzolamide / brimonidine - EMEA/H/C/003698/R/0014 Novartis Europharm Limited, Rapporteur: Robert James Hemmings, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Rhea Fitzgerald
SIRTURO - bedaquiline - EMEA/H/C/002614/R/0031, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga
SYLVANT - siltuximab - EMEA/H/C/003708/R/0029, Orphan Janssen-Cilag International NV, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Robert James Hemmings, 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

Empliciti - elotuzumab - EMEA/H/C/003967/II/0012 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Extension of Indication to include treatment in combination with pomalidomide and dexamethasone of adult patients with multiple myeloma. As a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 4.9, 5.1 5.2 and 6.6 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 RMP (version 2.0) is updated to reflect the new indication.” Request for 1 year of market protection for a new

indication (Article 14(11) of Regulation (EC) 726/2004)
Lynparza - olaparib - EMEA/H/C/003726/II/0023 AstraZeneca AB, Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Amelia Cupelli, “Extension of indication to include the use of Lynparza as a montherapy for the maintenance treatment of adult patients with newly diagnosed advanced BRCA-mutated high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete response or partial response) to first-line platinum-based chemotherapy. As a consequence, sections 4.1 (indication and posology) and 4.8 of the SmPC (summary profile and tabulated list of adverse reactions) are updated in order to include information on a single pivotal Phase 3 study (D0818C00001, referred to as SOLO 1). The Package Leaflet is updated in accordance. The updated pooled safety information for this submission has also been incorporated and aligned in the Capsule SmPC and PL.”
Opsumit - macitentan - EMEA/H/C/002697/II/0029, Orphan Actelion Registration Limited, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia, “Extension of Indication to include treatment of patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH), based on the pivotal study MERIT-1 (AC-055E201), together with 6 months of efficacy and safety data (cut-off date 17 October 2017) from its ongoing open-label extension study MERIT-2 (AC-055E202), as well as a drug-drug interaction (DDI) study (AC-055-122) of macitentan and rosuvastatine, a DDI study (AC-055-123) of macitentan and riociguat, and observational data from the OPUS Registry (OPsumit USers Registry; cut-off date of 17 April 2018). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 are being updated and the Package Leaflet is being updated accordingly. In addition, the MAH took the opportunity to implement editorial changes and to align the annexes with the latest QRD template and to update the

contact details of the local representatives in the Package Leaflet. An updated RMP version 9.2 was provided as part of the application."	
Translarna - ataluren - EMEA/H/C/002720/II/0047, Orphan PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Liana Gross-Martirosyan, "Extension of Indication to include non-ambulatory patients with Duchenne muscular dystrophy; This variation additionally presents, as supportive data, the final results of the long term clinical study PTC-124-GD-019-DMD (an Open-Label Study for Previously Treated Ataluren (PTC124) Patients with Nonsense Mutation Dystrophinopathy), submitted in line with the requirements of the Article 46 of the Paediatric Regulation. As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 8.0 has also been submitted."	
Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0191 Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Adrien Inoubli, "Extension of Indication based on results from interim Week 48 clinical study report (CSR) for Study GS-US-174-0144; a 'Randomized, Double-Blind Evaluation of the Antiviral Efficacy, Safety and Tolerability of Tenofovir Disoproxil Fumarate Versus Placebo in Pediatric Patients with Chronic Hepatitis B Infection'. Following changes have been proposed: 1) Viread film coated tablets (123 mg; 163 mg; 204 mg): new chronic hepatitis B (CHB) indication to include treatment of CHB in paediatric patients aged 6 to < 12 years 2) Viread granules 33 mg/g: extension of the existing CHB indication for Viread granules to include treatment of CHB in paediatric patients aged 2 to < 12 years. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC have been updated for Viread 123 mg, 163 mg and 204 mg. Sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been	

updated for Viread 245 mg, whereas Sections 4.1, 4.2, 4.4, 5.1 and 5.2. have been updated for Viread granules 33 mg/g.
The Package Leaflet has been updated accordingly for all the products concerned."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

BiResp Spiromax - budesonide / formoterol - EMEA/H/C/003890/II/0026
Teva Pharma B.V., Duplicate, Duplicate of DuoResp Spiromax, Rapporteur: Nithyanandan Nagercoil

Cinryze - C1 esterase inhibitor (human) - EMEA/H/C/001207/II/0064
Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus

Darzalex - daratumumab - EMEA/H/C/004077/II/0018/G, Orphan
Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac

DuoResp Spiromax - budesonide / formoterol - EMEA/H/C/002348/II/0026
Teva Pharma B.V., Rapporteur: Nithyanandan Nagercoil

Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0108/G
Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege

Fasenra - benralizumab - EMEA/H/C/004433/II/0008
AstraZeneca AB, Rapporteur: Nithyanandan Nagercoil

Foclivia - influenza virus surface antigens (inactivated) of strain A/Vietnam/1194/2004 (H5N1) - EMEA/H/C/001208/II/0038/G
Seqirus S.r.l, Rapporteur: Daniela Melchiorri

Herzuma - trastuzumab - EMEA/H/C/002575/II/0012
Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus

Kovaltry - octocog alfa - EMEA/H/C/003825/II/0017/G

Bayer AG, Rapporteur: Kristina Dunder

Miglustat Gen.Orph - miglustat - EMEA/H/C/004366/II/0003
Gen.Orph, Generic, Generic of Zavesca, Rapporteur: Milena Stain

Mircera - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/II/0070
Roche Registration GmbH, Rapporteur: Concepcion Prieto Yerro

Obizur - susoctocog alfa - EMEA/H/C/002792/II/0021
Baxalta Innovations GmbH, Rapporteur: Nithyanandan Nagercoil

PREVYMIS - letermovir - EMEA/H/C/004536/II/0005, Orphan
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson

Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0140
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Sancuso - granisetron - EMEA/H/C/002296/II/0053/G
Kyowa Kirin Holdings B.V., Rapporteur: Romaldas Mačiulaitis

SIRTURO - bedaquiline - EMEA/H/C/002614/II/0030, Orphan
Janssen-Cilag International NV, Rapporteur: Filip Josephson

Trazimera - trastuzumab - EMEA/H/C/004463/II/0002
Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus

Ucedane - carglumic acid - EMEA/H/C/004019/II/0002/G
Lucane Pharma, Generic, Generic of Carbaglu, Rapporteur: Eleftheria Nikolaidi

Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0040
MCM Vaccine B.V., Rapporteur: Bart Van der Schueren

Voncento - human coagulation factor VIII / human von willebrand factor - EMEA/H/C/002493/II/0035/G
CSL Behring GmbH, Rapporteur: Paula Boudewina van Hennik

WS1420
Ambirix-EMEA/H/C/000426/WS1420/0092
Twinrix Adult-EMEA/H/C/000112/WS1420/0126
Twinrix Paediatric-EMEA/H/C/000129/WS1420/0127
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Jan Mueller-Berghaus

WS1432
Ambirix-EMEA/H/C/000426/WS1432/0093
Twinrix Adult-EMEA/H/C/000112/WS1432/0127
Twinrix Paediatric-EMEA/H/C/000129/WS1432/0128
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Robert James Hemmings

WS1456
Infanrix hexa-EMEA/H/C/000296/WS1456/0247
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

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

Bronchitol - mannitol - EMEA/H/C/001252/II/0034, Orphan
Pharmaxis Pharmaceuticals Limited, Rapporteur: Nithyanandan Nagercoil, “Update of sections 4.8 and 5.1 of the SmPC in order to update the frequency of certain adverse events and to update the clinical safety and efficacy information based on the results of the clinical data from Study CF 303. This is a phase 3 safety and efficacy clinical trial in adult cystic fibrosis subjects. The package leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor

editorial changes in the product information and correct the Annex A."

Ferriprox - deferiprone - EMEA/H/C/000236/II/0126/G

Apotex Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update safety information on the use of Ferriprox in patients with renal or hepatic impairment, based on the final results of two clinical studies LA39-0412 (An Open-Label Study to Compare the Pharmacokinetic Profiles of a Single Dose of Ferriprox in Subjects with Impaired Renal Function and Healthy Volunteers) and LA40-0412 (An Open-Label Study to Compare the Pharmacokinetic Profiles of a Single Dose of Ferriprox in Subjects with Impaired Hepatic Function and Healthy Volunteers). The studies are listed as category 3 study in the RMP. The Package leaflet and labelling are updated accordingly. The RMP version 13.1 has also been submitted to include consequential changes regarding these two clinical studies minor changes requested to be addressed at the next regulatory procedure, as well as the RMP format is updated to conform to GVP Module V Rev 2 template.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make some minor edits in the PI."

Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0084

AstraZeneca AB, Rapporteur: Bart Van der Schueren, "Update of section 4.6 of the SmPC to include new information from a publication on breast-feeding. (Brady et al., 2018). The variation also includes recommendations from the Renewal procedure (EMEA/H/C/002617/0079) which included removal of the additional monitoring section, as well as updates from recommendations in the new EMA Guidelines for Vaccines. The Package Leaflet is updated accordingly.
In addition, the Marketing Authorisation Holder (MAH) took the opportunity to introduce minor editorial changes to the Product Information."

Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0097/G

CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, “Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to reflect the final results from the study IgPro20_3004: Multicenter, open-label extension study to investigate the long-term safety and efficacy of IgPro20 in maintenance treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) in subjects completing Study IgPro20_3003. The Package Leaflet is updated accordingly. Update of sections 4.2, 5.1 and 5.2 of the SmPC with the total number of patients with primary immunodeficiency (PID) based on the data from 7 previously submitted clinical trials in PID patients. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes in the PI and to bring the Labelling in line with the latest QRD template version 10.”	
Instanyl - fentanyl - EMEA/H/C/000959/II/0047/G Takeda Pharma A/S, Rapporteur: Alexandre Moreau, “Update of section 4.4. to revised the risks of respiratory depression and the risks in patients with Chronic Obstructive Pulmonary Disease based on cumulative saftey data respectively. Update of section 4.5 with regards interactions with others CNS depressants and skeletal muscle relaxants based on literature data. Update of section 4.8 to add loss of consciousness. PL is updtaed accordingly. the MAH took this opportunity to update the labelling in line with QRD latest templates.”	
Kyprolis - carfilzomib - EMEA/H/C/003790/II/0031, Orphan Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, “Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 to add a once-weekly dose regimen for carfilzomib (Kyprolis) at 20/70 mg/m2 in combination with dexamethasone (Kd) for the treatment of the currently indicated patient population. The MAH took the opportunity to implement editorial changes to the SmPC and Patient Information Leaflet (PIL) due to the revised excipients guideline (EMA/CHMP/302620/2017). The PIL is updated accordingly.”	

Remicade - infliximab - EMEA/H/C/000240/II/0217

Janssen Biologics B.V., Rapporteur: Kristina Dunder, “Update of section 4.8 of the SmPC in order to add the adverse drug reaction “acute generalised exanthematous pustulosis (AGEP)” with a frequency rare. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet.”

Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0053

Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, “Update of section 4.4 and 4.8 of the SmPC in order to extend the warning on cytogenetic abnormalities to reflect the incidence of new genetic abnormalities following data from study ELT116826 (AUS18T) – An open-label, single center, non-randomized, Phase 2, dose modification study Pilot Study of a Thrombopoietin-Receptor Agonist (TPO-R Agonist), Eltrombopag, in Aplastic Anemia Patients With Immunosuppressive-Therapy Refractory Thrombocytopenia. listed as a category 3 study in the RMP”

Rubraca - rucaparib - EMEA/H/C/004272/II/0003, Orphan

Clovis Oncology UK Limited, Rapporteur: Jorge Camarero Jiménez, “to update section 5.2 of the SmPC based on final results from Part 1 of study CO-338-45 this is a Phase 1, single-dose study of the disposition of [14C]-radiolabelled rucaparib in patients with advanced solid tumors the dossier has been updated to also include additional information on metabolite profilin. This was listed as Recommendation 3:

The MAH commits to submitting the results for Part 1 of clinical study CO-338 (mass balance study) as soon as available and to assess if further investigation is warranted to (1) further elucidate main pathways of metabolism, routes of elimination, and potential interactions of rucaparib and its metabolites; (2) to use the mass balance and metabolite profiling data to confirm the mean absolute oral bioavailability at the 600mg dose and clarify the reasons of low bioavailability. In light of the results of this study, further DDI study could be required. (Ref. Rcommendation 3, EMEA/H/C/04272 Response

to D180 LoOI)"	
Sprycel - dasatinib - EMEA/H/C/000709/II/0064 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Sinan B. Sarac, "Submission of results from existing and new PK analyses together with the review of the literature data on the dasatinib PK profile in fasted conditions to assess implications arising for the recommendation for administration, as requested by the CHMP."	
Trulicity - dulaglutide - EMEA/H/C/002825/II/0032 Eli Lilly Nederland B.V., Rapporteur: Greg Markey, "Update of section 4.4 of the SmPC, following a cumulative review of Acute Kidney Injury events undertaken upon request by PRAC (EPITT No 19204), to add information regarding the potential for dulaglutide to possibly contribute to the volume depletion event, which could indirectly contribute to the occurrence of AKI. The Package Leaflet has been updated accordingly."	
Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0011 Pfizer Limited, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC in order to add a warning about concomitant use of treatments inhibiting terminal complement activation."	
Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0005, Orphan Ipsen Pharma, Rapporteur: Martina Weise, "Update of section 5.2 of the SmPC in order to add information from an in vivo drug interaction study (study identifier: LX1606.1-110-NRM) to evaluate the effect of multiple doses of concomitant gastric acid reducers such as PPIs on the PK of telotristat ethyl, LP-778902."	
Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/II/0067 Bial - Portela & Cª, S.A., Rapporteur: Martina Weise, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect the long-term safety and efficacy data obtained from the open-label extensions (parts II to V) of the phase III study BIA-2093-305. The study was assessed in	

procedure EMA/H/C/988/P46 025."

Zostavax - shingles (herpes zoster) vaccine (live) - EMEA/H/C/000674/II/0120
MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC in order to add the adverse reactions Guillain-Barré syndrome and facial paralysis with frequency "very rare" following a review post-marketing cases; the Package Leaflet is updated accordingly."

WS1477
Lixiana-EMEA/H/C/002629/WS1477/0019
Roteas-EMEA/H/C/004339/WS1477/0007
Daiichi Sankyo Europe GmbH, Lead Rapporteur: Concepcion Prieto Yerro, "Update of sections 4.4, 4.8 and 5.1 of the SmPC for Lixiana and Roteas to update the clinical efficacy and safety information based on the final results from study DUI176b-D-U311, a phase IIIB prospective, randomised, open-label, blinded evaluator study to evaluate the efficacy and safety of low molecular weight heparin/edoxaban versus dalterparin in venous thromboembolism associated with cancer. In addition, the Worlsharing applicant (WSA) took the opportunity to combine the 15 mg, 30 mg and 60 mg strengths SmPCs, to delete 'aspirin' from section 2 of the Package Leaflet, to update the contact details of the Portuguese local representative in the Package Leaflet for Lixiana only, and to make some corrections to the German, Finnish, Italian, Lithuanian, Maltese and Portuguese translations."

B.6.10. CHMP-PRAC assessed procedures

Dificlir - fidaxomicin - EMEA/H/C/002087/II/0033
Astellas Pharma Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of an updated RMP version 10 in order to reflect the final outcome (Year 5) of the ClosER study (study AG2012-3459, Clostridium difficile European Resistance surveillance study).
The ClosER study was a prospective, longitudinal, pan-European, in vitro sentinel surveillance study of susceptibility of Clostridium difficile to

fidaxomicin and other antibiotics. The study is an additional pharmacovigilance activity (Category 3, MEA 002.4) included in the Dificlir RMP."	
Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0036 GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jean-Michel Dogné, "Update of section 4.4 of the SmPC in order to modify the warning related to the waning of protection against Plasmodium falciparum malaria over time. This update is based on final results from study MALARIA-076 listed as a category 3 study in the RMP. This was an open extension to the phase III, multi-centre study MALARIA-055 PRI (110021) to evaluate long-term efficacy, safety and immunogenicity of the GSK Biologicals' candidate malaria vaccine in infants and children. The RMP version 4.1 has also been submitted."	
Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0029/G Orexigen Therapeutics Ireland Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber, "Group of variations consisting of the: 2) C.I.3.b: to update section 4.8 on the list of adverse drug reactions and their corresponding frequencies following the PRAC outcome on PSUR procedure (PSUSA/10366/201709). 2) C.I.4: to update sections 4.2,4.4 and 5.2 of the SmPC to add results from a phase I open label parallel study to evaluate the pharmacokinetics of a single oral dose of extended-release combination of naltrexone and bupropion in subjects with normal hepatic function or varying degrees of impaired hepatic function and remove the recommendation to not use naltrexone/bupropion in patients with mild hepatic impairment. The existing warning has also been updated accordingly. The warning related to contraindications has also been aligned to section 4.3 to add end-stage renal failure patients. Consequentially an updated RMP (version 11) has also been submitted. In addition, the MAH takes the opportunity to	

update the warning on lactose to be in accordance with EC guideline on Guideline on "Excipients in the labelling and package leaflet of medicinal products for human use"."

SIRTURO - bedaquiline - EMEA/H/C/002614/II/0028, Orphan

Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.4 of the SmPC in order to update the safety information with inclusion of a statement on bedaquiline resistance, further to a request by the PRAC in the context of the assessment of PSUR procedure EMEA/H/C/PSUSA/00010074/201709 (LEG 011).

The RMP version 3.0 has also been submitted, updated based on the data triggering the SmPC update and to reflect completion of studies which were assessed in previous procedures.

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

TAGRISSO - osimertinib - EMEA/H/C/004124/II/0026

AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst, "C.I.11: Submission of an updated RMP version 12.0 following the completion of study D6030C00001 (BLOOM) (A Phase I, Open-label, Multicentre Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Anti-Tumour Activity of AZD9291 in Patients with EGFR Mutation Positive Advanced Stage Non-Small Cell Lung Cancer [NSCLC]; BLOOM in order to remove the following safety concerns included as missing information: Use in patients with ECOG performance status≥2" and "Use in patients with symptomatic brain metastases."

Toujeo - insulin glargine - EMEA/H/C/000309/II/0106

Sanofi-Aventis Deutschland GmbH, Duplicate, Duplicate of Lantus, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Submission of the final report from a completed Phase 3b study, EFC13799: "A randomized, open-label, 2-arm, parallel-group, multicenter, 26-week study assessing the safety and efficacy of HOE901-U300 versus Lantus

(insulin glargine 100 U/mL) in patients ≥ 65 years with treatment of diabetes mellitus type II (T2DM) inadequately controlled on antidiabetic regimens either including no insulin, or with basal insulin as their only insulin". The RMP (version 5) is updated to reflect the exposure data in elderly patients."	

B.6.11. PRAC assessed procedures

PRAC Led **Abraxane - paclitaxel - EMEA/H/C/000778/II/0092** Celgene Europe BV, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 17.0 in order to propose the reclassification and/or renaming of known safety concerns associated with the use of paclitaxel in accordance with the new Guideline on Good Pharmacovigilance Practices (GVP) Module V version 2"	
PRAC Led **Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0072** UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP (version 14.0) in order to revise the distribution's list of educational materials (addition of dermatologists) and to revise the RMP in line with the new RMP template (GVP Module V rev.2) including the update of the important identified risks and important potential risks. The PASS protocol for Study UP0038 designed to assess the effectiveness of the educational material is updated to add dermatologists to the healthcare professional study population, to remove Italy and Spain from study participation and to make additional administrative changes. In addition, the MAH took the opportunity to make some administrative changes in the RMP."	
PRAC Led **Colobreathe - colistimethate sodium - EMEA/H/C/001225/II/0039** Teva B.V., Rapporteur: Nithyanandan Nagercoil,	

PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, “Submission of the final report from study CLB-MD-08, a Category 3, non-interventional PASS. This is a Safety, Cross-sectional survey study to evaluate the effectiveness of the Colobreathe risk minimisation educational programme among healthcare professionals and patients. This submission also fulfils MEA 012.1.”

PRAC Led

Eurartesim - piperaquine tetraphosphate / artenimol - EMEA/H/C/001199/II/0032

Alfasigma S.p.A., Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, “Submission of an updated RMP version 15.2 (in line with the revision 2 of the RMP template) in order to close the Pregnancy Registry. In addition, the Marketing authorisation holder (MAH) took the opportunity to:

- Distribution of a new version of the educational material.
- Addition of two important potential risks: `Delayed haemolytic anaemia’ and `Severe skin reactions´, such as Stevens- Johnson syndrome and Toxic Epidermal Necrolysis.
- Limitation of the reproductive risk to the first trimester of pregnancy.
- Update on several studies.
- Inclusion of Eurartesim into the WHO Essential Medicines List.
- Update the MAH details.”

PRAC Led

Herceptin - trastuzumab - EMEA/H/C/000278/II/0147

Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, “Submission of the final report from the pregnancy registry (H4621g, MotHER) study listed as a category 3 study in the RMP. This is an observational study of pregnancy and pregnancy outcome in women with breast cancer treated with trastuzumab, pertuzumab in combination with trastuzumab, or ADO-trastuzumab emtansine during Pregnancy or within 7 months prior to conception. The RMP is being updated accordingly (version 20.0) and in response to comments discussed and received

in procedure EMEA/H/C/000278/II/140."

PRAC Led

Nulojix - belatacept -

EMEA/H/C/002098/II/0050/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 (IM103074 and IM103077) listed as category 3 studies in the RMP. Study IM103074 is an observational study designed to assess the pattern of use of balatacept in US transplant recipients in routine clinical practice. Study IM103077 is an observational study designed to assess the patterns of use of belatacept in renal transplantation using the collaborative transplant study.
An updated RMP (version 16.0) is submitted in order to reflect the results of the above studies. In addition, the MAH took the opportunity to update the RMP in line with the new RMP template (GVP Module V rev.2), to reflect minor editorial changes and to reflect the earlier completion dates for two remaining studies (IM103075 and IM103076) listed as category 3 studies in the RMP."

PRAC Led

Otezla - apremilast -

EMEA/H/C/003746/II/0023

Celgene Europe BV, Rapporteur: Peter Kiely, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Concepcion Prieto Yerro, "Submission of an updated RMP version 11.0 in order to reclassify and/or rename the known safety concerns associated with the use of apremilast in accordance with the new Guideline on GVP Module V. In addition, the RMP is converted to the RMP template Revision 2."

PRAC Led

Tasmar - tolcapone -

EMEA/H/C/000132/II/0061

Meda AB, Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, "Submission of an updated RMP version 7 in order to:
- reflect currently available data from post-marketing experience and patient exposure data;
- align the RMP with the new GVP RMP template

rev.2; - remove the important identified risk ‘dopaminergic effects due to increased bioavailability of co-administered levodopa (e.g. dyskinesia)’ and the potential risk ‘drug interactions with significant clinical consequence including sudden sleep onset’.”

B.6.12. CHMP-CAT assessed procedures

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

WS1469 **Glyxambi-EMEA/H/C/003833/WS1469/0016** **Jentadueto-EMEA/H/C/002279/WS1469/0046** **Trajenta-EMEA/H/C/002110/WS1469/0034** Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege
Hexacima-EMEA/H/C/002702/WS1455/0084/G **Hexaxim-EMEA/H/W/002495/WS1455/0089/G** **Hexyon-EMEA/H/C/002796/WS1455/0088/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

B.7. DOCUMENTS TABLED IN MMD AFTER THE CHMP PLENARY

B.7.1. Yearly Line listing for Type I and II variations

B.7.2. Monthly Line listing for Type I variations

B.7.3. Opinion on Marketing Authorisation transfer (MMD only)

B.7.4. Notifications in accordance with Article 61(3) of Council Directive 2001/83/EC (MMD only)

B.7.5. Request for supplementary information relating to Notification of Type I variation (MMD only)

B.7.6. Notifications of Type I Variations (MMD only)

C. Annex C - Post-Authorisation Measures (PAMs), (Line listing of Post authorisation measures with a description of the PAM. Procedures starting in that given month with assessment timetabled)

D. Annex D - Post-Authorisation Measures (PAMs), (Details on PAMs including description and conclusion, for adoption by CHMP in that given month, or finalised ones with PRAC recommendation and no adoption by CHMP needed)

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

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

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

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

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

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

G. ANNEX G

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

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

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 17-20 September 2018 CHMP plenary:

Oncology		
1.	(SME); Treatment of primary choroidal melanoma	The CHMP denied eligibility to PRIME and adopted the critical summary report.
2.	Treatment of patients with solid tumours	The CHMP denied eligibility to PRIME and adopted the critical summary report.
Haematology-haemostaseology		
3.	**Autologous CD34+ cells transduced with lentiviral vector encoding the human beta globin gene (OTL-300);** (SME); ATMP; Treatment of tranfusion-dependent β-thalassemia	The CHMP granted eligibility to PRIME and adopted the critical summary report.
Infectious Diseases		
4.	(SME);Treatment of recurrent Clostridium difficile infection	The CHMP denied eligibility to PRIME and adopted the critical summary report.

G.3.2. List of procedures starting in September 2018 for October 2018 CHMP adoption of outcomes

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