24 May 2019
EMA/CHMP/289313/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Agenda for the meeting on 27-29 May 2019

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

27 May 2019, 08:30 – 19:30, room 1C

28 May 2019, 08:30 – 19:30, room 1C

29 May 2019, 08:30 – 19:30, room 1C

Health and safety information

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

Disclaimers

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 27-29 May 2019. See (current) May 2019 CHMP minutes (to be published post June 2019 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 27-29 May 2019.

1.3. Adoption of the minutes

CHMP minutes for 23-26 April 2019.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. romosozumab - EMEA/H/C/004465

treatment of osteoporosis

Scope: Oral explanation

Action: Oral explanation to be held on Tuesday, 28 May 2019 at time 11:00

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

2.1.2. angiotensin II - EMEA/H/C/004930

treatment of hypotension in adults with distributive or vasodilatory shock who remain hypotensive despite fluid and vasopressor therapy

Scope: Possible Oral explanation

Action: Oral explanation to be held on Tuesday, 28 May 2019 at time 09:00

List of Outstanding Issues adopted on 28.03.2019. List of Questions adopted on 18.10.2018.

2.1.3. ibalizumab - EMEA/H/C/004961

treatment of adults infected with human immunodeficiency virus 1 (HIV-1) resistant to at least 1 agent in 3 different classes

Scope: Possible Oral Explanation, SAG Report

Action: Oral explanation to be held on Tuesday, 28 May 2019 at 14:00

List of Outstanding Issues adopted on 28.02.2019. List of Questions adopted on 11.12.2018.

2.2. Re-examination procedure oral explanations

2.2.1. Doxolipad - doxorubicin hydrochloride - EMEA/H/C/004110

TLC Biopharmaceuticals B.V.; treatment of breast and ovarian cancer

Scope: Oral explanation, Draft list of experts for the ad hoc expert group meeting held on 20 May 2019 adopted via written procedure on 16 May 2019

Action: Oral explanation to be held on Monday, 27 May 2019 at time 14:00

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

Opinion adopted on 31.01.2019. List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 14.09.2017.

2.3. Post-authorisation procedure oral explanations

No items

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

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

Univar BV; treatment of Wilson's disease

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.03.2019, 31.01.2019. List of Questions adopted on 28.06.2018.

3.1.2. L-lysine hydrochloride / L-arginine hydrochloride - EMEA/H/C/004541

reduction of renal radiation exposure during peptide-receptor radionuclide therapy (PRRT) with lutetium (^{177}Lu) oxodotreotide

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.03.2019. List of Questions adopted on 18.10.2018.

3.1.3. posaconazole - EMEA/H/C/005005

treatment of fungal infections

Scope: Opinion

Action: For adoption

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

3.1.4. posaconazole - EMEA/H/C/005028

treatment of fungal infections in adults

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.03.2019. List of Questions adopted on 18.10.2018.

3.1.5. edaravone - Orphan - EMEA/H/C/004938

Mitsubishi Tanabe Pharma GmbH; treatment of amyotrophic lateral sclerosis (ALS)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.04.2019, 28.02.2019. List of Questions adopted on 20.09.2018.

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

Emmaus Medical Europe Ltd; treatment of sickle cell disease

Scope: Opinion

Action: For adoption

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

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

3.2.1. dapagliflozin / saxagliptin / metformin hydrochloride - EMEA/H/C/004910

- Improvement of glycaemic control when metformin with or without sulphonylurea (SU) does not provide adequate glycaemic control and where simultaneous addition of dapagliflozin and saxagliptin is considered necessary – improvement of glycaemic control when metformin with or without SU and either dapagliflozin or saxagliptin does not provide adequate glycaemic control - when already being treated with dapagliflozin and saxagliptin and metformin.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 15.11.2018.

3.2.2. deferasirox - EMEA/H/C/005014

treatment of chronic iron overload

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 15.11.2018.

3.2.3. erlotinib - EMEA/H/C/005071

treatment of lung and pancreatic cancers

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 13.12.2018.

3.2.4. levodopa - EMEA/H/C/004786

treatment of symptoms of OFF periods in Parkinson's disease

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.09.2018.

3.2.5. siponimod - EMEA/H/C/004712

treatment of secondary progressive multiple sclerosis (SPMS)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 31.01.2019.

3.2.6. etanercept - EMEA/H/C/004711

treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, axial spondyloarthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, plaque psoriasis, paediatric plaque psoriasis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.09.2018.

3.2.7. delafloxacin - EMEA/H/C/004860

treatment of acute bacterial skin and skin structure infection (ABSSSI) in adults

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.09.2018.

3.2.8. crisaborole - EMEA/H/C/004863

treatment of mild to moderate atopic dermatitis

Scope: List of outstanding issues

Action: For adoption

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

3.2.9. tigecycline - EMEA/H/C/005114

- treatment of soft tissue and intra-abdominal infections

- complicated skin and soft tissue infections, excluding diabetic foot infections

- complicated intra-abdominal infections

should be used only in situations where it is known or suspected that other alternatives are not suitable

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 13.12.2018.

3.2.10. larotrectinib - Orphan - EMEA/H/C/004919

Bayer AG; treatment of adult and paediatric patients with locally advanced or metastatic solid tumours

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 28.03.2019. List of Questions adopted on 11.12.2018.

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

3.3.1. infliximab - EMEA/H/C/005020

treatment of rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, psoriasis and ulcerative colitis

Scope: List of questions

Action: For adoption

3.3.2. azacitidine - EMEA/H/C/005147

treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML) and acute myeloid leukemia (AML) and AML with >30% marrow blasts according to the WHO classification.

Scope: List of questions

Action: For adoption

3.3.3. azacitidine - EMEA/H/C/005075

treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML)

and acute myeloid leukemia (AML)

Scope: List of questions

Action: For adoption

3.3.4. cinacalcet - EMEA/H/C/005236

treatment of secondary hyperparathyroidism and hypercalcaemia

Scope: List of questions

Action: For adoption

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

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

Scope: List of questions

Action: For adoption

3.3.6. entrectinib - EMEA/H/C/004936

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

Scope: List of questions

Action: For adoption

3.3.7. alpelisib - EMEA/H/C/004804

indicated in postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, advanced breast cancer with a PIK3CA mutation in combination with fulvestrant after disease progression following an endocrine-based regimen

Scope: List of questions

Action: For adoption

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

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

Scope: List of questions

Action: For adoption

3.3.9. upadacitinib - EMEA/H/C/004760

treatment of moderate to severe active rheumatoid arthritis

Scope: List of questions

Action: For adoption

3.3.10. cholera vaccine, oral, live - EMEA/H/C/003876

indicated for active immunisation against disease caused by Vibrio cholerae serogroup, O1 in adults and children aged 6 years and older

Scope: List of questions

Action: For adoption

3.3.11. gilteritinib - Orphan - EMEA/H/C/004752

Accelerated assessment

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

Scope: List of questions

Action: For adoption

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

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

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

Scope: Letter from applicant dated 15 May 2019 requesting an extension of clock stop to respond to the list of outstanding issues adopted in April 2019.

Action: For adoption

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

3.4.2. imipenem / cilastatin / relebactam - EMEA/H/C/004808

indicated for the treatment of bacterial infections due to gram-negative microorganisms

Scope: Letter from applicant dated 10 May 2019 requesting an extension of clock stop to respond to the list of questions adopted in March 2019.

Action: For adoption

List of Questions adopted on 28.03.2019.

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

No items

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. ambrisentan - EMEA/H/C/004955

treatment of pulmonary arterial hypertension (PAH)

Scope: Withdrawal of initial marketing authorisation application

Action: For information

List of Outstanding Issues adopted on 31.01.2019. List of Questions adopted on 20.09.2018.

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. Nucala - mepolizumab - EMEA/H/C/003860/X/0018

GlaxoSmithKline Trading Services Limited

Rapporteur: Peter Kiely, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: “Extension application to introduce a new pharmaceutical form, solution for injection (in pre-filled syringe or in pre-filled pen).”

Action: For adoption

List of Questions adopted on 31.01.2019.

4.1.2. Tecentriq - atezolizumab - EMEA/H/C/004143/X/0017

Roche Registration GmbH

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

Scope: “Extension application to add a new strength of 840 mg (60 mg/ml) for Tecentriq concentrate for solution for infusion in a vial and a new indication (metastatic triple-negative breast cancer (TNBC)). The new indication applies only to the 840mg strength.”

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

Action: For adoption

List of Questions adopted on 31.01.2019.

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

No items

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

Astellas Pharma Europe B.V.

Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Scope: “Extension application to introduce a new pharmaceutical form associated with new strength (40 mg/ml granules for oral suspension) grouped with a type II variation (C.I.6.a) to include paediatric use of Dificlir in children from birth to less than 18 years of age.
The RMP (version 11.0) is updated in accordance.
Consequential updates have been made to the SmPC of Dificlir200 mg Film-coated tablet.
The labelling and package leaflet (PL) are updated accordingly.
The PL is also being amended to include a statement that Dificlir is essentially ‘sodium-free' (in accordance with the Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. The details of the local representative of the MAH in the Czech Republic are also updated.”

Action: For adoption

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

Pfizer Europe MA EEIG

Rapporteur: Joseph Emmerich, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ghania Chamouni

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

Action: For adoption

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

Merck Europe B.V.

Rapporteur: Filip Josephson, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Anette Kirstine Stark

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

Action: For adoption

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

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark

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

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

Action: For adoption

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

Merck Sharp & Dohme B.V.

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

Menno van der Elst

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

Action: For adoption

5.1.4. Lucentis - ranibizumab - EMEA/H/C/000715/II/0074/G

Novartis Europharm Limited

Rapporteur: Kristina Dunder, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include new indication for Lucentis vial presentation: treatment of retinopathy of prematurity (ROP) in preterm infants; as a consequence, sections 2, 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance.
In addition, RMP version 18.0 is also submitted.
B.IV.1.a.1 – To introduce a low volume high accuracy syringe, as a stand-alone medical device for the administration of the Lucentis 0.2mg paediatric dose (corresponding to 0.02 ml of the Lucentis 10 mg/ml solution for injection in vial presentations)."

Action: For adoption

Request for Supplementary Information adopted on 31.01.2019.

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

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Anette Kirstine Stark

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

Action: For adoption

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

Celgene Europe BV

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

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

Action: For adoption

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

Janssen-Cilag International NV

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

Scope: "Grouping of an Extension of indication to include patients 12 years of age and older for SIRTURO and a Type II variation to change the safety information in Section 4.9 of the SmPC. The extension of indication is supported by the Week 24 analysis of Cohort 1 (adolescent subjects aged ≥12 to <18 years) of Study TMC207-C211. Based on these data, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. An updated version of the RMP (version 3.2) was included in the submission."

Action: For adoption

Request for Supplementary Information adopted on 31.01.2019.

5.1.8. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0019

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 Tecentriq, in combination with nab-paclitaxel and carboplatin, indicated for the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC) who do not have EGFR mutant or ALK-positive NSCLC; 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. RMP version 9.0 has been submitted."

Action: For adoption

Request for Supplementary Information adopted on 31.01.2019.

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

UCB Pharma S.A.

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

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

Action: For adoption

Request for Supplementary Information adopted on 15.11.2018.

5.1.10. Zerbaxa - ceftolozane / tazobactam - EMEA/H/C/003772/II/0020

Merck Sharp & Dohme B.V.

Rapporteur: Bjorg Bolstad, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Adam Przybylkowski

Scope: “Extension of indication to include treatment of Nosocomial pneumonia, including ventilator associated pneumonia for Zerbaxa, based on results from the randomised, double-blind, multicentre clinical trial CXA-NP-11-04 (PN008).
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated.
The Package Leaflet is updated in accordance (sections 1, 2, 3, 4 and 6).
The applicant also took the opportunity to implement editorial changes in section 5.2 of the SmPC and to bring section 4.4 of the SmPC and section 2 of the PL in line with the latest Annex to the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. Version 2.1 of the RMP was also submitted.”

Action: For adoption

Request for Supplementary Information adopted on 28.03.2019.

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

GlaxoSmithKline (Ireland) Limited

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

Scope: “Update of sections 4.1. and 5.1 of the SmPC in order to update the efficacy information regarding the benefit on disease exacerbations of umeclidinium and umeclidinium/vilanterol from the CTT116855 study (InforMing the PAthway of COPD Treatment [IMPACT]) and the benefit on disease exacerbations of vilanterol from the HZC113782 study (Study to Understand Mortality and Morbidity [SUMMIT]).
The Package Leaflet is updated in accordance.”

Action: For adoption

Request for Supplementary Information adopted on 31.01.2019.

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

GlaxoSmithKline (Ireland) Limited

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

Scope: “Update of sections 4.1. and 5.1 of the SmPC in order to update the efficacy information regarding the benefit of umeclidinium and umeclidinium/vilanterol from the CTT116855 study (InforMing the PAthway of COPD Treatment [IMPACT]).
The Package Leaflet is updated in accordance.”

Action: For adoption

Request for Supplementary Information adopted on 31.01.2019.

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

No items

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

No items

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. givosiran - H0004775

indicated for the treatment of acute hepatic porphyria in adults and adolescents

Scope: Briefing note and the rapporteurs’ recommendation on the request for accelerated assessment

Action: For adoption

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

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Fabrazyme - Agalsidase Beta - EMEA/H/C/000370/MEA 057.10

Genzyme Europe BV; treatment of Fabry disease

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Outi Mäki-Ikola

Scope: Fabry registry - MAH's responses to the fifth biennial report (MEA 57.9) related to additional follow up of current and future patients treated with low dose regimens

Action: For discussion

9.1.2. Zalmoxis - nalotimagene carmaleucel - EMEA/H/C/002801/R/0015 - Orphan, ATMP

MolMed S.p.A

Rapporteur: Johannes Hendrikus Ovelgonne, Co-Rapporteur: Sol Ruiz, CHMP Coordinator of Rapporteur: Paula Boudewina van Hennik, CHMP Coordinator Co-Rapporteur: Maria Concepcion Prieto Yerro

Scope: Request for Supplementary Information

Action: For adoption

9.1.3. Zalmoxis - nalotimagene carmaleucel - EMEA/H/C/002801/II/0016 - Orphan, ATMP

MolMed S.p.A

Rapporteur: Johannes Hendrikus Ovelgonne, Co-Rapporteur: Sol Ruiz, CHMP Coordinator of Rapporteur: Paula Boudewina van Hennik, CHMP Coordinator Co-Rapporteur: Maria Concepcion Prieto Yerro

Scope: The MAH is proposing to terminate study TK008 (specific obligation for the conditional marketing authorisation (CMA)) and replace it with study TK013

Request for Supplementary Information

Action: For adoption

9.1.4. RoActemra - tocilizumab - EMEA/H/C/000955

Roche Registration GmbH

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

Scope: Report for Roactemra LEG 055 which was reviewed by the PRAC during the May plenary, DHPC and communication plan intended to inform prescribers on the identified risk of hepatotoxicity associated with the use of RoActemra

Action: For adoption

10. Referral procedures

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

No items

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

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

MAHs: various

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

Rapporteurs for involved CAPs:

Eliquis (APIXABAN):
Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Nithyanandan Nagercoil;

Pradaxa (DABIGATRAN ETEXILATE):
Rapporteur: Mark Ainsworth, Co-Rapporteur: Joseph Emmerich;

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

Scope: List of outstanding issues

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

Action: For adoption

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

No items

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

No items

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

No items

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

10.6.1. Methocarbamol/Paracetamol– EMEA/H/A-31/XXX

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

Referral Rapporteur: TBC, Referral Co-Rapporteur: TBC

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

Action: For discussion

EMA received a notification from DE (BfArM) requesting the initiation of an Article 31 procedure for the fixed dose combination methocarbamol/paracetamol, based on concerns on efficacy (due to the dose of methocarbamol and role of paracetamol in the combination) and potential interactions between its active ingredients, which arose during the assessment of generic MAAs.

In the EU/EEA the combination is only authorised in Spain (since 1968), for use in the short-term, symptomatic treatment of painful muscle spasms associated with acute musculoskeletal disorders and generic MAAs referencing to the Spanish MA are currently under assessment in United Kingdom and Germany (as reference Member State).

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

10.11.1. Basiron AC – benzoyl peroxide, hydrous – EMEA/H/A-13/1475

MAHs: Galderma Nordic AB

Re-examination Rapporteur: Romaldas Maciulaitis, Re-examination Co-Rapporteur: Alexandre Moreau

Initial Referral Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege

Scope: Request for withdrawal for re-examination

Action: For information

This procedure concerns a Type II Quality WS variation (SE/H/xxxx/WS/190). The notification received by the reference authority (SE) on 26/10/2018, notifying of the start of a referral under Article 13 of Commission regulation (EC) No 1234/2008.

11. Pharmacovigilance issue

11.1. Early Notification System

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

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

Action: For information

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 CHMP Co-opted Member

Election of CHMP Co-opted Member with the area of expertise:

Expertise in biostatistics, principally on clinical trial methodology, and at least basic knowledge of the EU regulatory framework

Action: For election

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 13-16 May 2019

Action: For information

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

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 22-24 May 2019

Action: For information

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 13-15 May 2019

Action: For information

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at May 2019 PDCO

Action: For information

Report from the PDCO meeting held on 27-29 May 2019

Action: For information

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 21-23 May 2019

Action: For information

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 27-29 May 2019

Action: For information

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

14.3.1. Scientific Advice Working Party (SAWP)

Chair: Anja Schiel

Report from the SAWP meeting held on 13-16 May 2019. Table of conclusions

Action: For information

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

14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 21-22 May 2019.

Action: For adoption

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP 20-22 May 2019 meeting to CHMP for adoption:

- 16 reports on products in scientific advice and protocol assistance
- 4 reports on products in pre-authorisation procedures
- 4 reports on products in plasma master file

Action: For adoption

14.3.4. Respiratory Drafting Group (RDG)

Chair: Karolina Toerneke

Scope: Respiratory drafting Group advice to PDCO on a PIP for broncholitis obliterans syndrome

Action: For discussion

14.3.5. Antimicrobial Advice ad hoc Expert Group (AMEG)

Scope: Overview of comments received during the public consultation on the AMEG scientific advice on the preliminary risk profiling

Action: For discussion

Scope: Overview of comments received during the public consultation on the AMEG scientific advice on the categorisation of antimicrobials

Action: For discussion

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

No items

16. 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)*

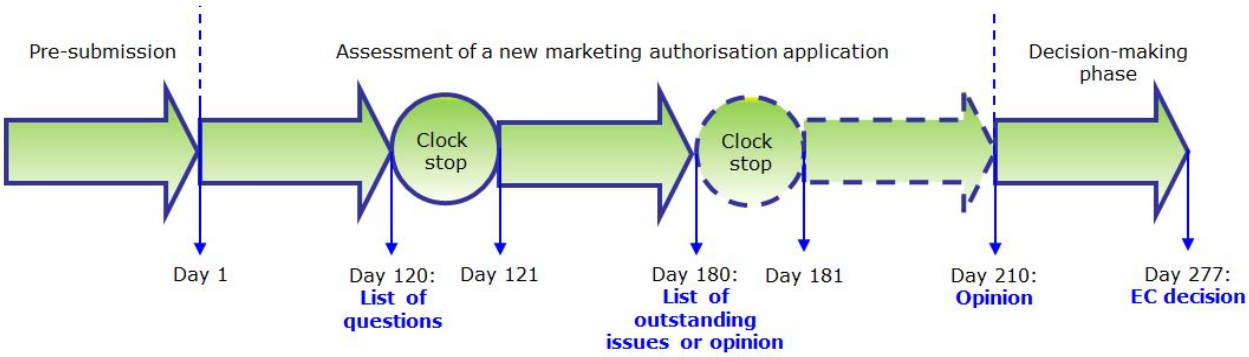
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

24 May 2019
EMA/CHMP/289436/2019

Annex to 27-29 May 2019 CHMP Agenda

Pre-submission and post-authorisations issues

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A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for
May 2019: **For adoption**

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

Final Outcome of Rapporteurship allocation for
May 2019: **For adoption**

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

Abasaglar - insulin glargine -
EMEA/H/C/002835/R/0023
Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Amelia Cupelli
Request for Supplementary Information adopted on 28.03.2019.

Duloxetine Lilly - duloxetine -
EMEA/H/C/004000/R/0015
Eli Lilly Nederland B.V., Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Maria del Pilar Rayon

Ketoconazole HRA - ketoconazole -
EMEA/H/C/003906/R/0014, Orphan
Laboratoire HRA Pharma, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Željana Margan Koletić

VIZAMYL - flutemetamol (18F) -
EMEA/H/C/002557/R/0017

GE Healthcare AS, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber
Request for Supplementary Information adopted on 28.03.2019.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Adjupanrix - pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - EMEA/H/C/001206/R/0062
GlaxoSmithkline Biologicals SA, Informed Consent of Pandemrix (EXP), Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 26.04.2019.

Brimica Genuair - aclidinium / formoterol fumarate dihydrate - EMEA/H/C/003969/R/0026
AstraZeneca AB, Duplicate, Duplicate of Duaklir Genuair, Rapporteur: Ewa Balkowiec Iskra, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Adam Przybylkowski

Cyramza - ramucirumab - EMEA/H/C/002829/R/0031
Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Kolbeinn Gudmundsson (IS) (MNAT with IS for Clinical Efficacy, IS for Coordination, IS for Clinical Safety, FI for Quality, FI for Non-Clinical, LT for Clinical Pharmacology), PRAC Rapporteur: Brigitte Keller-Stanislawski

Duaklir Genuair - aclidinium / formoterol fumarate dihydrate - EMEA/H/C/003745/R/0026
AstraZeneca AB, Rapporteur: Ewa Balkowiec Iskra, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Adam Przybylkowski

Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/R/0080
Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, Co-Rapporteur: Joseph Emmerich, PRAC Rapporteur: Ana Sofia Diniz Martins

Lymphoseek - tilmanocept - EMEA/H/C/002085/R/0016

Norgine B.V., Rapporteur: Jayne Crowe, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Rugile Pilviniene

Moventig - naloxegol - EMEA/H/C/002810/R/0028
Kyowa Kirin Holdings B.V., Rapporteur: Bart Van der Schueren, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Ronan Grimes

MULTAQ - dronedarone - EMEA/H/C/001043/R/0042
sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Menno van der Elst

OFEV - nintedanib - EMEA/H/C/003821/R/0025, Orphan
Boehringer Ingelheim International GmbH, Rapporteur: Jayne Crowe, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica Mirošević Skvrce

Rezolsta - darunavir / cobicistat - EMEA/H/C/002819/R/0031
Janssen-Cilag International NV, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli

Tadalafil Mylan - tadalafil - EMEA/H/C/003787/R/0014
Mylan S.A.S, Generic, Generic of Cialis, Rapporteur: Kolbeinn Gudmundsson, PRAC Rapporteur: Maria del Pilar Rayon

B.2.3. Renewals of Conditional Marketing Authorisations

Translarna - ataluren - EMEA/H/C/002720/R/0051, Orphan
PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Liana Gross-Martirosyan
Request for Supplementary Information adopted on 26.04.2019.

Zalmoxis - nalotimagene carmaleucel - EMEA/H/C/002801/R/0015, Orphan, ATMP
MolMed S.p.A, Rapporteur: Johannes Hendrikus Ovelgonne, Co-Rapporteur: Sol Ruiz, CHMP Coordinators: Paula Boudewina van Hennik and Maria Concepcion Prieto Yerro, PRAC Rapporteur:
See agenda 9.1

Brigitte Keller-Stanislawski

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 13-16 May 2019 PRAC:

Signal of persistent sexual dysfunction after drug withdrawal

Serotonin and noradrenaline reuptake inhibitors (SNRI); Selective serotonin reuptake inhibitors (SSRI); Vortioxetine – CYMBALTA; DULOXETINE LILLY; DULOXETINE MYLAN; DULOXETINE ZENTIVA; XERISTAR; YENTREVE (CAP & NAP)

PRAC recommendation on a variation: **For adoption**

Signal of interaction with boosted antiviral human immunodeficiency virus (HIV) therapy leading to insufficient inhibition of platelet aggregation

Clopidogrel; clopidogrel/acetylsalicylic acid; Lopinavir, ritonavir; ritonavir - CLOPIDOGREL APOTEX, CLOPIDOGREL BGR, CLOPIDOGREL HCS, CLOPIDOGREL KRKA, CLOPIDOGREL KRKA D.D., CLOPIDOGREL MYLAN, CLOPIDOGREL RATIOPHARM, CLOPIDOGREL RATIOPHARM GMBH, CLOPIDOGREL TAD, CLOPIDOGREL TEVA, CLOPIDOGREL ZENTIVA, GREPID, ISCOVER, PLAVIX, ZYLLT; CLOPIDOGREL/ACETYLSALICYLIC ACID ZENTIVA, DUOPLAVIN, KALETRA, LOPINAVIR/RITONAVIR MYLAN, NORVIR, RITONAVIR (CAP & NAP)

PRAC recommendation on a variation: **For adoption**

Signal of colitis microscopic

Pantoprazole – CONTROLOC CONTROL, PANTOLOC CONTROL, PANTOZOL CONTROL, SOMAC CONTROL (CAP & NAP)

PRAC recommendation on a variation: **For adoption**

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its May 2019 meeting:

EMEA/H/C/PSUSA/00000060/201809
(adefovir)
CAPS:
Hepsera (EMEA/H/C/000485) (adefovir dipivoxil), Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Adrien Inoubli, "Period Covered From: 21/09/2015 To: 20/09/2018"

EMEA/H/C/PSUSA/00000547/201810
(carbidopa / entacapone / levodopa)
CAPS:
Corbilta (EMEA/H/C/002785) (levodopa / carbidopa / entacapone), Orion Corporation, Rapporteur: Outi Mäki-Ikola
Levodopa/Carbidopa/Entacapone Orion (EMEA/H/C/002441) (levodopa / carbidopa / entacapone), Orion Corporation, Rapporteur: Outi Mäki-Ikola
Stalevo (EMEA/H/C/000511) (levodopa / carbidopa / entacapone), Orion Corporation, Rapporteur: Outi Mäki-Ikola
NAPS:
LEVODOPA/CARBIDOPA/ENTACAPONE TORRENT - TORRENT PHARMA (UK) LTD
PRAC Rapporteur: Kirsti Villikka, "18 Oct 2015 to 17 Oct 2018"

EMEA/H/C/PSUSA/00000939/201810
(deferasirox)
CAPS:
EXJADE (EMEA/H/C/000670) (deferasirox), Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

EMEA/H/C/PSUSA/00002919/201810
(thalidomide)
CAPS:
Thalidomide Celgene (EMEA/H/C/000823) (thalidomide), Celgene Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "10 October 2017 - 09 October 2018"

EMEA/H/C/PSUSA/00003010/201809
(trastuzumab)
CAPS:
Herceptin (EMEA/H/C/000278) (trastuzumab), Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus
Herzuma (EMEA/H/C/002575) (trastuzumab), Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus
KANJINTI (EMEA/H/C/004361) (trastuzumab), Amgen Europe B.V., BREDA, Rapporteur: Jan Mueller-Berghaus
Ontruzant (EMEA/H/C/004323) (trastuzumab), Samsung Bioepis NL B.V., Rapporteur: Koenraad Norga
Trazimera (EMEA/H/C/004463) (trastuzumab), Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "08 Nov 2017 to 24 Sep 2018"

EMEA/H/C/PSUSA/00010029/201810
(dapagliflozin)
CAPS:
Edistride (EMEA/H/C/004161) (dapagliflozin), AstraZeneca AB, Rapporteur: Kristina Dunder
Forxiga (EMEA/H/C/002322) (dapagliflozin), AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "05 October 2017 to 04 October 2018"

EMEA/H/C/PSUSA/00010213/201810
(delamanid)
CAPS:
Deltyba (EMEA/H/C/002552) (delamanid), Otsuka Novel Products GmbH, Rapporteur: Greg Markey, PRAC Rapporteur: Jean-Michel Dogné, "Period Covered From: 28/04/2018 To: 27/10/2018"

EMEA/H/C/PSUSA/00010306/201810
(sofosbuvir / ledipasvir)
CAPS:
Harvoni (EMEA/H/C/003850) (ledipasvir / sofosbuvir), Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, "Period Covered From: 10/10/2017 To: 09/10/2018"

EMEA/H/C/PSUSA/00010318/201810 (nintedanib (oncology indications)) CAPS: **Vargatef** (EMEA/H/C/002569) (nintedanib), Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Agni Kapou, “Period Covered From: 15/10/2017 To: 15/10/2018”	
EMEA/H/C/PSUSA/00010319/201810 (nintedanib (respiratory indication)) CAPS: **OFEV** (EMEA/H/C/003821) (nintedanib), Boehringer Ingelheim International GmbH, Rapporteur: Jayne Crowe, PRAC Rapporteur: Nikica Mirošević Skvrce, “Period Covered From: 15/10/2017 To: 15/10/2018”	
EMEA/H/C/PSUSA/00010449/201811 (cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide) CAPS: **Genvoya** (EMEA/H/C/004042) (elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide), Gilead Sciences Ireland UC, Rapporteur: Greg Markey, PRAC Rapporteur: Amelia Cupelli, “From: 04/11/2017 To: 04/11/2018”	

B.4. EPARs / WPARs

Ambrisentan Mylan - ambrisentan - EMEA/H/C/004985 MYLAN S.A.S, treatment of pulmonary arterial hypertension (PAH), Generic, Generic of Volibris, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Cabazitaxel Teva - cabazitaxel - EMEA/H/C/004951 Teva B.V., treatment of prostate cancer, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Doptelet - avatrombopag - EMEA/H/C/004722 Dova Pharmaceuticals Ireland Limited, treatment of thrombocytopenia, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Dovato - dolutegravir / lamivudine - EMEA/H/C/004909 ViiV Healthcare B.V., treatment of Human	For information only. Comments can be sent to the EPL in case necessary.

Immunodeficiency Virus type 1 (HIV-1), Fixed combination application (Article 10b of Directive No 2001/83/EC)	
Esperoct - turoctocog alfa pegol - EMEA/H/C/004883, Orphan Novo Nordisk A/S, Treatment and prophylaxis of bleeding in patients with haemophilia A, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Grasustek - pegfilgrastim - EMEA/H/C/004556 Juta Pharma GmbH, reduction in the duration of neutropenia and the incidence of febrile neutropenia, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
LIBTAYO - cemiplimab - EMEA/H/C/004844 Regeneron Ireland U.C., as monotherapy, indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Sixmo - buprenorphine - EMEA/H/C/004743 L. Molteni & C. dei Fratelli Alitti Societa di Esercizio S.p.A., Substitution treatment for opioid drug dependence, Known active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Striascan - ioflupane (123i) - EMEA/H/C/004745 CIS BIO International, indicated for detecting loss of functional dopaminergic neuron terminals in the striatum, Generic, Generic of DaTSCAN, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Talzenna - talazoparib - EMEA/H/C/004674 Pfizer Europe MA EEIG, 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., New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Temybric Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/005254 GlaxoSmithKline Trading Services, treatment of adult patients with chronic obstructive pulmonary	For information only. Comments can be sent to the EPL in case necessary.

disease (COPD), Informed Consent of Trelegy Ellipta, Informed consent application (Article 10c of Directive No 2001/83/EC)	
Ultomiris - ravulizumab - EMEA/H/C/004954, Orphan Alexion Europe SAS, treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Xromi - hydroxycarbamide - EMEA/H/C/004837 Nova Laboratories Ireland Limited, prevention of complications of Sickle Cell disease, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Zynteglo - autologous cd34+ cell enriched population that contains hematopoietic stem cells transduced with lentiglobin bb305 lentiviral vector encoding the beta-a-t87q-globin gene - EMEA/H/C/003691, Orphan, ATMP bluebird bio (Netherlands) B.V, treatment of transfusion-dependent β-thalassaemia (TDT), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Aimovig - erenumab - EMEA/H/C/004447/II/0003/G Novartis Europharm Limited, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 28.03.2019.	
BeneFIX - nonacog alfa - EMEA/H/C/000139/II/0156/G Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 02.05.2019. Request for Supplementary Information adopted on 28.03.2019.	Positive Opinion adopted by consensus on 02.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Benepali - etanercept - EMEA/H/C/004007/II/0042/G	Request for supplementary information adopted with a specific timetable.

Samsung Bioepis NL B.V., Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 02.05.2019.	
Busilvex - busulfan - EMEA/H/C/000472/II/0030/G Pierre Fabre Medicament, Rapporteur: Jorge Camarero Jiménez Request for Supplementary Information adopted on 02.05.2019.	Request for supplementary information adopted with a specific timetable.
Evicel - human fibrinogen / human thrombin - EMEA/H/C/000898/II/0067 Omrix Biopharmaceuticals N. V., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 02.05.2019.	Positive Opinion adopted by consensus on 02.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Flixabi - infliximab - EMEA/H/C/004020/II/0038 Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 02.05.2019, 14.03.2019.	Request for supplementary information adopted with a specific timetable.
Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0004/G Seqirus Netherlands B.V., Rapporteur: Sol Ruiz Opinion adopted on 23.05.2019.	Positive Opinion adopted by consensus on 23.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Insuman - insulin human - EMEA/H/C/000201/II/0128/G Sanofi-Aventis Deutschland GmbH, Rapporteur: Bart Van der Schueren Opinion adopted on 16.05.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0073 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri	
Macimorelin Aeterna Zentaris - macimorelin - EMEA/H/C/004660/II/0001 Aeterna Zentaris GmbH, Rapporteur: Martina Weise Opinion adopted on 02.05.2019.	Positive Opinion adopted by consensus on 02.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Miglustat Gen.Orph - miglustat - EMEA/H/C/004366/II/0003 Gen.Orph, Generic, Generic of Zavesca, Rapporteur: Milena Stain Request for Supplementary Information adopted on 08.11.2018.	

Movymia - teriparatide - EMEA/H/C/004368/II/0012 STADA Arzneimittel AG, Duplicate, Duplicate of Terrosa, Rapporteur: Milena Stain Opinion adopted on 23.05.2019.	Positive Opinion adopted by consensus on 23.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Myalepta - metreleptin - EMEA/H/C/004218/II/0004, Orphan Aegerion Pharmaceuticals B.V., Rapporteur: Bart Van der Schueren Request for Supplementary Information adopted on 02.05.2019.	Request for supplementary information adopted with a specific timetable.
Natpar - parathyroid hormone - EMEA/H/C/003861/II/0013/G, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Bart Van der Schueren Request for Supplementary Information adopted on 31.01.2019.	
Ogivri - trastuzumab - EMEA/H/C/004916/II/0003/G MYLAN S.A.S, Rapporteur: Koenraad Norga Request for Supplementary Information adopted on 02.05.2019.	Request for supplementary information adopted with a specific timetable.
Onpattro - patisiran - EMEA/H/C/004699/II/0004/G, Orphan Alnylam Netherlands B.V., Rapporteur: Kristina Dunder	
Orphacol - cholic acid - EMEA/H/C/001250/II/0025, Orphan Laboratoires CTRS, Rapporteur: Greg Markey Request for Supplementary Information adopted on 28.02.2019, 11.10.2018.	
Prasugrel Mylan - prasugrel - EMEA/H/C/004644/II/0003/G Mylan S.A.S, Generic, Generic of Efient, Rapporteur: Alar Irs Request for Supplementary Information adopted on 16.05.2019.	Request for Supplementary Information adopted with a specific timetable.
Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0029/G CSL Behring GmbH, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 02.05.2019.	Request for supplementary information adopted with a specific timetable.
Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0132 GlaxoSmithkline Biologicals SA, Rapporteur:	

Kristina Dunder Request for Supplementary Information adopted on 28.03.2019.	
Terrosa - teriparatide - EMEA/H/C/003916/II/0010 Gedeon Richter Plc., Rapporteur: Milena Stain Opinion adopted on 23.05.2019.	Positive Opinion adopted by consensus on 23.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0016/G Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 14.03.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tysabri - natalizumab - EMEA/H/C/000603/II/0113/G Biogen Netherlands B.V., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 04.04.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Visudyne - verteporfin - EMEA/H/C/000305/II/0098/G Novartis Europharm Limited, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 04.04.2019.	
Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0056/G Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez	
WS1464/G **Revatio-EMEA/H/C/000638/WS1464/0084/G** **Viagra-EMEA/H/C/000202/WS1464/0100/G** Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 23.05.2019. Request for Supplementary Information adopted on 21.03.2019.	Positive Opinion adopted by consensus on 23.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1500/G **HyQvia-EMEA/H/C/002491/WS1500/0045/G** **Kiovig-EMEA/H/C/000628/WS1500/0086/G**	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 17.01.2019.	
WS1502 **Fertavid-EMEA/H/C/001042/WS1502/0042** **Puregon-EMEA/H/C/000086/WS1502/0100** Merck Sharp & Dohme B.V., Lead Rapporteur: Nithyanandan Nagercoil Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 07.03.2019, 06.12.2018.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1567 **Ambirix-EMEA/H/C/000426/WS1567/0097** **Twinrix Adult-EMEA/H/C/000112/WS1567/0132** **Twinrix Paediatric-EMEA/H/C/000129/WS1567/0133** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 16.05.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1600/G **Aflunov-EMEA/H/C/002094/WS1600/0049/G** **Foclivia-EMEA/H/C/001208/WS1600/0044/G** Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 23.05.2019.	Request for supplementary information adopted with a specific timetable.
Hexacima-EMEA/H/C/002702/WS1575/0088/G **Hexaxim-EMEA/H/W/002495/WS1575/0093/G** **Hexyon-EMEA/H/C/002796/WS1575/0092/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus	

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

Adenuric - febuxostat - **EMEA/H/C/000777/II/0051** Menarini International Operations Luxembourg

S.A., Rapporteur: Andrea Laslop, “Update of section 5.1 of the SmPC in order to include the results of the clinical safety study CARES (TMX-67_301), to compare the cardiovascular outcomes of febuxostat and allopurinol in subjects with gout and cardiovascular comorbidities; this is a Multicenter, Randomized, Active-Control, Phase 3B Study. In addition, the Marketing authorisation holder (MAH) took the opportunity to provide a consolidated Module 2.7.6 in order to list all the synopsis of individual studies in a unique tabular format.” Request for Supplementary Information adopted on 28.03.2019, 13.12.2018, 04.10.2018.	
Bosulif - bosutinib - EMEA/H/C/002373/II/0037 Pfizer Europe MA EEIG, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, “Update of sections 4.6 and 5.3 of the SmPC based on final results from An Oral (Gavage) Study of the Effects of PF-05208763 on Pre- and Postnatal Development, Including Maternal Function in Rats listed as a category 3 study in the RMP. The Package leaflet is updated accordingly. The updated RMP version 4.5 has also been submitted.” Opinion adopted on 16.05.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Brilique - ticagrelor - EMEA/H/C/001241/II/0044 AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.4 of the SmPC in order to add a warning on Thrombotic Thrombocytopenic Purpura (TTP) and update of section 4.8 of the SmPC to include TTP as new adverse drug reaction with a frequency ‘unknown’, based on a safety review. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make some formatting corrections throughout the product information.”	
Brilique - ticagrelor - EMEA/H/C/001241/II/0045 AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, “Update of section 4.4 of the SmPC in order to add a new warning on interference with laboratories tests regarding platelet function tests to diagnose heparin induced	

thrombocytopenia (HIT) based on as safety review."	
Brinavess - vernakalant - EMEA/H/C/001215/II/0034 Correvio, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8 and 5.1 of the SmPC based on the final results from the non-interventional PASS SPECTRUM study, listed as a category 3 study in the RMP, in order to fulfil MEA 026.5; SPRECTRUM (6621-019) study is a prospective observational registry study to characterise normal conditions of use, dosing and safety following administration of vernakalant IV sterile concentrate." Request for Supplementary Information adopted on 16.05.2019, 14.02.2019.	Request for supplementary information adopted with a specific timetable.
Cetrotide - cetrorelix - EMEA/H/C/000233/II/0068 Merck Europe B.V., Rapporteur: Martina Weise, "Update of section 4.2 of the SmPC based on literature review to add an alternative option for the treatment initiation to start once the leading follicle(s) reach a size that could lead to premature LH (Luteinizing Hormone) surge and ovulation. The Package Leaflet (PL) is updated in accordance. Correction in section 3 of the PL to regarding the timing of ovulation induction. In addition, the Marketing authorisation holder (MAH) took the opportunity to delete the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.0." Request for Supplementary Information adopted on 28.02.2019, 18.10.2018.	
Cinryze - C1 esterase inhibitor (human) - EMEA/H/C/001207/II/0069 Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC following a company review of the safety data base. The PL is updated accordingly."	
Defitelio - defibrotide - EMEA/H/C/002393/II/0039, Orphan Gentium S.r.l., Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC to amend the mechanism of action with new data on non-clinical studies identified from published literature." Opinion adopted on 02.05.2019.	Positive Opinion adopted by consensus on 02.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Request for Supplementary Information adopted on 14.03.2019.

Eliquis - apixaban - EMEA/H/C/002148/II/0059

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.3, 4.4 and 4.5 of the SmPC based on the current European Society of Cardiology (ESC) guideline for direct oral anti-coagulants (DOACs) and the literature including the AXAFA-AFNET 5 study, a major investigator's sponsored trial with apixaban, in order to include an exception to the contraindicated concomitant treatment with any other anticoagulant agent for heparin co-administration during catheter ablation for atrial fibrillation. In addition, the Marketing authorisation holder (MAH) took the opportunity to clarify the wording in section 4.2 of the SmPC to include a reference to transesophageal echocardiogram (TEE) guided cardioversion." Request for Supplementary Information adopted on 28.02.2019.

EXJADE - deferasirox - EMEA/H/C/000670/II/0066

Novartis Europharm Limited, Rapporteur: Alexandre Moreau, "To update the Exjade SmPC (Section 5.1) to reflect the results of clinical study CICL670A2302 (TELESTO) with Exjade in patients with myelodysplatic syndrome (MDS)."

Eylea - aflibercept - EMEA/H/C/002392/II/0052

Bayer AG, Rapporteur: Alexandre Moreau, "Update of section 5.1 of the SmPC in order to reflect the final results from ALTAIR (SN17668) study; this is a randomized, open-label phase 4 study evaluating the efficacy and safety of repeated doses of intravitreal aflibercept with variable treatment intervals in Japanese subjects with neovascular age-related macular degeneration. In addition, the Marketing authorisation holder (MAH) took the opportunity to include minor editorial changes in section 5.1 of the SmPC."

Fasenra - benralizumab - EMEA/H/C/004433/II/0013

AstraZeneca AB, Rapporteur: Fátima Ventura, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect the final results from study D3250C00021 (BORA) listed as a category 3 in

the RMP; this is a randomised phase 3 study to evaluate the safety and tolerability of benralizumab in asthmatic adults and adolescents on inhaled corticosteroid plus long-acting β2 agnostic. In addition, section 4.2 of the SmPC is updated to reflect the extended PIP waiver age group" Request for Supplementary Information adopted on 11.04.2019, 14.02.2019.	
Firdapse - amifampridine - EMEA/H/C/001032/II/0060, Orphan BioMarin International Limited, Rapporteur: Kristina Dunder, "Update section 5.1 of the SmPC to include results from study LMS-003: a double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of amifampridine in patients with Lambert-Eaton Myasthenic Syndrome (LEMS)." Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 17.01.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Gilenya - fingolimod - EMEA/H/C/002202/II/0053 Novartis Europharm Limited, Rapporteur: Alexandre Moreau, "Type II (C.I.4): - to update section 4.4 of the SmPC (subsection 'Return of disease activity (rebound)' and subsection 'Stopping therapy') to add information to prescriber's on the timing of reported events and further recommendations on monitoring of patients. - to update section 4.6 of the SmPC to add a warning for women stopping treatment for the purpose of becoming pregnant and for pregnant women, and addition of a cross-reference to section 4.4 subsection 'Return of disease activity (rebound)'. - to update section 4.8 of the SmPC to add a new adverse reaction 'Severe exacerbation of disease after Gilenya discontinuation' with frequency 'Not known'. The package leaflet is updated accordingly." Request for Supplementary Information adopted on 07.03.2019.	
Humira - adalimumab - EMEA/H/C/000481/II/0187 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC to reflect results from the final	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

report from study M11-327: A Multicenter Open-Label Study of the Long-term Safety and Efficacy of the Human Anti-TNF Monoclonal Antibody Adalimumab in Subjects with Non-infectious Intermediate Uveitis, Posterior Uveitis, or Panuveitis; listed as a category 3 study in the RMP. Furthermore editorial changes and a brief description of the study design were also added to section 5.1 of the SmPC." Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 14.03.2019.	
IBRANCE - palbociclib - EMEA/H/C/003853/II/0016 Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to update with information following submission of the final results from the pivotal Study A5481023 "A double blind, Phase 3 trial of fulvestrant with or without palbociclib in pre- and postmenopausal women with hormone receptor positive, HER2-negative metastatic breast cancer that progressed on prior endocrine therapy" listed as a recommendation at the time of initial MA." Request for Supplementary Information adopted on 02.05.2019, 31.01.2019.	Request for supplementary information adopted with a specific timetable.
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0048, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, "Update of section 4.4 of the SmPC Special warnings and precautions for use in order to add a warning under 'bleeding-related events' based on the final clinical study reports results to evaluate the risks of major hemorrhage with the administration of IMBRUVICA (ibrutinib)). The study is listed in section III.2 additional Pharmacovigilance Activities A non-interventional PASS clinical study report (CSR) for serious haemorrhage in the RMP. In addition, the Marketing authorisation holder (MAH) took the opportunity to include a minor edit in the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 14.03.2019.	
Increlex - mecasermin - EMEA/H/C/000704/II/0059 Ipsen Pharma, Rapporteur: Outi Mäki-Ikola,	Request for supplementary information adopted with a specific timetable.

"Submission of the final analysis for the Category 3, Additional Pharmacovigilance Activity MEA 020.3, on Lowest Effective Dose for mecasermin. No changes to the SmPC or Patient Leaflet are proposed as part of this final analysis on Lowest Effective Dose of mecasermin." Request for Supplementary Information adopted on 16.05.2019.	
Kanuma - sebelipase alfa - EMEA/H/C/004004/II/0019, Orphan Alexion Europe SAS, Rapporteur: Bart Van der Schueren, "Submission of the final report from study LAL-CL04, in order to fulfil this recommendation (REC). This is an open label multicentre extension study to evaluate the long-term safety, tolerability and efficacy of sebelipase alfa in adult subjects with liver dysfunction due to lysosomal acid lipase deficiency who previously received treatment in study LAL-CL01." Request for Supplementary Information adopted on 21.03.2019.	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0071 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "To update sections 4.2, 4.8, 5.1 and 5.2 of the SmPC based on interim results from study KEYNOTE-051; this is a ongoing Phase I/II, single-arm study to evaluate the PK, pharmacodynamics, toxicity, safety, and anti-tumour activity of pembrolizumab in paediatric participants (Measure 2 of PIP01). Additionally, the results of study Study PD018 / PA-0064; evaluation of expression of PD-1, PD-L1, and PD-L2 in archival paediatric tumour tissues, were submitted (Measure 1 of PIP01)." Request for Supplementary Information adopted on 02.05.2019.	Request for supplementary information adopted with a specific timetable.
Kolbam - cholic acid - EMEA/H/C/002081/II/0028, Orphan Retrophin Europe Ltd, Rapporteur: Constantinos Markopoulos, "Submission of the final report from study CAC-002-01, listed as a category 3 study in the RMP. This is a Phase 3, open-label, single arm, non-randomized study investigating cholic acid in the treatment of subjects with inborn errors of bile acid metabolism. The study was a continuation study that included eligible subjects who had previously received	

cholic acid in studies CAC-91-10-10 or CAC-001-01 as well as newly diagnosed subjects." Request for Supplementary Information adopted on 28.02.2019.	
Kovaltry - octocog alfa - EMEA/H/C/003825/II/0022 Bayer AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of the RMP version 2.0 in line with the GVP revision 2 and the new RMP template." Opinion adopted on 16.05.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Lynparza - olaparib - EMEA/H/C/003726/II/0028 AstraZeneca AB, Rapporteur: Alexandre Moreau, "Update of section 5.2 of the SmPC in order to include information on the in vitro effect of olaparib on UGT enzymes based on results from in vitro assays. In addition, the MAH is proposing to change the due date for submission of the final CSR of the phase IV, open label, single arm study (D0816C00012/ORZORA) in patients with relapsed platinum sensitive ovarian cancer who are in response following platinum-based chemotherapy and who carry loss of function germline or somatic BRCA mutations, listed as a PAES in the Annex II." Opinion adopted on 16.05.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Mekinist - trametinib - EMEA/H/C/002643/II/0033 Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.4 and 4.8 of the SmPC to introduce a warning and new ADRs related to severe cutaneous adverse reactions (SCARs) as per request in the outcome of EMEA/H/C/PSUSA/00010084/201808 for Dabrafenib. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some editorial changes in sections 4.4, 4.6 and 4.8 of the SmPC." Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 14.03.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Menveo - meningococcal group a, c, w135 and y conjugate vaccine - EMEA/H/C/001095/II/0083 GSK Vaccines S.r.l, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.5 of the SmPC in	

order to include reference to concomitant administration with Meningococcal group B vaccine, based on results from study V72_56, previously submitted and assessed as part of procedure P46/035 for Menveo. The Package Leaflet (Section 2) is updated accordingly." Request for Supplementary Information adopted on 28.03.2019.	
Natpar - parathyroid hormone - EMEA/H/C/003861/II/0018/G, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Bart Van der Schueren, "Update of sections 4.4 and 4.8 of the SmPC in order to include information related to the potential risk of hypersensitivity reactions based on the review of cumulative postmarketing safety data, as well as the postmarketing cases of hypersensitivity with a frequency of unknown. Update of section 4.4 of the SmPC in order to include information related to the potential risk of seizure due to severe hypocalcemia, to add a warning based on the review of cumulative postmarketing safety data. The Package Leaflet has been revised accordingly." Request for Supplementary Information adopted on 23.05.2019.	Request for supplementary information adopted with a specific timetable.
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0146 CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC in order to add decreased neutrophil count to the list of adverse reactions with the frequency unknown. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to sections 4.2, 4.4, 4.8 and 5.1 of the SmPC and to the Package Leaflet." Opinion adopted on 02.05.2019.	Positive Opinion adopted by consensus on 02.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0147 CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of section 2 of the SmPC in order to update the IgG subclass values according to performed analyses. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

local representatives for Bulgaria in the Package Leaflet." Opinion adopted on 16.05.2019.	
Repatha - evolocumab - EMEA/H/C/003766/II/0033 Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, "Update of section 4.8 of the SmPC in order to update the safety information with regards to the adverse reaction "Influenza-like illness" with a frequency of Uncommon following the assessment of influenza-like illness with evolocumab in both the clinical database and postmarketing database. The Package Leaflet Section 4 was updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement changes to the package leaflet Section 2 subsequent to the revised Annex to the EC guideline on excipients in the labelling (EMA/CHMP/302620/2017) to update the wording for sodium."	
Spinraza - nusinersen - EMEA/H/C/004312/II/0013/G, Orphan Biogen Netherlands B.V., Rapporteur: Bruno Sepodes, "C1.3.b (Type II): to update sections 4.8 and 5.1 of the SmPC following assessment of the final CSR for Study CS3A (Procedure number: EMA/H/C/4312/P46/007). Study CS3A was a phase 2 open-label multiple dose study to Assess the Efficacy, Safety, Tolerability, and Pharmacokinetics of Multiple Doses of Nusinersen (ISIS 396443) Delivered Intrathecally to Patients with Infantile-Onset Spinal Muscular Atrophy. 3xC.I.4 (Type II): to update sections 4.8 and 5.1 of the SmPC to reflect safety, efficacy, and immunogenicity data from the interim analyses of studies SM201 and CS11, and results of SM202, Part 1. SM202 (EMBRACE) is a 2-part Phase 2 study in subjects with infantile- and later-onset SMA not eligible to participate in Studies CS3B or CS4. CS11 (SHINE) is an on-going open label extension Phase 3 study for subjects with infantile and later onset SMA who previously participated in investigational studies of nusinersen, including Studies CS3A, CS12, CS3B, and CS4 and SM202. SM201 (NURTURE) is an on-going multicentre, Phase 2, open label study in infants with genetically diagnosed, presymptomatic SMA."	Positive Opinion adopted by consensus on 02.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 02.05.2019.	
Symtuza - darunavir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004391/II/0017/G Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update the safety information based on week-96 results from studies TMC114FD2HTX3001 (AMBER) "A Phase 3, randomized, active-controlled, double-blind study to evaluate efficacy and safety of D/C/F/TAF once daily fixed-dose combination regimen versus a regimen consisting of DRV/COBI FDC co-administered with FTC/TDF FDC in ARV treatment-naïve HIV-1 infected subjects", and study TMC114IFD3013 (EMERALD)) "A Phase 3, randomized, active-controlled, open-label study to evaluate switching to a D/C/F/TAF once-daily single-tablet regimen versus continuing the current regimen consisting of a boosted protease inhibitor combined with FTC/TDF in virologically-suppressed, HIV-1 infected subjects.", both listed as category 3 studies in the RMP. The Package Leaflet is updated accordingly. The RMP version 5.0 (in version 2 of the RMP template) has also been submitted to reflect the study results and revise due dates for category 3 studies GS-US-311-1717 and GS-US-292-0109. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.2 of the SmPC and Package Leaflet to include advice in the event of vomiting in line with the approved Genvoya SmPC, make minor editorial changes in the SmPC; as well as to update the list of local representatives in the Package Leaflet in line with the latest QRD template version 10.0."	
Tafinlar - dabrafenib - EMEA/H/C/002604/II/0038 Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC in order to update information on fertility, pregnancy and lactation after routine review of the company core data sheet, taking into consideration the original source documentation from GSK (former MAH), current scientific knowledge, published literature, as well as health authority and working group guidelines. The	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Package leaflet is being updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some editorial changes in section 4.4 and 4.8 of the SmPC and in section 4 of the package leaflet." Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 14.03.2019.	
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0023 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to include new ADRs identified in IMmotion150 and IMmotion151 studies. The revision of the list of ADRs is supported by a drug safety report reflecting the ADRs in the updated pool of patients for monotherapy (n=3178) and combination therapy (n=1345). The Package Leaflet is updated accordingly." Opinion adopted on 02.05.2019.	Positive Opinion adopted by consensus on 02.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tremfya - guselkumab - EMEA/H/C/004271/II/0010 Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, "Update of sections 4.8 and 5.1 of the SmPC to add the long term 3-year clinical data from the two ongoing clinical studies CNTO1959PSO3001 (VOYAGE 1) and CNTO1959PSO3002 (VOYAGE 2) in subjects with plaque psoriasis." Request for Supplementary Information adopted on 02.05.2019, 14.03.2019.	Request for supplementary information adopted with a specific timetable.
Veltassa - patiromer - EMEA/H/C/004180/II/0007 Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Jayne Crowe, "Update of sections 4.2, 4.5 and 5.1 of the SmPC to reflect the results of study RLY5016-401; an Open-Label, Randomized, Parallel Group Phase 4 Study of the Efficacy and Safety of Patiromer for Oral Suspension With or Without Food for the Treatment of Hyperkalemia (TOURMALINE). The PL has been updated accordingly." Opinion adopted on 02.05.2019. Request for Supplementary Information adopted on 14.03.2019, 17.01.2019.	Positive Opinion adopted by consensus on 02.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Verzenios - abemaciclib - EMEA/H/C/004302/II/0003 Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC in	

order to add a criterion for discontinuing abemaciclib in the event of specific hepatic changes based on available safety data. In addition, the Marketing authorisation holder (MAH) took the opportunity to make editorial changes to section 5.1 of the SmPC."	
XALKORI - crizotinib - EMEA/H/C/002489/II/0062 Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, "Submission of the review of the PK profile of the crizotinib lactam metabolite, PF-06260182 in subjects or patients treated with single agent crizotinib, and discussion of the clinical relevance of these findings derived from the following reports: A8081001, A8081002, A8081005, A8081006, A8081007, A8081012, A8081014 and A8081020, in order to fulfill a CHMP recommendation. Based on the data discussed as part of this variation, no update of the SmPC is warranted."	
Xarelto - rivaroxaban - EMEA/H/C/000944/II/0064 Bayer AG, Rapporteur: Kristina Dunder, "Submission of the final report from an interventional phase III study (COMMANDER HF, 2.5 mg rivaroxaban compared to placebo)." Request for Supplementary Information adopted on 16.05.2019.	Request for supplementary information adopted with a specific timetable.
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 28.03.2019, 20.09.2018.	
WS1566 **Biktarvy-EMEA/H/C/004449/WS1566/0017** **Descovy-EMEA/H/C/004094/WS1566/**	Positive Opinion adopted by consensus on 02.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

0041 **Genvoya-EMEA/H/C/004042/WS1566/0061** **Odefsey-EMEA/H/C/004156/WS1566/0041** **Vemlidy-EMEA/H/C/004169/WS1566/0019** Gilead Sciences Ireland UC, Lead Rapporteur: Bruno Sepodes, "Update of section 4.8 of the SmPC following a safety review by the MAH assessing the clinical evidence of a causal association between tenofovir alafenamide-containing products and two adverse events, angioedema and urticaria. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement minor linguistic amendments and editorial changes to the Odefsey and Vemlidy products information." Opinion adopted on 02.05.2019.	recommendation.
WS1588 **Aluvia-EMEA/H/W/000764/WS1588/0109** **Kaletra-EMEA/H/C/000368/WS1588/0177** **Norvir-EMEA/H/C/000127/WS1588/0154** AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.3 and 4.5 of the SmPC in order to include information on the contraindication with neratinib and interactions with abemaciclib, neratinib, glecaprevir/pibrentasvir. In addition, the Worksharing Applicant (WSA) took the opportunity to update section 4.5 of the Kaletra and Aluvia SmPCs to add information on the interaction of lopinavir/ritonavir with sofosbuvir/velpatasvir/voxilaprevir. The Package Leaflets are updated accordingly."	
WS1605 **Lyrica-EMEA/H/C/000546/WS1605/0097** **Pregabalin** **Pfizer-EMEA/H/C/003880/WS1605/0027** Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, "Addition in the SmPC section 4.5 of the wording on the risk of death, including in patients who are substance abusers." Request for Supplementary Information adopted on 23.05.2019.	Request for supplementary information adopted with a specific timetable.
WS1607 **Kisplyx-EMEA/H/C/004224/WS1607/0023** **Lenvima-EMEA/H/C/003727/WS1607/**	Request for supplementary information adopted with a specific timetable.

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Eisai GmbH, Lead Rapporteur: Bart Van der Schueren, “Update of section 5.2 of the SmPC in order to include information about the results of Study E7080-A001- 010, “A Multicenter Phase 0 Study in Healthy Subjects and Subjects with Either Hepatic or Renal Impairment to Obtain Plasma for Assessment in Vitro Lenvatinib Protein Binding”.”
Request for Supplementary Information adopted on 23.05.2019.

B.5.3. CHMP-PRAC assessed procedures

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 28.02.2019, 20.09.2018.

Avonex - interferon beta-1a - EMEA/H/C/000102/II/0182/G
Biogen Netherlands B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, “2x type II (C.I.4):
1) Update of sections 4.3 and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054).
2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding

following a review of studies, case reports and literature articles.
The Package leaflet has been updated accordingly.
This submission fulfils MEA 87.2 and 84."
Request for Supplementary Information adopted on 28.02.2019.

Benlysta - belimumab - EMEA/H/C/002015/II/0065

GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning on suicidality and depression based on interim results from study BEL115467 listed in the Annex II; this is a Randomized, Double-Blind, Placebo-Controlled 52-Week Study to Assess Adverse Events of Special Interest in Adults with Active, Autoantibody-Positive Systemic Lupus Erythematosus Receiving Belimumab; the Package Leaflet is updated accordingly. The RMP version 30 has also been submitted. In addition, the Marketing authorisation holder (MAH) is proposing a DHPC letter and a communication plan."
Request for Supplementary Information adopted on 28.03.2019.

Betaferon - interferon beta-1b - EMEA/H/C/000081/II/0124/G

Bayer AG, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "2x type II (C.I.4):
1) Update of sections 4.3 and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054).
2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles.
The Package leaflet has been updated accordingly.
This submission fulfils MEA 024.2 and 21.
An updated RMP version 4.1 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes' and an update of the EU-RMP template (rev.2)."

Request for Supplementary Information adopted on 28.02.2019.	
Champix - varenicline - EMEA/H/C/000699/II/0074 Pfizer Europe MA EEIG, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, “Update of sections 4.2, 5.1 and 5.2 of the SmPC to reflect results of the paediatric study A3051073 (MEA 047) " A Phase 4, Twelve-Week, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Dose-Ranging Study With Follow-Up, Evaluating The Safety And Efficacy Of Varenicline For Smoking Cessation In Healthy Adolescent Smokers." The PL is updated accordingly. RMP version 11.1 was submitted.” Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 14.03.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Darzalex - daratumumab - EMEA/H/C/004077/II/0027, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Update of sections 4.4 and 4.8 of the SmPC to add new safety information on the recently identified risk of Hepatitis B reactivation (HBV). Consequently the PIL is proposed to be updated. A revision of the RMP (v. 5) is included in the submission. The MAH also proposes a DHPC to inform prescribers on the newly identified risk.”	
Extavia - interferon beta-1b - EMEA/H/C/000933/II/0096/G Novartis Europharm Limited, Informed Consent of Betaferon, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, “2x type II (C.I.4): 1) Update of sections 4.3 and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054). 2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles. The Package leaflet has been updated accordingly.	

This submission fulfils MEA 022.2 and 019. An updated RMP version 4.1 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes' and an update of the EU-RMP template (rev. 2)." Request for Supplementary Information adopted on 28.02.2019.	
Fasenra - benralizumab - EMEA/H/C/004433/II/0014/G AstraZeneca AB, Rapporteur: Fátima Ventura, PRAC Rapporteur: David Olsen, "B.IV.1.c – To add an autoinjector delivery device, Fasenra 30 mg solution for injection in pre-filled pen. C.I.4 – Update of sections 4.2, 6.4, 6.5, 6.6 of the SmPC in order to update the information for self-administration for Fasenra 30 mg solution for injection in pre-filled syringe. The labelling and the package leaflet are updated accordingly. In addition, the RMP (version 2.0) is updated to reflect the information about the new presentation, to include additional information about completed studies (ALIZE, GREGALE, AMES, GREGO), to add updated exposure data post MAA approval, and to reflect additional details on the post-authorisation safety studies (Pregnancy registry (D3250R00026) and Malignancy Post Authorization Safety Study (D3250R00042)). Furthermore, the RMP is revised in line with the RMP template (GVP Module V rev.2)." Request for Supplementary Information adopted on 28.02.2019.	
Ferriprox - deferiprone - EMEA/H/C/000236/II/0128 Apotex B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update section 4.4 of the SmPC and the patient/carer reminder card in order to update and change the recommended frequency of ANC monitoring throughout Ferriprox treatment from a weekly basis to every week for the first six months of Ferriprox therapy, once every two weeks after six months of Ferriprox therapy, and to monthly after one year of therapy. The package leaflet has been updated accordingly. The RMP version 13.2 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update minor linguistic amendments in the HU and MT product information."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 16.05.2019, 29.11.2018.	
Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0034, Orphan Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final results of the pivotal study BO21005/GOYA to address the additional pharmacovigilance activities required in the EU RMP. Consequently the updated RMP version 5.0 has been submitted." Request for Supplementary Information adopted on 16.05.2019.	Request for supplementary information adopted with a specific timetable.
Jakavi - ruxolitinib - EMEA/H/C/002464/II/0040 Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "Update of section 5.3 of the SmPC based on final results from studies from the juvenile toxicity studies 1570143 (dose range finding juvenile study) and 157014 (juvenile development study). An updated RMP version 10 was submitted accordingly. The RMP was also updated in line with the template of the GVP Module V Rev.2 (EMA/838713/2011 Rev 2). Finally, the RMP changes requested by the PRAC in the latest PSUR (PSUSA-10015-201802) have been also implemented in this RMP. In addition, the MAH has taken the opportunity to align this RMP to the revised RMP template and to the GVP Module V Rev.2 (EMA/838713/2011 Rev 2)." Opinion adopted on 16.05.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Jakavi - ruxolitinib - EMEA/H/C/002464/II/0041 Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "Update of section 4.5 of the SmPC based on the final results of a Drug-Drug Interaction (DDI) study INC4242A2106, fulfilling a Post-Authorisation Measure (MEA 0016) requested as part of a previous type II variation (Procedure No. EMEA/H/C/002464/II/0025). The study INC4242A2106 evaluated the effect of multiple doses of fluconazole on the pharmacokinetics of ruxolitinib administered as a single dose in an open-label, crossover study in healthy subjects. An updated RMP version 10 was submitted accordingly. Furthermore, the RMP	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

template was adapted to revision 2 in line with GVP Module V Rev.2 (EMA/838713/2011 Rev 2).” Opinion adopted on 16.05.2019.	
Mimpara - cinacalcet - EMEA/H/C/000570/II/0062/G Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “Update of section 4.2 of the SmPC to provide additional information with reference to switching from etelcalcetide to Mimpara (cinacalcet), upon request by PRAC following the assessment of the etelcalcetide PSUR (dated 14 June 2018). Further, the term ‘silica, dental type’ has been replaced by ‘Amorphous silicon dioxide’ in SmPC section 6.1. An updated RMP version 9.0 was provided as part of the application in order to align the RMP with the GVP Module V (template Rev 2) with consequential reclassification of existing safety concerns.” Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 14.03.2019, 29.11.2018.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
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: 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"."
Request for Supplementary Information adopted on 28.02.2019, 15.11.2018.

Nucala - mepolizumab - EMEA/H/C/003860/II/0021

GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information based on final results from Study 200363 Part B and two open label extension (OLE) studies (201312 and MEA115666) listed as category 3 studies in the RMP. These are interventional post-authorisation safety studies conducted to assess the long-term (52 weeks) safety and tolerability of mepolizumab when administered subcutaneously to patients aged 6 to 11 years old with severe eosinophilic asthma (study 200363 Part B), to describe the long-term safety profile of mepolizumab (MEA115666), and to provide extended treatment to subjects from study MEA115661 and further describe long-term safety in these subjects (study 201312).
The RMP (version 5.0) has also been submitted to reflect the completion of the studies and to be aligned with GVP Module V, rev.2 template."
Request for Supplementary Information adopted on 14.03.2019.

Pelgraz - pegfilgrastim - EMEA/H/C/003961/II/0005

Accord Healthcare S.L.U., Rapporteur: Sol Ruiz, PRAC Rapporteur: Menno van der Elst

Plegridy - peginterferon beta-1a - EMEA/H/C/002827/II/0052/G

Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ulla Wändel Liminga, "2x type II (C.I.4):
1) Update of section 4.3, and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054).

2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles.
The Package leaflet has been updated accordingly.
This submission fulfils MEA 8.2 and 002.
An updated RMP version 4.1 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes' and an update of the EU-RMP template (rev. 2)."
Request for Supplementary Information adopted on 28.02.2019.

PREVYMIS - letermovir - EMEA/H/C/004536/II/0011, Orphan
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.4 and 4.5 of the SmPC in order to update the safety information following the final results of a clinical pharmacology trial entitled "A Study to Assess the Effect of Rifampin on the Single-Dose and Steady-State Pharmacokinetics of MK-8228 in Healthy Adult Subjects" (MK-8228-038) listed as a category 3 study in the RMP; the Package Leaflet is updated accordingly. The RMP version 2.1 has also been submitted."

Rebif - interferon beta-1a - EMEA/H/C/000136/II/0137/G
Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "2x type II (C.I.4):
1) Update of sections 4.3, 4.6 and 5.3 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054).
2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles.
The Package leaflet has been updated accordingly.
This submission fulfils MEA 43.2 and 39.
An updated RMP version 10.0 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes'

and an update of the EU-RMP template (rev.2)." Request for Supplementary Information adopted on 28.02.2019.

ReFacto AF - moroctocog alfa - EMEA/H/C/000232/II/0151

Pfizer Europe MA EEIG, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, "To update sections 4.8 Undesirable effects and 5.1 Pharmacodynamic effects of the SmPC based on the final results from study 3082B2-313 (B1831001 - "An Open-Label Study to Evaluate Prophylaxis Treatment, and to Characterize the Efficacy, Safety, and Pharmacokinetics of B-Domain Deleted Recombinant Factor VIII Albumin Free (Moroctocog Alfa [AF_CC]) in Children with Hemophilia A") listed as an additional pharmacovigilance activity in the Risk Management Plan (RMP; MEA 116). The RMP version 13.0 has also been submitted.
In addition, the SmPC is being brought in line with the revised guidelines on core SmPC for human plasma derived and recombinant coagulation factor VIII products (Revision 3) in sections 4.2 Posology and Method of Administration, 4.4 Special warnings and special precautions for use, 4.8 Undesirable effects and 5.1 Pharmacodynamic effects."

Tecentriq - atezolizumab - EMEA/H/C/004143/II/0024

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add a warning regarding the risk of immune-related myositis identified during a comprehensive analysis of patients treated with Tecentriq. The additional risk minimisations in Annex 2D are also updated. Furthermore a DHPC is being proposed to inform about the risk of immune-related myositis. The Package Leaflet is updated accordingly. The RMP version 11.0 has also been submitted."

Venclyxto - venetoclax - EMEA/H/C/004106/II/0020, Orphan

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, PRAC Rapporteur: Eva Jirsová, "Update of sections 4.2 and 5.2 of the SmPC in order to include that no dose adjustment is recommended in patients with mild

or moderate hepatic impairment; a 50% dose reduction of ventoclax is recommended based on final results from study M15-342 (A Study to Evaluate the Safety and Pharmacokinetics of a Single Dose of Ventoclax in Female Subjects with Mild, Moderate, or Severe Hepatic Impairment) listed as a category 3 study in the RMP; the Package Leaflet is updated accordingly. The RMP version 3.4 has also been submitted." Request for Supplementary Information adopted on 28.02.2019.	
Xiapex - collagenase clostridium histolyticum - EMEA/H/C/002048/II/0107 Swedish Orphan Biovitrum AB (publ), Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, "Update of sections 4.4 and 5.1 of the SmPC to update the efficacy and safety information following the final results from study AUX-CC-810: Long-term Safety, Curvature Deformity, Characterization, and Immunogenicity over time in Subjects Previously Treated with AA4500 for Peyronie's Disease in Studies AUX-CC-802, AUX-CC-803, AUC-X-CC-804, and AUX-CC-806; listed as a category 3 study in the RMP. The RMP version 14.1 has also been submitted. In addition, the Marketing authorisation holder took the opportunity to introduce minor editorial changes to SmPC and Package Leaflet." Request for Supplementary Information adopted on 28.03.2019.	
Yervoy - ipilimumab - EMEA/H/C/002213/II/0063 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4 and 4.8 of the SmPC and of annex II in order to add safety information regarding Graft Versus Host Disease (GVHD) in allogeneic hematopoietic stem cell transplant (HSCT) recipients after treatment with ipilimumab. The update is based on a review of post-marketing data. The Package Leaflet and the RMP (version 25.0) is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some editorial changes in the PI and RMP and to include some changes in the RMP due to previous procedures." Request for Supplementary Information adopted	

on 17.01.2019.	
WS1490 **IKERVIS-EMEA/H/C/002066/WS1490/0014** **Verkazia-EMEA/H/C/004411/WS1490/0001** Santen Oy, Lead Rapporteur: Peter Kiely, Lead PRAC Rapporteur: Jan Neuhauser, "Submission of an updated RMP version 7.0 in order to implement RMP revision 2 template, as a consequence safety concerns have been updated: all safety concerns were moved from important safety concerns to the new section of Risks not considered important for inclusion in the list of safety concerns in the RMP. The milestones for VERKAZIA PASS have also been updated. In addition, the MAH is proposing to align IKERVIS SmPC section 4.4 on concomitant therapy and effects on immune system with VERKAZIA SmPC in order to harmonize the routine risk minimization measures for both products. The MAH took this opportunity to implement the latest QRD template and the safety features for IKERVIS." Request for Supplementary Information adopted on 11.04.2019, 14.02.2019.	
WS1582 **Actraphane-EMEA/H/C/000427/WS1582/0076** **Actrapid-EMEA/H/C/000424/WS1582/0070** **Insulatard-EMEA/H/C/000441/WS1582/0073** **Mixtard-EMEA/H/C/000428/WS1582/0077** **Protaphane-EMEA/H/C/000442/WS1582/0072** Novo Nordisk A/S, Lead Rapporteur: Sinan B. Sarac, Lead PRAC Rapporteur: Hans Christian Siersted, "To update the Human Insulin RMP to version 3.0 in order to reclassify the risk of 'Medication errors' (including human error-related medication errors) from an important potential risk to an important identified risk following a Pharmacovigilance Risk Assessment Committee (PRAC) request (EMEA/H/C/PSUSA/00001753/201710) and in accordance with the Good practice guide on risk minimisation and prevention of medication	Request for supplementary information adopted with a specific timetable.

errors, issued by the PRAC in 2015. Furthermore, in accordance with the updated GVP Module V guidance on RMPs, the Worksharing Applicant (WSA) proposed to remove this risk as it is fully characterised and managed through routine pharmacovigilance and no additional pharmacovigilance activities or additional risk minimisation measures are planned or being currently undertaken. Information regarding the avoidance of accidental mix-ups/medication errors is included in the PIL for the concerned products. In consequence, section 4.4 of the SmPC was updated in order to add a warning on accidental mix-ups/medication. Additionally, the WSA took the opportunity include minor updates to Annex IIIA to bring the PI in line with the latest QRD template version." Request for Supplementary Information adopted on 16.05.2019.	
WS1599 **Rixathon-EMEA/H/C/003903/WS1599/0020** **Riximyo-EMEA/H/C/004729/WS1599/0020** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus, Lead PRAC Rapporteur: Anette Kirstine Stark, "Submission of the final report from study (GP13-301) listed as a category 3 study in the RMP. This is a randomized, controlled double-blind Phase III trial to compare the efficacy, safety and pharmacokinetics of GP2013 plus cyclophosphamide, vincristine, prednisone vs. MabThera plus cyclophosphamide, vincristine, prednisone, followed by GP2013 or MabThera maintenance therapy in patients with previously untreated advanced stage follicular lymphoma. The RMP version 4.0 has also been submitted." Request for Supplementary Information adopted on 16.05.2019.	Request for supplementary information adopted with a specific timetable.

B.5.4. PRAC assessed procedures

PRAC Led **Bydureon - exenatide - EMEA/H/C/002020/II/0059** AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final	Request for supplementary information adopted with a specific timetable.

CSR for Study H80-MC-B016; a modified Prescription-Event Monitoring Program (Modified PEM) to be conducted in the UK, enrolling patients with Type 2 diabetes mellitus, to quantify the incidence of acute pancreatitis in the first 12 months after initiating treatment with prescription exenatide once weekly. An updated RMP version 33 was provided as part of the application. The provision of the final CSR addresses Post-authorisation Measure MEA 010.5." Request for Supplementary Information adopted on 16.05.2019.	
PRAC Led **Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0074/G** UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from studies (RA0021 and RA005) listed as a category 3 studies in the RMP. Study RA0021 (ARTIS registry) is to provide short- and long-term safety data from the use of certolizumab pegol (CZP) in Sweden for rheumatoid arthritis (RA) patients. Study RA005 (NBD registry) is to obtain safety and outcome data on RA patients receiving CZP and other RA treatments. In addition, the MAH submitted interim results for two ongoing registries studies (RA0020/RABBIT and RA0022/BSRBR). Study RA0020/RABBIT is a German long-term observation of biologics/ DMARD in RA. Study RA0022/BSRBR is a longitudinal observational study of patients with RA treated with biologic agents, and prospective surveillance study for adverse events." Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 17.01.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Firazyr - icatibant - EMEA/H/C/000899/II/0047, Orphan** Shire Pharmaceuticals Ireland Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Update of Risk Management Plan (RMP) in order to reflect the finalisation of the paediatric study HGT-FIR-086, update the main safety concerns following results of the paediatric study HGT-FIR-086 and remove study	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

HGT-FIR-086 as an additional PV activity. In addition the RMP was reformatted to comply with the requirements of the new EU RMP template. The requested variation proposed amendments to the Risk Management Plan (RMP).” Opinion adopted on 16.05.2019.	
PRAC Led **Forsteo - teriparatide - EMEA/H/C/000425/II/0050/G** Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Alexandre Moreau, “Submission of the final study reports of the European Union (EU) components of two post-authorisation safety studies (PASS); Study B3DMC-GHBX(2.2) and Study B3D-MC-GHBX(2.3b) both US population-based comparative cohort studies undertaken to evaluate a potential association between teriparatide and adult Osteosarcoma. An updated RMP version 7.0 was submitted as part of the application.” Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 14.02.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Gardasil - human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) - EMEA/H/C/000703/II/0081** MSD Vaccins, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, “Update of the RMP to version 14.0 to update the list of safety concerns by removing the important identified risks syncope with fall resulting in injury, the important potential risks: viral type replacement and convulsion, and the missing information: immunogenicity, unanticipated safety signals and long-term safety, and in order to incorporate information from completed category 3 post-approval measure and scientific information on the safety profile of the qHPV vaccine.” Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 14.03.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Hemangiol - propranolol - EMEA/H/C/002621/II/0019**	Request for supplementary information adopted with a specific timetable.

PIERRE FABRE DERMATOLOGIE, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, “Update of Package Leaflet in order to strengthen the warning on Hypoglycemia and Bronchospasm following completion of Drug Utilisation Study (DUS) performed in Germany and France to evaluate off-label use and effectiveness of RMM in a real-life clinical setting (MEA 002). In additions editorial changes has been introduced in section 4.4 of the SmPC as well as changes in the PL in accordance with QRD template 10.0. RMP version 3.1 has been submitted in order to updates the additional RMMs as a consequence of the results of the DUS.” Request for Supplementary Information adopted on 16.05.2019, 14.02.2019.	
PRAC Led **Keytruda - pembrolizumab - EMEA/H/C/003820/II/0068** Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “C.I.11: Submission of an updated RMP version 23.1 in order to discuss the effectiveness of the educational materials put in place for Keytruda at the time of the initial marketing authorization and to provide a proposal to update these materials as well as to revise the safety specification as requested by PRAC during PSUSA/00010403/2018 procedure.” Request for Supplementary Information adopted on 16.05.2019, 14.03.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Neuraceq - florbetaben (18F) - EMEA/H/C/002553/II/0028** Life Radiopharma Berlin GmbH, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, “Submission of the final report from non-interventional PASS study FBB-01_02_13 listed as a category 3 study in the RMP. This is a prospective observational study to assess effectiveness of the training and risk minimisation measures recommended for the usage of the diagnostic agent NeuraCeq in the post-authorisation clinical situation. The RMP version 3.9 has also been submitted.”	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 16.05.2019.	
PRAC Led **ProQuad - measles, mumps, rubella and varicella vaccine (live) - EMEA/H/C/000622/II/0134** MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP (version 6.1) in order to adhere to Version 2 of the RMP template. As a consequence, the following changes are carried out: - Removal of the important identified risks febrile seizure, fever, measles-like rash, and thrombocytopenia and the addition of disseminated disease caused by Oka/Merck vaccine virus strain. - The important potential risks varicella-like or herpes zoster-like rashes, potential central nervous system events, potential transmission of varicella vaccine virus strain, exposure of immunocompromised individuals, hypersensitivity including anaphylaxis and injection-site reactions are also removed. - Additionally, secondary transmission of Oka/Merck vaccine virus strain in susceptible high-risk individuals leading to severe clinical consequences is included. - The important missing information 'categories exposure during pregnancy' and 'safety and immunogenicity in patients less than 9 months' of age is also removed." Request for Supplementary Information adopted on 16.05.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Sutent - sunitinib - EMEA/H/C/000687/II/0073** Pfizer Europe MA EEIG, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, "C.I.11: Submission of an updated RMP version 17 in order to review the list of safety concerns to make it more risk proportionate based on any available safety data. The updates are in line with the new GVP Module V (Rev 2) guidelines and new RMP template." Request for Supplementary Information adopted on 16.05.2019, 17.01.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led	Request for supplementary information adopted

Vectibix - panitumumab - EMEA/H/C/000741/II/0093 Amgen Europe B.V., Rapporteur: Bjorg Bolstad, PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Bjorg Bolstad, "Submission of RMP version 23 for panitumumab to align the important identified and potential risks and missing information with the EMA guideline on Good Pharmacovigilance Practices Module V (Rev. 2). As a result Annex II has been updated. The MAH is taking the opportunity to update sections 4.2 and 4.4 to include the table on dose modification previously located in the section 4.4. The section 4.4 is also updated to implement the latest excipient guideline recommendation on sodium content. In addition, minor corrections are introduced in the section 4.8 of the SmPC and in the list of the local representatives." Request for Supplementary Information adopted on 16.05.2019.	with a specific timetable.
PRAC Led **Votrient - pazopanib - EMEA/H/C/001141/II/0054** Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 17.0 in order to postpone CSR submission for "COMPARZ" study and its substudy, to reflect PRAC recommendations for additional assessments of some risks, to revise the list of safety concerns, and to adapt to GVP template." Request for Supplementary Information adopted on 16.05.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Zydelig - idelalisib - EMEA/H/C/003843/II/0046** Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the clinical study report for study GS-EU-313-4226, A Cross-Sectional Post-Authorization Safety Study to Assess Healthcare Provider Awareness of Risks Associated with Zydelig in the European Union; this is a category 3 PASS study to assess the effectiveness of additional risk minimization measures by determining the level of knowledge of haematologists and oncologists (who manage patients with CLL or FL) about the infection risks	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

associated with Zydelig treatment and the corresponding recommendation to minimize these risks as outlined in the SmPC and communicated in the direct healthcare professional communication (DHPC). This is to fulfill RMP post-authorisation measure MEA 016." Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 14.03.2019.	
PRAC Led **WS1536** **Levitra-EMEA/H/C/000475/WS1536/0064** **Vivanza-EMEA/H/C/000488/WS1536/0060** Bayer AG, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of the final clinical study report of study 12912 a non-interventional PASS (category 3 study) to investigate the NAION (Non-arteritic anterior ischemic optic neuropathy) risk associated with PDE5 inhibitors together with a consequential update of the RMP." Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 14.03.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1543** **Ultibro Breezhaler-EMEA/H/C/002679/WS1543/0029** **Ulunar Breezhaler-EMEA/H/C/003875/WS1543/0029** **Xoterna Breezhaler-EMEA/H/C/003755/WS1543/0033** Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth, Lead PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final study report of the Category I Post-Authorisation Safety Study (PASS) CQVA149A2402 (Multinational database cohort study in Europe in COPD patients, to assess the incidence rates and hazard ratios of various safety outcomes in new users of indacaterol/glycopyrronium compared to new users of comparator drugs (at the drug-class level). The Product Information has been updated by the removal of the black triangle and amendments in Annex II.D (Conditions or restrictions with regard	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

to the safe and effective use of the medicinal product). The RMP version 5.0 has been submitted accordingly." Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 14.03.2019.	
PRAC Led **WS1581** **Rasilez-EMEA/H/C/000780/WS1581/0123** **Rasilez HCT-EMEA/H/C/000964/WS1581/0093** Noden Pharma DAC, Lead Rapporteur: Daniela Melchiorri, Lead PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of an updated RMP version 14 in order to update the template in line with GVP Module V Rev2 required, add new important potential risk of non-melanoma skin cancer (related to Rasilez HCT only), and remove several important risks and missing information items as per PRAC endorsement of PSUR 12."	
PRAC Led **WS1586** **Anoro Ellipta-EMEA/H/C/002751/WS1586/0028** **Laventair Ellipta-EMEA/H/C/003754/WS1586/0031** GlaxoSmithKline (Ireland) Limited, Lead Rapporteur: Jayne Crowe, Lead PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of an updated RMP version 8.0 following Annual Renewal Procedure (EMEA/H/C/4002751/R/0022/ EMEA/H/C/003754/R/0025) commitments to remove the important identified risks of Hypersensitivity and Paradoxical bronchospasm (which may be life-threatening) from the list of safety concerns and to update all relevant sections of the RMP accordingly. MAH is also proposing to remove some additional risks (narrow angle glaucoma, Bladder outflow obstruction and urinary retention, Safety in pregnancy and lactation, Safety in long-term use, Safety in severe hepatic impairment), which have not been previously discussed with EMA." Request for Supplementary Information adopted on 16.05.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **WS1596**	Request for supplementary information adopted with a specific timetable.

Humalog-EMEA/H/C/000088/WS1596/0172 **Liprolog-EMEA/H/C/000393/WS1596/0133** Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Annika Folin, "Submission of the final report from on-going review of adverse drug events related to Humalog MEA/028 and Liprolog MEA/021, listed as a category 3 study in the RMP. This is a post approval safety surveillance programme for lot-specific adverse event review to evaluate any potential change in frequency of hypersensitivity, immunogenicity, and lack of drug effect (LODE) events for insulin lispro synthesized via streamlined KPB (sKPB) process." Request for Supplementary Information adopted on 16.05.2019.	
PRAC Led **WS1603** **Pregabalin Mylan-EMEA/H/C/004078/WS1603/0013** **Pregabalin Mylan Pharma-EMEA/H/C/003962/WS1603/0011** Mylan S.A.S, Generic, Generic of Lyrica, Lead PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "To align the RMP with the originator (updated as part of procedure EMEA/H/C/000546/WS1364/0092). In addition the RMP is updated to the latest template and is also harmonised for all pregabalin marketing authorisations procedures for which Mylan has an approved RMP." Request for Supplementary Information adopted on 16.05.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **WS1608** **Filgrastim Hexal-EMEA/H/C/000918/WS1608/0049** **Zarzio-EMEA/H/C/000917/WS1608/0050** Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "The scope of the above mentioned variation application is to align on the due dates and deliverables for the post-authorization measure, MEA007. The due date is extended from Dec 2019 to March 2020, to combine the annual safety report (ASR) with the 5-year interim clinical study report (CSR) in	Request for supplementary information adopted with a specific timetable.

2020 and the final CSR in 2024 and for the MEA to cover the entire duration of study EP06-501." Request for Supplementary Information adopted on 16.05.2019.

B.5.5. CHMP-CAT assessed procedures

Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0005/G, ATMP

CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder, "Update of the product information to reflect the study results of the 36-month follow up data for trial cod 16 HS 13 and the final study report with 60-month follow-up data for trial cod 16 HS 14.
Study cod 16 HS 13, is a Prospective, randomised, open label, multicentre Phase-III clinical trial to compare the efficacy and safety of the treatment with the autologous chondrocyte transplantation product co.don chondrosphere (ACT3D-CS) with microfracture in subjects with cartilage defects of the knee with a defect size between 1 and 4 cm2.
Study cod 16 HS 14, is a Prospective, randomised, open label, multicentre Phase-II clinical trial to investigate the efficacy and safety of the treatment of large defects (4-10 cm2) with three different doses of the autologous chondrocyte transplantation product co.don chondrosphere (ACT3D-CS) in subjects with cartilage defects of the knee."

YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0007, Orphan, ATMP

Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

B.5.6. CHMP-PRAC-CAT assessed procedures

Zalmoxis - nalotimagene carmaleucel - EMEA/H/C/002801/II/0016, Orphan, ATMP

MolMed S.p.A, Rapporteur: Johannes Hendrikus Ovelgonne, Co-Rapporteur: Sol Ruiz, CHMP Coordinator: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Brigitte Keller-Stanislawski, "The MAH is proposing to terminate the study TK008 (specific obligation for the CMA) and

See agenda 9.1

replace it with study TK013”

B.5.7. PRAC assessed ATMP procedures

PRAC Led **Alofisel - darvadstrocel - EMEA/H/C/004258/II/0006, Orphan, ATMP** Takeda Pharma A/S, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, “Submission of an updated RMP version 7 in order to propose replacement of the observational PASS study (Category 3) with two separate studies: a long-term safety extension of the ADMIRE-CD II study and a retreatment PASS. The European multi-database linkage study is added for the assessment of the potential risk of tumorgenicity.”	

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

WS1541 **Abasaglar-EMEA/H/C/002835/WS1541/** **Humalog-EMEA/H/C/000088/WS1541/0173** **Liprolog-EMEA/H/C/000393/WS1541/0134** Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 23.05.2019.	Request for supplementary information adopted with a specific timetable.
WS1560 **Renvela-EMEA/H/C/000993/WS1560/0048** **Sevelamer carbonate Winthrop-EMEA/H/C/003971/WS1560/0019** Genzyme Europe BV, Lead Rapporteur: Bart Van der Schueren, “To introduce new presentation with new dosing spoon for Renvela (EU/1/09/521/009) and Sevelamer carbonate Winthrop (EU/1/14/952/006) 0.8 g powder for oral suspension sachet. This variation fulfils commitment to develop a suitable device which would allow the accurate administration of the minimum 0.4g increments of sevelamer carbonate, that was undertaken during the line extension procedures. In addition, the MAH took the opportunity to	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

introduce editorial changes in the product informaiton." Opinion adopted on 16.05.2019. Request for Supplementary Information adopted on 14.03.2019.	
WS1562/G **Aflunov-EMEA/H/C/002094/WS1562/0047/G** **Foclivia-EMEA/H/C/001208/WS1562/0042/G** Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri Opinion adopted on 02.05.2019. Request for Supplementary Information adopted on 28.03.2019.	Positive Opinion adopted by consensus on 02.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1572 **Juluca-EMEA/H/C/004427/WS1572/0014** **Tivicay-EMEA/H/C/002753/WS1572/0049** ViiV Healthcare B.V., Lead Rapporteur: Janet Koenig Opinion adopted on 16.05.2019.	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1576/G **Blitzima-EMEA/H/C/004723/WS1576/0021/G** **Ritemvia-EMEA/H/C/004725/WS1576/0021/G** **Rituzena-EMEA/H/C/004724/WS1576/0022/G** **Truxima-EMEA/H/C/004112/WS1576/0023/G** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz Opinion adopted on 02.05.2019.	Positive Opinion adopted by consensus on 02.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1579 **Axura-EMEA/H/C/000378/WS1579/0081** **Memantine Merz-EMEA/H/C/002711/WS1579/0017** Merz Pharmaceuticals GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro Request for Supplementary Information adopted on 26.04.2019.	
WS1583 **M-M-RVAXPRO-EMEA/H/C/000604/WS1583/0094** **ProQuad-EMEA/H/C/000622/WS1583/0133** MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus	Positive Opinion adopted by consensus on 16.05.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 16.05.2019.	
WS1590 **Segluromet-EMEA/H/C/004314/WS1590/0006** **Steglatro-EMEA/H/C/004315/WS1590/0006** **Steglujan-EMEA/H/C/004313/WS1590/0008** Merck Sharp & Dohme B.V., Lead Rapporteur: Kristina Dunder, "To update sections 4.4 and 4.8 of the SmPC in order to implement the PRAC Recommendation on the signal of Fournier's gangrene for SGLT-2 inhibitors. The Package leaflet is being updated accordingly. In addition, the MAH is proposing an additional text the package leaflet to include the frequency of Fournier's gangrene, in alignment with the SmPC."	
WS1595 **Kalydeco-EMEA/H/C/002494/WS1595/0078** **Symkevi-EMEA/H/C/004682/WS1595/0009** Vertex Pharmaceuticals (Ireland) Limited, Lead Rapporteur: Maria Concepcion Prieto Yerro, "To provide a final Environmental Risk Assessement report." Request for Supplementary Information adopted on 16.05.2019.	Request for supplementary information adopted with a specific timetable.

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

Yervoy - ipilimumab - EMEA/H/C/002213/II/0063 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4 and 4.8 of the SmPC and of annex II in order to add safety information regarding Graft Versus Host Disease (GVHD) in allogeneic hematopoietic stem cell transplant (HSCT) recipients after treatment with ipilimumab. The update is based on a review of post-marketing data. The Package Leaflet and the RMP (version 25.0) is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some editorial changes in the PI and RMP and to include some changes in the RMP due to previous procedures."	The MAH withdrew the procedure on 10.05.2019.

Request for Supplementary Information adopted on 17.01.2019. Withdrawal request submitted on 10.05.2019.	

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

PRAC Led **Cerdelga - eliglustat - EMEA/H/C/003724/II/0020, Orphan** Genzyme Europe BV, PRAC Rapporteur: Eva A. Segovia, "Submission of the final report from study ELIGLC06912 listed as a category 3 study in the RMP (MEA006). This is a Drug Utilization Study of Eliglustat in the United States (US) Population Using MarketScan Database and the International Collaborative Gaucher Group Registry. Consequently, submission of an updated RMP version 6 in order to reflect the submission of the final data for study ELIGLC06912. In addition, RMP version 6.0 has been aligned with the Guideline on GVP - Module V, revision 2 and the related new EU RMP template has been implemented." Request for Supplementary Information adopted on 14.03.2019.	Updated Timetable
WS1524 **HyQvia-EMEA/H/C/002491/WS1524/0048** **Kiovig-EMEA/H/C/000628/WS1524/0090** Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 14.03.2019.	Request for an extension to the clock stop to respond to the Request for Supplementary Information adopted in March 2019.

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

cabazitaxel - EMEA/H/C/005178 treatment of adult patients with metastatic castration resistant prostate cancer previously treated with a docetaxel-containing regimen
azacitidine - EMEA/H/C/005300 Treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML) and acute myeloid leukemia (AML)
glasdegib - EMEA/H/C/004878, Orphan Pfizer Europe MA EEIG, treatment of newly

diagnosed de novo or secondary acute myeloid leukaemia

doxorubicin - EMEA/H/C/005194
treatment of breast cancer, ovarian cancer, progressive multiple myeloma and AIDS-related Kaposi's sarcoma

indacaterol / glycopyrronium / mometasone - EMEA/H/C/005061
treatment of asthma and to reduce asthma exacerbations

fingolimod - EMEA/H/C/005191
treatment of multiple sclerosis

lacosamide - EMEA/H/C/005243
treatment of epilepsy

teriparatide - EMEA/H/C/005087
treatment of osteoporosis

teriparatide - EMEA/H/C/005388
treatment of osteoporosis

luspatercept - EMEA/H/C/004444, Orphan
Celgene Europe BV, - treatment of adult patients with very low- to intermediate-risk myelodysplastic syndromes (MDS)-associated anaemia; - the treatment of adult patients with beta-thalassaemia (β-thalassaemia)-associated anaemia who require RBC transfusions.

semaglutide - EMEA/H/C/004953
treatment of type 2 diabetes mellitus

trastuzumab - EMEA/H/C/005066
treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)

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

Kymriah - tisagenlecleucel - EMEA/H/C/004090/X/0010, Orphan, ATMP
Novartis Europharm Limited, Rapporteur: Rune Kjeken, Co-Rapporteur: Dariusz Sladowski, CHMP Coordinator: Ingrid Wang and Ewa Balkowiec Iskra

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

bortezomib - EMEA/H/C/005074
treatment of multiple myeloma

List of Questions adopted on 31.01.2019.

fostamatinib - EMEA/H/C/005012
indicated for the treatment of thrombocytopenia
List of Questions adopted on 31.01.2019.

emapalumab - EMEA/H/C/004386, Orphan
Novimmune B.V., treatment of paediatric patients with primary haemophagocytic lymphohistiocytosis (HLH)
List of Questions adopted on 13.12.2018.

Imraldi - adalimumab - EMEA/H/C/004279/X/0019/G
Samsung Bioepis NL B.V., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Ulla Wändel Liminga, “Extension application to introduce a new presentation of 40 mg/0.8 ml solution for injection in a vial, to allow the administration to paediatric patients requiring less than a full 40mg dose.
C.I.z - To update the Product Information for the pre-filled syringe (EU/1/17/1216/001-004) and pre-filled pen (EU/1/17/1216/005-008) presentations in line with the dosage regimen changes introduced with the extension application.
The RMP (version 3.0) is updated in accordance. In addition, the applicant took the opportunity to implement minor editorial changes ”
List of Questions adopted on 28.03.2019.

omadacycline tosilate - EMEA/H/C/004715
treatment of community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI) in adults
List of Questions adopted on 31.01.2019.

rituximab - EMEA/H/C/004807
treatment of Non-Hodgkin's lymphoma (NHL), Chronic lymphocytic leukaemia (CLL) and Rheumatoid arthritis
List of Questions adopted on 18.10.2018.

netarsudil - EMEA/H/C/004583
indicated for the reduction of elevated intraocular pressure (IOP) in adults with open-angle glaucoma or ocular hypertension.
List of Questions adopted on 31.01.2019.

quizartinib - EMEA/H/C/004468, Orphan
Daiichi Sankyo Europe GmbH, treatment of acute myeloid leukaemia

List of Questions adopted on 29.01.2019.

onasemnogene abeparvovec -
EMEA/H/C/004750, Orphan, ATMP
AveXis Netherlands B.V., treatment of
treatment of spinal muscular atroophy (SMA)
List of Questions adopted on 22.02.2019.

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

Chenodeoxycholic acid Leadiant -
chenodeoxycholic acid -
EMEA/H/C/004061/S/0010, Orphan
Leadiant GmbH, Rapporteur: Constantinos Markopoulos, PRAC Rapporteur: Adam Przybylkowski

Elaprase - idursulfase -
EMEA/H/C/000700/S/0080
Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst

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

Cerdelga - eliglustat -
EMEA/H/C/003724/R/0022, Orphan
Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Eva A. Segovia

Exviera - dasabuvir -
EMEA/H/C/003837/R/0045
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Maria del Pilar Rayon

SCENESSE - afamelanotide -
EMEA/H/C/002548/R/0026, Orphan
Clinuvel Europe Limited, Rapporteur: Janet Koenig, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Martin Huber

Senshio - ospemifene -
EMEA/H/C/002780/R/0028
Shionogi B.V., Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Joseph Emmerich, PRAC Rapporteur: Kirsti Villikka

Sevelamer carbonate Winthrop - sevelamer carbonate - EMEA/H/C/003971/R/0022

Genzyme Europe BV, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Laurence de Fays

Tyverb - lapatinib - EMEA/H/C/000795/R/0060
Novartis Europharm Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Annika Folin

Vectibix - panitumumab - EMEA/H/C/000741/R/0094
Amgen Europe B.V., Rapporteur: Bjorg Bolstad, Co-Rapporteur: Constantinos Markopoulos, PRAC Rapporteur: David Olsen

Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/R/0054
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Maria del Pilar Rayon

Xadago - safinamide - EMEA/H/C/002396/R/0032
Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Rhea Fitzgerald

Xydalba - dalbavancin - EMEA/H/C/002840/R/0028
Allergan Pharmaceuticals International Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Rugile Pilviniene

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

Darzalex - daratumumab - EMEA/H/C/004077/II/0029, Orphan
Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Extension of indication to extend the existing therapeutic indication for Darzalex (daratumumab) in combination with lenalidomide and dexamethasone (Rd) for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for

autologous stem cell transplant (ASCT); as a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP (Version 6, Succession 1) has also been submitted."

Darzalex - daratumumab - EMEA/H/C/004077/II/0030, Orphan

Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Extension of indication to extend the existing therapeutic indication for DARZALEX (daratumumab) in combination with bortezomib, thalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant (ASCT); as a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP (Version 6, Succession 1) has also been submitted."

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

Eli Lilly Nederland B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Amelia Cupelli, "Extension of indication to include a new indication for Trulicity; "to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke), in adults with type 2 diabetes mellitus who have multiple cardiovascular risk factors without established cardiovascular disease, and in adults with type 2 diabetes mellitus with established cardiovascular disease."

The data supporting this new indication is derived from Study GBDJ (Researching Cardiovascular Events with a Weekly INcretin in Diabetes (REWIND)); a single pivotal Phase 3 long-term cardiovascular outcomes study, which assessed the efficacy and safety of treatment with once-weekly injection of dulaglutide 1.5 mg when added to glucose-lowering regimen of patients with type 2 diabetes (T2D), compared to the addition of a once weekly placebo injection. This study is a post-authorisation measure (PAM) (MEA 004) included in the dulaglutide RMP.

As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are being updated and the Package

Leaflet is updated accordingly.
In addition, the MAH is taking the opportunity to update the wording of the existing indication in section 4.1 of the SmPC and to implement a minor change in section 5.1 of the SmPC, in the glycaemic control summary subsection, based on the results from the dulaglutide study as add-on to sodium-glucose co-transporter 2 inhibitor therapy which was assessed as part of II/25.
An updated RMP version 3.1 was provided as part of the application."

Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/II/0015
Pfizer Ireland Pharmaceuticals, Rapporteur: Bjorg Bolstad, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Rugile Pilviniene,
"Extension of indication to include paediatric patients aged 3 months to less than 18 years for Zavicefta (for the treatment of cIAI and cUTI), based on data from paediatric studies D4280C00014, C3591004 and C3591005 and the population PK modelling/simulation analyses (CAZ-MS-PED-01 and CAZ-MS-PED-02).
As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2, 6.3 and 6.6 of the SmPC are updated in order to reflect this additional population, the paediatric posology, paediatric safety information, the description of the clinical trials and handling instructions for paediatric dosing.
The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct the sodium content to SmPC sections 2 and 4.4 and PL section 2 and the volumes of distribution of ceftazidime and avibactam in SmPC section 5.2.
Furthermore, the MAH is also introducing a correction in the Czech SmPC to add missing values in the table in SmPC section 5.1.
The RMP version 3.0 has also been submitted."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Advate - octocog alfa - EMEA/H/C/000520/II/0100
Baxter AG, Rapporteur: Jan Mueller-Berghaus

AMGEVITA - adalimumab - EMEA/H/C/004212/II/0017
Amgen Europe B.V., Rapporteur: Kristina Dunder

Atazanavir Mylan - atazanavir -

EMEA/H/C/004048/II/0012
Mylan S.A.S, Generic, Generic of Reyataz,
Rapporteur: Bjorg Bolstad

Atriance - nelarabine -
EMEA/H/C/000752/II/0047/G
Novartis Europharm Limited, Rapporteur: Sinan
B. Sarac

Cimzia - certolizumab pegol -
EMEA/H/C/001037/II/0079/G
UCB Pharma S.A., Rapporteur: Kristina Dunder

Erelzi - etanercept -
EMEA/H/C/004192/II/0018
Sandoz GmbH, Rapporteur: Johann Lodewijk
Hillege

Eylea - aflibercept -
EMEA/H/C/002392/II/0053
Bayer AG, Rapporteur: Alexandre Moreau

Kovaltry - octocog alfa -
EMEA/H/C/003825/II/0023
Bayer AG, Rapporteur: Kristina Dunder

NovoRapid - insulin aspart -
EMEA/H/C/000258/II/0128
Novo Nordisk A/S, Rapporteur: Kristina Dunder

Omnitrope - somatropin -
EMEA/H/C/000607/II/0060
Sandoz GmbH, Rapporteur: Johann Lodewijk
Hillege

OPDIVO - nivolumab -
EMEA/H/C/003985/II/0067/G
Bristol-Myers Squibb Pharma EEIG, Rapporteur:
Jorge Camarero Jiménez

Rebif - interferon beta-1a -
EMEA/H/C/000136/II/0141
Merck Europe B.V., Rapporteur: Filip Josephson

Skyrizi - risankizumab -
EMEA/H/C/004759/II/0002/G
AbbVie Deutschland GmbH & Co. KG,
Rapporteur: Peter Kiely

Voncento - human coagulation factor VIII /
human von willebrand factor -
EMEA/H/C/002493/II/0041/G
CSL Behring GmbH, Rapporteur: Paula
Boudewina van Hennik

WS1630

Bretaris Genuair-EMEA/H/C/002706/WS1630/0041
Eklira Genuair-EMEA/H/C/002211/WS1630/0041
AstraZeneca AB, Lead Rapporteur: Ewa Balkowiec Iskra

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

Amglidia - glibenclamide - EMEA/H/C/004379/II/0004, Orphan
Ammtek, Rapporteur: Martina Weise, "Update of sections 4.2 and 5.1 of the SmPC to reconcile posology instructions with the actual use of the product in clinical practice in order to avoid overdosing, to harmonise sections related to "Dosage adjustments and long-term treatment management" and remove reference to the off-label use of crushed tablets. This update is based on recently published literature, the ISPAD consensus guideline, and in line with the NEOGLI CSR.
In addition, the applicant took the opportunity to make editorial corrections."

Brintellix - vortioxetine - EMEA/H/C/002717/II/0022/G
H. Lundbeck A/S, Rapporteur: Bart Van der Schueren, "Update of sections 4.8 and 5.1 of the SmPC in order to describe effects of vortioxetine on treatment-emergent sexual dysfunction based on the outcome of 2 prospective clinical studies (Studies 318 and 4001).
Update of sections 4.4 and 5.2 of the SmPC in order to reflect the outcome of study 401 in subjects with severe hepatic impairment."

Cosentyx - secukinumab - EMEA/H/C/003729/II/0051
Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include additional dosing information for Ankylosing Spondylitis (AS) patients based on final results from study CAIN457F2314; this is a randomized, double-blind, double dummy, placebo controlled, parallel-group, Phase 3 multicenter study of secukinumab versus placebo to demonstrate efficacy at 16 weeks and to assess long-term efficacy up to Week 156 in patients with active

AS; the Package Leaflet is updated accordingly."

CRYSVITA - burosumab -
EMEA/H/C/004275/II/0004, Orphan
Kyowa Kirin Holdings B.V., Rapporteur: Kristina Dunder, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC, to reflect the results of Study UX023-CL301, a phase III study undertaken to further assess the efficacy, safety and pharmacodynamics in paediatric patients aged 1-12 years with X-linked Hypophosphataemia (XLH). The provision of the final CSR addresses Specific Obligation 2 (ANX 002) and the requirements of article 46 of the paediatric regulation. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the SmPC to increase readability."

Deltyba - delamanid -
EMEA/H/C/002552/II/0037, Orphan
Otsuka Novel Products GmbH, Rapporteur: Koenraad Norga, "xC.I.13 MIC report as amendment to CSR 242-09-213"

Keytruda - pembrolizumab -
EMEA/H/C/003820/II/0075
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Update of section 5.1 of the SmPC in order to reflect the updated results from study KEYNOTE-010 listed as a category 3 study in the RMP with a data cutoff of 16 March 2018. Study KEYNOTE-010 is a controlled phase II/III trial that randomized a total of 1034 previously-treated subjects with advanced or metastatic NSCLC whose tumors express PD-L1 to receive pembrolizumab at 2 mg/kg Q3W or 10 mg/kg Q3W or docetaxel at 75 mg/m2 Q3W. In addition, the MAH took the opportunity of this variation to include additional instructions in section 4.5 of the SmPC to clarify the use of corticosteroids in subjects treated with pembrolizumab in combination with other chemotherapeutic agents. The Package Leaflet is updated accordingly."

Keytruda - pembrolizumab -
EMEA/H/C/003820/II/0076
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "To update section 5.1 of the SmPC based on final results from study KEYNOTE-052 (KN052) listed as a PAES in Annex II; this is a single arm Phase II Clinical Trial of

pembrolizumab in subjects with advanced/unresectable or metastatic urothelial cancer (1st line)."

Kyntheum - brodalumab - EMEA/H/C/003959/II/0011
LEO Pharma A/S, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC "Mechanism of action" subsection with information about the cytokine IL-17C."

Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0024
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Joseph Emmerich, "Submission of the final clinical report from the Phase 3 study M16-126 (A Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Glecaprevir (GLE)/Pibrentasvir (PIB) in Adults with Chronic Hepatitis C Virus (HCV) Genotype 5 or 6 Infection)."

Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0025
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Joseph Emmerich, "Update of sections 4.2, 4.8 and 5.1 of the SmPC to shorten the treatment duration in treatment-naïve subjects with compensated cirrhosis and Hepatitis C virus GT1, 2, 4, 5, or 6 infection, from 12 to 8 weeks, based on interim results from study M16-135 (A Single Arm, Open-Label Study to Evaluate the Efficacy and Safety of Glecaprevir (GLE)/Pibrentasvir (PIB) in Treatment Naïve Adults with Chronic Hepatitis C Virus (HCV) Genotype 1 - 6 Infection and Compensated Cirrhosis). In addition, the marketing authorisation holder took the opportunity to revise the submission date of the final CSR for the hepatocellular carcinoma recurrence study in Annex IID."

Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0026
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Joseph Emmerich, "Update of section 5.1 of the SmPC in order to reflect data from two Asian regional Phase 3 studies: study M15-592 (VOYAGE-1 - A Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of ABT-493/ABT-530 in Treatment-Naïve and Treatment-Experienced, Non-Cirrhotic Asian

Adults with Chronic Hepatitis C Virus Genotype (GT) 1 to GT6 Infection With or Without Human Immunodeficiency Virus Co-Infection) and study M15-593 (VOYAGE-2 - An Open-Label Study to Evaluate the Efficacy and Safety of ABT-493/ABT-530 in Treatment-Naïve and Treatment-Experienced Asian Adults With Chronic Hepatitis C Virus Genotype (GT) 1 to GT6 Infection With Compensated Cirrhosis and With or Without Human Immunodeficiency Virus Co-Infection)."	
Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0007, Orphan Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, "Update of sections 4.8 and 5.1 of the SmPC based on safety and efficacy data for paediatric patients with relapsed or refractory AML from a systematic literature review."	
Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0008, Orphan Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, "Update the SmPC Section 4.2 to specify the dose and schedule for the second induction. Furthermore, a statement in SmPC Section 4.2 was added to increase awareness about the actual recommended (maximum) dose of Mylotarg and information regarding traceability added to Section 4.4. In addition, the Marketing authorisation holder (MAH) took the opportunity to include minor editorial changes in sections 4.2, 4.4, 4.8 and 5.2 of the SmPC and to make minor updates to bring the PI in line with the latest QRD template version."	
OPDIVO - nivolumab - EMEA/H/C/003985/II/0065 Bristol-Myers Squibb Pharma EEIG, Co-Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update posology and clinical related information based on interim results from Phase 3b/4 Study CA209384 (A Dose Frequency Optimization, Phase IIIB/IV Trial of Nivolumab 240 mg Every 2 Weeks vs Nivolumab 480 mg Every 4 weeks in Subjects with Advanced or Metastatic Non-small Cell Lung Cancer who Received Up to 12 Months of Nivolumab at 3 mg/kg or 240 mg Every 2 Weeks) and further supported by pharmacometric analyses in subjects with 2L+ NSCLC."	

OPDIVO - nivolumab -
EMEA/H/C/003985/II/0069
Bristol-Myers Squibb Pharma EEIG, Co-Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.2, 5.1 and 6.6 of the SmPC in order to introduce a new dosing regimen and schedule for adjuvant treatment of melanoma based on population PK data and Exposure-Response (E-R) Efficacy analysis. The Packalge leaflet has been updated accordingly."

Qtern - saxagliptin / dapagliflozin -
EMEA/H/C/004057/II/0024
AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, "Update of sections 4.2, 4.4 and 5.1 of the SmPC with information on the glycaemic efficacy and renal safety of dapagliflozin in patients with Type 2 Diabetes Mellitus and moderate renal impairment (CKD 3A) based on final results from study D1690C00024 (DERIVE) (dapagliflozin), and to reflect a change in renal cut-off value for saxagliptin. The package leaflet is updated accordingly.
The RMP version 4.1 has also been submitted.
In addition, the MAH took the opportunity to update SmPC sections 2, 4.8, 5.2 and Annex II to include the required excipient information in relation to sodium levels and lactose following the update to the Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal products for human use", as well as to bring the PI in line with EMA guidance ("Compilation of QRD decisions on stylistic matters in product information", EMA/25090/2002 Rev.18, published 08 December 2017)."

Tecentriq - atezolizumab -
EMEA/H/C/004143/II/0028
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC with new ADRs identified in IMpower132 study. This change is supported by safety data as presented in a drug safety report referring to the IMpower132 safety report (report 1089805) previously submitted to the Agency. The package leaflet is updated accordingly."

TECFIDERA - dimethyl fumarate -
EMEA/H/C/002601/II/0059
Biogen Netherlands B.V., Rapporteur: Martina

Weise, “Update of sections 4.8 and 5.1 of the SmPC in order to add the efficacy and safety information based on final results from study 109MS311, a multicentre extension study to determine the long-term safety and efficacy in paediatric subjects with RRMS (final study report already submitted under P46- 020). The Package Leaflet is updated accordingly.”

Translarna - ataluren - EMEA/H/C/002720/II/0053/G, Orphan

PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, “C.I.4: Update of section 5.3 of the SmPC in order to update the safety information based on final results Charles River 9001126 Three-month juvenile toxicology and toxicokinetic study planned in neonatal dogs listed as category 3 study in the RMP (MEA-005).
C.I.13 Submission of the final report from study WIL-523008 listed as category 3 study in the RMP (MEA/003). This is a Seven-day tolerability and pharmacokinetic study in neonatal dogs.
C.I.13 Submission of the final report from study WIL-523009 listed as category 3 study in the RMP (MEA/004). This is a One-month juvenile dose range-finding toxicology and toxicokinetic study planned in neonatal dogs age correlating with dosing in newborn paediatric patients to 2 years of age.
C.I.13 Submission of the final report from study (Charles River 5700755 listed as category 3 study in the RMP (MEA/0024). This is a 28-day investigational toxicology and toxicokinetic study of ataluren in juvenile beagle dogs with an 8-week recovery period – Category 3.”

Tremfya - guselkumab - EMEA/H/C/004271/II/0014

Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, “Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information based on final results from the phase 3 Eclipse study CNTO1959PSO3009, comparing guselkumab (Tremfya) and secukinumab (Cosentyx) for the treatment of moderate to severe plaque psoriasis.”

Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0014, Orphan

Ipsen Pharma, Rapporteur: Martina Weise, “To update sections 4.2 and 5.2 of the SmPC

following final results from study LX1606-111; this is a Phase 1, open-label, parallel-group study to evaluate the single-dose pharmacokinetics of Telotristat Ethyl in Male and Female Subjects with Severe Hepatic Impairment and Matched Subjects with Normal Function; the Package Leaflet is updated accordingly."

PRAC Led

WS1601

Glyxambi-EMEA/H/C/003833/WS1601/0022

Jentadueto-EMEA/H/C/002279/WS1601/0051

Trajenta-EMEA/H/C/002110/WS1601/0038

Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of sections 4.2 and 5.1 of the Trajenta SmPC, update of sections 4.2, 4.4 and 5.1 of the Jentadueto SmPC and section 5.1 of the Glyxambi SmPC, based on the final results from study 1218.74 (CAROLINA study) listed as a category 3 study in the RMP of Jentadueto and Trajenta, in order to fulfil Trajenta MEA 008.1 and Jentadueto MEA 001.1; this is a phase III randomized, parallel group, double blind study to evaluate Cardiovascular safety of linagliptin versus glimepiride in patients with type 2 diabetes mellitus at high cardiovascular risk. The Package Leaflet for Trajenta is updated accordingly. The RMP version 13.0 for Jentadueto and Trajenta and version 5.0 for Glyxambi have also been submitted. In addition, the Worksharing applicant (WSA) took the opportunity to make corrections throughout the product information for Glyxambi and Jentadueto and to make corrections to the Bulgarian, French, Swedish translations for Glyxambi."

WS1627

Eviplera-EMEA/H/C/002312/WS1627/0099

Odefsey-EMEA/H/C/004156/WS1627/0042

Gilead Sciences Ireland UC, Lead Rapporteur: Johann Lodewijk Hillege, "Update of section 4.9 of the Eviplera and Odefsey SmPCs in order to remove the recommendation to use oral activated charcoal in the event of an overdose of

rilpivirine and replace it with a general guidance to contact poison control. In addition the MAH has taken the opportunity to update the lactose wording in section 4.4 of the SmPC and section 2 of the PL of Eviplera, according to the annex to the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use', as well as update section 5.1 of the Eviplera SmPC to reflect the full waiver for the Eviplera PIP. The MAH has also taken the opportunity to introduce minor administrative updates in the product information for both for Eviplera and Odefsey."

WS1637
Ebymect-EMEA/H/C/004162/WS1637/0039
Edistride-EMEA/H/C/004161/WS1637/0032
Forxiga-EMEA/H/C/002322/WS1637/0051
Xigduo-EMEA/H/C/002672/WS1637/0050
AstraZeneca AB, Lead Rapporteur: Kristina Dunder, "Update of sections 4.4 (Special warnings and precautions for use) and 4.8 (Undesirable effects) of the SmPC of dapagliflozin-containing products with respect to the Fournier's gangrene class labelling language, following results from the DECLARE study (a Multicentre, Randomized, Double-Blind, Placebo-Controlled cardiovascular outcome trial in Patients with Type 2 Diabetes). The Package Leaflet is updated accordingly."

WS1647/G
Mirapexin-EMEA/H/C/000134/WS1647/0091/G
Sifrol-EMEA/H/C/000133/WS1647/0082/G
Boehringer Ingelheim International GmbH, Lead Rapporteur: Mark Ainsworth,

B.6.10. CHMP-PRAC assessed procedures

Benlysta - belimumab - EMEA/H/C/002015/II/0067
GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 5.1 of the SmPC based on final results from study BEL115471/

HGS1006-C1112 listed as a category 3 study in the RMP; this is a Phase 3/4, multicenter, randomized, double-blind, placebo-controlled, 52-week study to evaluate the efficacy and safety of belimumab in African-American/Black subjects with systemic lupus erythematosus. The RMP version 31 has also been submitted."

BYETTA - exenatide - EMEA/H/C/000698/II/0069

AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Submission of a justification for extrapolating exenatide once weekly clinical data (previously assessed for Bydureon) to exenatide twice daily (Byetta) in order to include the latest agreed RMP versions for Bydureon (v30, v31s2 and v32s2) also in the dossier for Byetta. As a consequence, the removal of the important potential risk 'Cardiac Events' is proposed also for Byetta."

Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0003/G

Sanofi Pasteur, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Sonja Hrabcik, "C.I.13 grouping: Submission of the final report from studies CYD14 and CYD15 listed as category 3 studies in the RMP. These are the final results of the pivotal efficacy studies including amendments to long-term efficacy follow-up (to capture the full range of dengue disease in the study population prospectively i.e. return to active detection of all symptomatic dengue cases) and long-term safety monitoring. No changes to the PI or RMP identified are proposed at this stage. Minor updates of the RMP will follow."

Giotrif - afatinib - EMEA/H/C/002280/II/0031

Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "Update of sections 4.4 and 4.8 of the SmPC in order to add gastrointestinal (GI) perforation as an additional side effect based on summarises of clinical trial and post-marketing safety data. The Package Leaflet and the RMP are updated accordingly. The RMP version 8.0 has been submitted including also the update of the RMP due to transition to the revision 2 template as per pharmacovigilance guidance and taking in

consideration the recommendation received during renewal procedure EMEA/H/C/002280/R/0026. In addition the MAH took the opportunity to correct some typographical errors in the German, Austrian and Spanish PIs, to include a linguistic review comments received from Czech Authority during linguistic review of procedure EMEA/H/C/002280/R/0026 in the SmPC and to update the list of the local representatives for Austria in the package leaflet."

Insuman - insulin human - EMEA/H/C/000201/II/0130

Sanofi-Aventis Deutschland GmbH, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Jean-Michel Dogné, "Submission of the final report from a completed Phase 3 study, HUBIN-L-05335, listed as a category 3 post-authorisation efficacy / safety study in the RMP. This study covers the evaluation of Insuman Implantable 400 IU/mL in patients with Type 1 diabetes treated with the Medtronic MiniMed Implantable Pump System using Insuplant 400 IU/mL, addressing the Post-Authorisation Measure MEA040.
In this application, the RMP v4.0 combines the updates related to HUBIN-L-05335 study final results and the approval of amended protocol V2 of the ongoing Post Authorization Safety Study HUBIN-C-06380 (MEA/047.4 & MEA/047.5, concerning PRAC decision: EMA/PRAC/256519/2018 dated 17-May-2018; updates are limited to Annex 3 of Part VII)."

Reagila - cariprazine - EMEA/H/C/002770/II/0010

Gedeon Richter Plc., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ana Sofia Diniz Martins, "Submission of in vitro metabolism study report (R188-A15) and consequential update of the Risk Management Plan"

TAGRISSO - osimertinib - EMEA/H/C/004124/II/0029

AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2 and 5.2 of the SmPC in order to reflect the outcome of study D5160C00035, an open-label, Phase I study to assess the pharmacokinetics, safety and tolerability of osimertinib following a single oral

80 mg dose to patients with advanced solid tumours and normal renal function or severe renal impairment. This study was a Category 3 study in the EU-RMP. The RMP version 13 has also been submitted."

TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0058

Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Submission of CSR of study 109MS310, an open-label study to assess the effects of Tecfidera on lymphocyte subsets in subjects with relapsing remitting multiple sclerosis, listed as category 3 study in the RMP.
The RMP (version 10.1) has been updated as a consequence of the completion of this study. The revised RMP also includes updates to reflect safety information available through to the data lock point of 24 January 2019 and to align with the EU RMP Module V (revision 2.01)."

Tyverb - lapatinib - EMEA/H/C/000795/II/0062

Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "Submission of the final report from study EGF117165/LAP016A2206 listed as an obligation in the Annex II of the Product Information. This is an open-label, phase II study to evaluate biomarkers associated with response to subsequent therapies in subjects with HER2-positive metastatic breast cancer receiving treatment with trastuzumab in combination with lapatinib or chemotherapy.
The Annex II and the RMP are updated to reflect the completion of this study. The RMP version 36.0 has also been submitted to address the PRAC recommendation from the last PSUR review."

Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0015, Orphan

Ipsen Pharma, Rapporteur: Martina Weise, PRAC Rapporteur: Adam Przybylkowski, "To update section 5.1 of the SmPC based on final results from study LX1606.1-302.CS (TELEPATH) listed as a category 3 study in the RMP; this is a multicentre, phase III, long-term extension study to further evaluate the safety and tolerability of telotristat etiprate in patients with carcinoid syndrome (CS). The updated RMP version 4.0 has

also been submitted, also updating to GVP Module V (Rev 2).”

B.6.11. PRAC assessed procedures

PRAC Led **Komboglyze - saxagliptin / metformin hydrochloride -** **EMEA/H/C/002059/II/0046** AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of an updated RMP version 15 in order to implement the revised GVP template Rev.2. As a result, the list of safety concerns has been revised and a number of important identified risks, important potential risks and missing information have been reclassified and have been removed from the RMP.”
PRAC Led **Noxafil - posaconazole -** **EMEA/H/C/000610/II/0057** Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Alexandre Moreau, “Submission of an updated RMP (version 15.1) in order to bring it in line with the guidance included in Good Pharmacovigilance Practices (GVP) Module V (Rev. 2), with the consequent applicable re-evaluation of some safety concerns. In addition to the above updates, the MAH took the opportunity to include data from the completed clinical trial in paediatric subjects PN097 (the CSR for which was submitted to the Agency in February 2019: P46 029), and update the due date for submission of the final report for the ongoing post-marketing efficacy trial PN069 (changed from December 2019 to 4th quarter of 2020).”
PRAC Led **Rebetol - ribavirin -** **EMEA/H/C/000246/II/0086** Merck Sharp & Dohme B.V., PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Joseph Emmerich, “Submission of an updated RMP version 5.1 in order to revise safety concerns for ribavirin based on GVP module V (rev. 2) guidance. In addition, the MAH took the

opportunity to revise the safety concerns of ribavirin in light of the current era of IFN free regimen, as requested in a previous PSUSA procedure (EMEA/H/C/PSUSA/00010007/201707)."

PRAC Led

Stayveer - bosentan - EMEA/H/C/002644/II/0027

Janssen-Cilag International NV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final report from study AC-052-516, (a category 1 study). This is a non-interventional observational study of the disease characteristics and outcomes of PAH in children and adolescents in real-world clinical settings.
The RMP version 10 has also been submitted. The RMP has been updated in line with GVP module 2."

PRAC Led

Tracleer - bosentan - EMEA/H/C/000401/II/0091

Janssen-Cilag International NV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final report from study AC-052-516, (a category 1 study). This is a non-interventional observational study of the disease characteristics and outcomes of PAH in children and adolescents in real-world clinical settings.
The RMP version 10 has also been submitted. The RMP has been updated in line with GVP module 2."

PRAC Led

Tremfya - guselkumab - EMEA/H/C/004271/II/0013

Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of RMP to remove exposure during lactation as missing information."

PRAC Led

Tysabri - natalizumab - EMEA/H/C/000603/II/0114

Biogen Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte

Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, “Update of the RMP (version 25.0) with information related to extended interval dosing that will be added to the educational materials. Annex IID of the PI also reflects the above changes.”

B.6.12. CHMP-CAT assessed procedures

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0011, Orphan, ATMP

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

Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0008, ATMP

CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder

YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0008, Orphan, ATMP

Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

PRAC Led

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0034, ATMP

Amgen Europe B.V., Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, “To update the RMP for Imlygic to version 7.0 in order to add 2 category 3 studies (Studies 20180062 and 20180099), as well as an internal evaluation of managed distribution process metrics, to evaluate the effectiveness of additional risk minimization measures (aRMM).”

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

WS1585
Infanrix
hexa-EMEA/H/C/000296/WS1585/0258
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1593
Ambirix-EMEA/H/C/000426/WS1593/0098
Twinrix Adult-EMEA/H/C/000112/WS1593/0133
Twinrix Paediatric-EMEA/H/C/000129/WS1593/0134
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1602/G
Leganto-EMEA/H/C/002380/WS1602/0030/G
Neupro-EMEA/H/C/000626/WS1602/0084/G
UCB Pharma S.A., Lead Rapporteur: Bruno Sepodes

WS1615
Actraphane-EMEA/H/C/000427/WS1615/0078
Actrapid-EMEA/H/C/000424/WS1615/0072
Insulatard-EMEA/H/C/000441/WS1615/0075
Levemir-EMEA/H/C/000528/WS1615/0093
Mixtard-EMEA/H/C/000428/WS1615/0079
Protaphane-EMEA/H/C/000442/WS1615/0074
Ryzodeg-EMEA/H/C/002499/WS1615/0032
Tresiba-EMEA/H/C/002498/WS1615/0038
Xultophy-EMEA/H/C/002647/WS1615/0030
Novo Nordisk A/S, Lead Rapporteur: Sinan B. Sarac

WS1621
Bexsero-EMEA/H/C/002333/WS1621/0077
Menveo-EMEA/H/C/001095/WS1621/0087
GSK Vaccines S.r.l, Lead Rapporteur: Johann

Lodewijk Hillege

WS1623
Hexacima-EMEA/H/C/002702/WS1623/0091
Hexaxim-EMEA/H/W/002495/WS1623/0096
Hexyon-EMEA/H/C/002796/WS1623/0095
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

WS1626/G
Glyxambi-EMEA/H/C/003833/WS1626/0023/G
Jardiance-EMEA/H/C/002677/WS1626/0044/G
Synjardy-EMEA/H/C/003770/WS1626/0040/G
Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege

WS1638
Trevicta-EMEA/H/C/004066/WS1638/0023
Xeplion-EMEA/H/C/002105/WS1638/0044
Janssen-Cilag International NV, Lead Rapporteur: Kristina Dunder

WS1642/G
Rixathon-EMEA/H/C/003903/WS1642/0024/G
Riximyo-EMEA/H/C/004729/WS1642/0024/G
Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus

Hexacima-EMEA/H/C/002702/WS1624/0090/G
Hexaxim-EMEA/H/W/002495/WS1624/0095/G
Hexyon-EMEA/H/C/002796/WS1624/0094/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 26-29 May 2019 CHMP plenary:

G.3.2. List of procedures starting in May 2019 for June 2019 CHMP adoption of outcomes

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