24 June 2019
EMA/CHMP/354403/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Agenda for the meeting on 24-27 June 2019

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

24 June 2019, 13:00 – 19:30, room 1C

25 June 2019, 08:30 – 19:30, room 1C

26 June 2019, 08:30 – 19:30, room 1C

27 June 2019, 08:30 – 15:00, 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).

Temporary visiting address Spark building ● Orlyplein 24 ● 1043 DP Amsterdam ● The Netherlands
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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 24-27 June 2019. See (current) June 2019 CHMP minutes (to be published post July 2019 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 24-27 June 2019

1.3. Adoption of the minutes

CHMP minutes for 27-29 May 2019.

ORGAM minutes for 17 June 2019.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. cannabidiol - Orphan - EMEA/H/C/004675

GW Pharma (International) B.V.; Adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS)

Scope: Oral explanation, SAG Report

Action: Oral explanation to be held on Tuesday, 25 June 2019 at time 14:00

List of Outstanding Issues adopted on 26.04.2019, 31.01.2019, 15.11.2018. List of Questions adopted on 31.05.2018.

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

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

Scope: Oral explanation

The list of questions to the BSWP was adopted via written procedure on 12.06.2019.

Action: Oral explanation to be held on Monday, 24 June 2019 at time 16:30

List of Outstanding Issues adopted on 29.05.2019, 28.03.2019. List of Questions adopted on 11.12.2018.

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

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

Novartis Europharm Limited

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

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

Oral explanation

Action: Oral explanation to be held on Monday, 24 June 2019 at time 14:30

Request for Supplementary Information adopted on 28.02.2019, 15.11.2018, 26.07.2018.

See 5.1

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

PTC Therapeutics International Limited

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

Scope: "Extension of indication to include non-ambulatory patients with Duchenne muscular dystrophy; this variation additionally presents, as supportive data, the final results of the long term clinical study PTC-124-GD-019-DMD (an Open-Label Study for Previously Treated Ataluren (PTC124) Patients with Nonsense Mutation Dystrophinopathy), submitted in line with the requirements of the Article 46 of the Paediatric Regulation.
As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.
The RMP version 8.0 has also been submitted."

Oral explanation

Action: Oral explanation to be held on Tuesday, 25 June 2019 at time 11:00

Request for Supplementary Information adopted on 28.02.2019, 13.12.2018.

See 5.1

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. azacitidine - EMEA/H/C/005300

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

and acute myeloid leukemia (AML)

Scope: Opinion

Action: For adoption

3.1.2. romosozumab - EMEA/H/C/004465

Treatment of osteoporosis

Scope: Opinion

Action: For adoption

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

3.1.3. 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: Opinion

Action: For adoption

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

3.1.4. lacosamide - EMEA/H/C/005243

treatment of epilepsy

Scope: Opinion

Action: For adoption

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

3.2.1. bortezomib - EMEA/H/C/005074

treatment of multiple myeloma

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 31.01.2019.

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

indicated for the secondary prevention of atherothrombotic events

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 31.01.2019.

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

Accelerated assessment

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 24.04.2019.

3.2.4. fostamatinib - EMEA/H/C/005012

indicated for the treatment of thrombocytopenia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 31.01.2019.

3.2.5. emapalumab - Orphan - EMEA/H/C/004386

Novimmune B.V.; treatment of paediatric patients with primary haemophagocytic lymphohistiocytosis (HLH).

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 13.12.2018.

3.2.6. rituximab - EMEA/H/C/005387

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

Scope: List of outstanding issues

Action: For adoption

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

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

Scope: List of outstanding issues

Action: For adoption

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

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

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 31.01.2019.

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

Accelerated assessment

Roche Registration GmbH; Treatment of mature B cell lymphomas

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 24.04.2019.

3.2.10. rituximab - EMEA/H/C/004807

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 18.10.2018.

3.2.11. netarsudil - EMEA/H/C/004583

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 31.01.2019.

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

Daiichi Sankyo Europe GmbH; treatment of acute myeloid leukaemia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 29.01.2019.

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

Accelerated assessment

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.02.2019.

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

3.3.1. brolucizumab - EMEA/H/C/004913

treatment of neovascular (wet) age-related macular degeneration (AMD)

Scope: List of questions

Action: For adoption

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

Accelerated assessment

Ebola Vaccine

Scope: List of questions

Action: For adoption

3.3.3. cefiderocol - EMEA/H/C/004829

Accelerated assessment

treatment of infections due to aerobic Gram-negative bacteria

Scope: List of questions

Action: For adoption

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

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

Scope: List of questions

Action: For adoption

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

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

Scope: List of questions

Action: For adoption

3.3.6. methylthioninium chloride - EMEA/H/C/002776

is indicated as an aid for the enhanced visualization and detection of colorectal lesions in adult patients undergoing screening / surveillance colonoscopy for colorectal cancer. An increased detection of colorectal lesions translates into an increase in the adenoma detection rate (ADR).

Scope: List of questions

Action: For adoption

3.3.7. bempedoic acid - EMEA/H/C/004958

treatment of primary hypercholesterolaemia or mixed dyslipidaemia

Scope: List of questions

Action: For adoption

3.3.8. bempedoic acid / ezetimibe - EMEA/H/C/004959

treatment of primary hypercholesterolaemia or mixed dyslipidaemia

Scope: List of questions

Action: For adoption

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

SciPharm Sarl; treatment of thromboembolic pulmonary hypertension (CTEPH)

Scope: List of questions

Action: For adoption

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

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

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

Scope: Letter from applicant dated 12 June 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 15.11.2018.

3.4.2. adalimumab - EMEA/H/C/004879

treatment of juvenile idiopathic arthritis, paediatric plaque psoriasis, paediatric Crohn's disease, paediatric uveitis

Scope: Letter from applicant dated 12 June 2019 requesting an extension of clock stop to respond to the list of questions adopted in March 2019

Action: For adoption

List of Question adopted on 28.03.2019.

3.4.3. budesonide / glycopyrronium / formoterol fumarate dihydrate - EMEA/H/C/004983

as a maintenance treatment in adult patients with moderate to very severe chronic obstructive pulmonary disease (COPD)

Scope: Letter from applicant dated 24 May 2019 requesting an extension of clock stop to

respond to the list of questions adopted in April 2019.

Action: For adoption

List of questions adopted on 26.04.2019.

3.4.4. erlotinib - EMEA/H/C/005071

treatment of lung and pancreatic cancers

Scope: Letter from applicant dated 17 June 2019 requesting an extension of clock stop to respond to the list of outstanding issues adopted in May 2019.

Action: For adoption

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

3.4.5. crisaborole - EMEA/H/C/004863

treatment of mild to moderate atopic dermatitis

Scope: Letter from applicant dated 19 June 2019 requesting an extension of clock stop to respond to the list of outstanding issues adopted in May 2019.

Action: For adoption

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

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

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

Emmaus Medical Europe Ltd; treatment of sickle cell disease

Scope: Appointment of re-examination rapporteurs, draft timetable

Letter from the applicant dated 11 June 2019 requesting a re-examination of the opinion adopted on 29 May 2019.

Action: For adoption

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

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

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

4.1.1. Imraldi - adalimumab - EMEA/H/C/004279/X/0019/G

Samsung Bioepis NL B.V.

Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "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 "

Action: For adoption

List of Questions adopted on 28.03.2019.

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 840 mg strength."

Action: For adoption

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

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

Pfizer Europe MA EEIG

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

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

Action: For adoption

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

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

Eli Lilly Nederland B.V.

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

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

Action: For adoption

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

GlaxoSmithKline (Ireland) Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include patients aged 5 years and older in the current approved indication for Benlysta (belimumab powder for solution for infusion 120 mg/ml and 400 mg/ml) based on the results of the safety, efficacy and pharmacokinetics study in patients aged 5 years to 17 years (BEL114055). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated with safety and efficacy information.
Update of sections 4.2, 5.1 and 5.2 of the SmPC for Benlysta (belimumab, solution for injection in pre-filled pen and pre-filled syringe, 200 mg) to reflect the paediatric data available for the intravenous formulation. The Package Leaflet is updated accordingly.

The RMP version 28.0 is submitted to reflect the results of the study and to bring it in line with the GVP Module V RMP template version 2.0. In addition, the MAH took the opportunity to make some editorial changes in the product information and bring it in line with the latest QRD template version 10.0."

Action: For adoption

Request for Supplementary Information adopted on 28.02.2019.

5.1.2. Cyramza - ramucirumab - EMEA/H/C/002829/II/0027

Eli Lilly Nederland B.V.

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

Scope: "Extension of indication to include Cyramza indicated as monotherapy for the treatment of adult patients with hepatocellular carcinoma who have an alpha fetoprotein (AFP) of ≥ 400 ng/mL, after prior sorafenib therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in accordance. The Package Leaflet is updated in accordance. RMP version 8.1 has been submitted."

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

Action: For adoption

Request for Supplementary Information adopted on 28.03.2019, 15.11.2018.

5.1.3. Dupixent - dupilumab - EMEA/H/C/004390/II/0012

sanofi-aventis groupe

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

Scope: "Extension of indication to extend the adult atopic dermatitis indication to the paediatric, 12 years to 17 years (adolescent) patients under Article 8 of the Paediatric Regulation (1901/2006). This study is submitted in accordance with the requirement of Article 46."

Action: For adoption

Request for Supplementary Information adopted on 31.01.2019.

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

sanofi-aventis groupe

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

Scope: "Extension of Indication to include a new indication in adult patients with chronic rhinosinusitis with nasal polyposis. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.
An updated RMP is submitted (V 4.0)"

Action: For adoption

5.1.5. Fiasp - insulin aspart - EMEA/H/C/004046/II/0010

Novo Nordisk A/S

Rapporteur: Kristina Dunder, Co-Rapporteur: Ingrid Wang, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to include treatment of children and adolescents aged 1 year and above based on data from the phase 3b clinical trial NN1218-4101(assessed as part of PAM P46-002, fulfilled), supported by data from the Clinical Pharmacology trials NN1218-4371 (PAM P46-003, submitted on the 02-Jan-2019) and NN1218-3888 which was included in the initial MAA. As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC and the corresponding sections of the Package Leaflet are updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make other non-related minor or editorial changes were implemented throughout the EU PI to increase readability/consistency."

Action: For adoption

Request for Supplementary Information adopted on 26.04.2019.

5.1.6. Imbruvica - ibrutinib - Orphan - EMEA/H/C/003791/II/0046

Janssen-Cilag International NV

Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication for Imbruvica; to broaden the current indication and apply for an extension of indication with respect to include treatment of adult patients with Waldenström's macroglobulinaemia (WM) in combination with rituximab. This proposed broaden indication is supported by the final clinical study report results of phase 3 study PCYC-1127-CA. As a consequence, sections 4.1 and 4.8 of the SmPC are updated. No changes were required to the broaden indication for the Package Leaflet. In addition, the Marketing authorisation holder (MAH) took the opportunity to update in the SmPC and Package Leaflet with minor editorial/administrative changes.
An updated version of the Imbruvica EU Risk Management Plan (RMP) (version 12) is also included in this submission."

Action: For adoption

Request for Supplementary Information adopted on 28.02.2019.

5.1.7. Imbruvica - ibrutinib - Orphan - EMEA/H/C/003791/II/0047

Janssen-Cilag International NV

Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication for Imbruvica (ibrutinib); to extend the existing chronic lymphocytic leukaemia (CLL) indication to include combination use with obinutuzumab for the treatment of adult patients with previously untreated CLL. This proposed indication is supported by the data from the phase 3 study PCYC-1130-CA. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated, in 4.1 to include the extended indication, in 4.8 to update the safety information to include long term safety (supported by results of study 3038-1) and section 5 to update the existing CLL label studies with long term efficacy data for

CLL (supported by long term efficacy results of study PCYC-1112-CA and PCYC-1116-CA). The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the SmPC and Package Leaflet with minor editorial/administrative changes.
An updated version of the Imbruvica EU Risk Management Plan (RMP) (version 12) is also included in this submission."

Action: For adoption

Request for Supplementary Information adopted on 28.02.2019.

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

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication to include, as monotherapy or in combination with platinum and 5-fluorouracil (5-FU) Chemotherapy, first-line treatment of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) in adults for Keytruda; based on the results from KEYNOTE-048, a randomized, multi-center, open-label phase 3 study investigating pembrolizumab, or pembrolizumab plus platinum plus 5-FU chemotherapy versus platinum plus 5-FU plus cetuximab in subjects with first-line recurrent or metastatic HNSCC.
As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. An updated version of the RMP (Version 22.1) is also being submitted."

Action: For adoption

Request for Supplementary Information adopted on 28.03.2019.

5.1.9. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0069

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 first line treatment of advanced or metastatic renal cell carcinoma (RCC) as combination therapy of pembrolizumab together with axitinib based on the results of the first Interim Analysis (IA1) from the pivotal study, KN426, an ongoing, Phase 3, randomized, open-label, multicenter, global study, to evaluate the efficacy and safety of pembrolizumab in combination with axitinib versus sunitinib in previously untreated subjects with advanced/metastatic RCC. It also includes supportive data from KEYNOTE-427 Cohort A (pembrolizumab monotherapy) and a Sponsored Study A4061051 (axitinib monotherapy). 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 Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.
The risk management plan (RMP) Version 24.1 is submitted."

Action: For adoption

Request for Supplementary Information adopted on 26.04.2019.

5.1.10. Lonsurf - trifluridine / tipiracil - EMEA/H/C/003897/II/0012

Les Laboratoires Servier

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Annika Folin

Scope: "Extension of indication to include Lonsurf indicated for the treatment of adult patients with metastatic gastric cancer including adenocarcinoma of the gastroesophageal junction, who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, platinum-, and either a taxane- or irinotecan-based chemotherapy. 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) took the opportunity to update the list of local representatives in the Package Leaflet. RMP version 6.1 has also been submitted and updated in accordance with Template Rev 2."

Action: For adoption

Request for Supplementary Information adopted on 31.01.2019.

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

Novartis Europharm Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

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

Action: For adoption

Request for Supplementary Information adopted on 28.02.2019.

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

Boehringer Ingelheim International GmbH

Rapporteur: Jayne Crowe, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica Mirošević Skvrce

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

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

Action: For adoption

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

Novartis Europharm Limited

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

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

Oral explanation

Action: For adoption

Request for Supplementary Information adopted on 28.02.2019, 15.11.2018, 26.07.2018.

See 2.3

5.1.14. Stelara - ustekinumab - EMEA/H/C/000958/II/0071

Janssen-Cilag International NV

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

Scope: "Extension of indication for Stelara to include treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic or have medical contraindications to such therapies. As a consequence, the SmPC, Package Leaflet and RMP have been updated."

Action: For adoption

Request for Supplementary Information adopted on 26.04.2019.

5.1.15. Suliqua - insulin glargine / lixisenatide - EMEA/H/C/004243/II/0011

sanofi-aventis groupe

Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include "treatment of adults with insufficiently controlled type 2 diabetes mellitus to improve glycaemic control as an adjunct to diet and exercise in addition to other oral medicinal products for the treatment of diabetes" based on the phase 3 Study EFC13794; a 26-week randomized, open-label, active controlled, parallel-group, study assessing the efficacy and safety of the insulin glargine/lixisenatide fixed ratio combination in adults with Type 2 Diabetes inadequately controlled on GLP-1 receptor agonist and metformin (alone or with pioglitazone and/or SGLT2 inhibitors), followed by a fixed ratio combination single-arm 26-week extension period. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated and the Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to update the contact details of the local representatives in Denmark, the Netherlands and the UK in the Package Leaflet and to implement minor editorial changes in the annexes. An updated RMP version 4.0 was provided as part of the application."

Action: For adoption

5.1.16. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0018

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 carboplatin and etoposide, indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC) for Tecentriq; 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 8.0 has been submitted"

Action: For adoption

Request for Supplementary Information adopted on 31.01.2019.

5.1.17. Toujeo - insulin glargine - EMEA/H/C/000309/II/0108

Sanofi-Aventis Deutschland GmbH

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include new population for Toujeo. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

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

PTC Therapeutics International Limited

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

Scope: "Extension of indication to include non-ambulatory patients with duchenne muscular dystrophy; this variation additionally presents, as supportive data, the final results of the long term clinical study PTC-124-GD-019-DMD (an Open-Label Study for Previously Treated Ataluren (PTC124) Patients with Nonsense Mutation Dystrophinopathy), submitted in line with the requirements of the Article 46 of the Paediatric Regulation.
As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 8.0 has also been submitted."

Oral explanation

Action: For adoption

Request for Supplementary Information adopted on 28.02.2019, 13.12.2018.

See 2.3

5.1.19. Victoza - liraglutide - EMEA/H/C/001026/II/0049

Novo Nordisk A/S

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Menno van der Elst

Scope: “Extension of indication to include treatment of children and adolescents (age 10-17 years) with T2D based on Study NN2211-1800; a Phase 1 clinical pharmacology, multi-centre, randomised, double-blind placebo controlled trial, and Study NN2211-3659; a Phase 3a efficacy and safety, multi-centre, randomised, parallel group, placebo controlled trial with a 26-week double blind period followed by a 26-week open label period (main part). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, and 5.2 of the SmPC are being updated and the Package Leaflet is updated accordingly.
Additionally, in accordance with the guideline from 2017 about excipients, the MAH took the opportunity to include sodium in SmPC section 4.4 and the Package Leaflet.
An updated RMP version 30 was provided as part of the application.”

Action: For adoption

Request for Supplementary Information adopted on 28.03.2019.

5.1.20. 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 29.05.2019, 28.03.2019.

5.1.21. Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0041

Pfizer Ireland Pharmaceuticals

Rapporteur: Alar Irs, PRAC Rapporteur: Maia Uusküla

Scope: “Extension of indication to include paediatric patients from birth to less than 2 months old for Zinforo; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated based on results from study D3720C00009 (C2661002) an open-label, multicentre study to evaluate the safety, tolerability, pharmacokinetics, and efficacy of ceftaroline in neonates and young infants with late-onset sepsis. The Package Leaflet is updated in accordance. The RMP (v 17.0) has also been submitted.”

Action: For adoption

Request for Supplementary Information adopted on 28.02.2019.

5.1.22. WS1539
Ebymect - dapagliflozin / metformin - EMEA/H/C/004162/WS1539/0035

Edistride - dapagliflozin - EMEA/H/C/004161/WS1539/0029
Forxiga - dapagliflozin - EMEA/H/C/002322/WS1539/0048
Xigduo - dapagliflozin / metformin - EMEA/H/C/002672/WS1539/0046

AstraZeneca AB

Lead Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: "Update of sections 4.1, 4.2, 4.4, 4.8, and 5.1 of Forxiga, Edistride, Xigduo and Ebymect SmPCs to modify the current indication for improvement of glycaemic control based on final results from study D1693C00001 (DECLARE), which is listed as a category 3 study in the RMP (Forxiga: MEA 005):
- For the prevention of new or worsening HF or CV death
- For the prevention of new or worsening nephropathy
The Package Leaflets (PL) are updated accordingly. The updated dapagliflozin Risk Management Plan (RMP) version 17 and dapagliflozin/metformin fixed dose combination (FDC) RMP version 11 have also been submitted.
In addition, the Worksharing applicant took the opportunity to correct a typo error in Edistride marketing authorisation number in section 8 of SmPC and add the latest renewal date for Xigduo in section 9 of SmPC. Besides, the lactose wording in SmPC section 4.4 has been updated in line with the updated excipient guideline. The revised PI also include proposals for minor administrative changes for consistency throughout the PI."

Action: For adoption

Request for Supplementary Information adopted on 26.04.2019.

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

Aventis Pharma S.A.

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

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

Action: For adoption

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

8.2. 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. 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

Scope: "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."

Action: For discussion

Request for Supplementary Information adopted on 29.05.2019, 28.02.2019, 20.09.2018.

9.1.2. Kyprolis - carfilzomib - EMEA/H/C/003790/II/0031, Orphan

Amgen Europe B.V.

Rapporteur: Jorge Camarero Jiménez

Scope: "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 to add a once-weekly dose regimen for carfilzomib (Kyprolis) at 20/70 mg/m^2 in combination with dexamethasone (Kd) for the treatment of the currently indicated patient population. The MAH took the opportunity to implement editorial changes to the SmPC and Patient Information Leaflet (PIL) due to the revised excipients guideline (EMA/CHMP/302620/2017). The PIL is updated accordingly."

Action: For adoption

Request for Supplementary Information adopted on 28.02.2019, 15.11.2018.

9.1.3. OPDIVO - nivolumab - EMEA/H/C/003985/II/0065

Bristol-Myers Squibb Pharma EEIG

Co-Rapporteur: Paula Boudewina van Hennik

Scope: "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."

Action: For discussion

9.1.4. Optimark (withdrawn) – gadoversetamide - EMEA/H/C/000745/ANX/014.11

Guerbet

Lead Rapporteur: Greg Markey
Scope: Long-term effects study ALS-Gd64/001 on gadolinium accumulation in the bone for gadoversetamide, gadoteric acid, gadobutrol, gadoxetic acid, gadopentetic acid and gadodiamide containing medicinal products.

Request for PRAC advice was adopted via written procedure on 07.06.2019

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

No items

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

No items

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

10.4.1. Flurbiprofen Geiser – oromucosal spray – EMEA/H/A-29(4)/1487

Geiser Pharma S.L.

Rapporteur: TBC, Co-Rapporteur: TBC

Scope: Start of procedure, Appointment of rapporteurs, List of questions, Timetable

Action: For adoption

The applicant has submitted a hybrid application under Article 10(3) of Directive 2001/83/EC for Flurbiprofen Geiser 8.75mg oromucosal spray. NL is of the opinion that the therapeutic equivalence between the reference and test product has not been adequately demonstrated since no clinical trials have been submitted and the justification for the lack of conducting any clinical trials is not considered acceptable.

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. Bacterial lysates-containing based medicinal products for respiratory conditions - EMEA/H/A-31/1465

MAH various

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

Scope: List of Outstanding Issues

Action: For adoption

Review of the benefit-risk balance following notification by AIFA in Italy on 8 June 2018 of a referral under Article 31 of Directive 2001/83/EC.

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

MAH various

Rapporteur: Ondrej Slanar, Co-Rapporteur: Janet Koenig

Scope: List of outstanding issues

Action: For adoption

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

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

List of Oustanding Issues adopted on 28. March 2019. List of questions adopted on 13 December 2018.

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

June 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. Area of expertise of CHMP Co-opted Member

Discussion on area of expertise in light of the expiry of the mandate of co-opted member Sol Ruiz on 21/07/2019.

The area of expertise of Sol Ruiz is quality and safety (biological) in advanced therapies (gene, cell and tissue therapies).

Action: For discussion

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 11-14 June 2019

Action: For information

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

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 19-21 June 2019

Action: For information

14.2.3. Paediatric Committee (PDCO)

PIPs reaching D30 at June 2019 PDCO

Action: For information

Report from the PDCO meeting held on 25-28 June 2019

Action: For information

14.2.4. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 18-20 June 2019

Action: For information

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

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 25-27 June 2019

Action: For information

Questions to Pharmacokinetics Working Party on Bioequivalence for orally inhaled products containing beclomethasone diproprionate (BDP)

Action: For adoption

Questions to Pharmacokinetics Working Party – need to measure both enantiomers as proof of bioequivalence

Action: For adoption

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 11-14 June 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

PRAC advice on liposomal formulations and non-liposomal formulations of doxorubicin

Action: For discussion

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP June 2019 meeting to CHMP for adoption:

- 20 reports on products in scientific advice and protocol assistance

- 10 reports on products in pre-authorisation procedures
- 1 report on products in post-authorisation procedures
- 4 reports on products in plasma master file

Action: For adoption

14.3.4. Blood Product Working Party (BPWP)

Chair: Jacqueline Kerr

Election of BPWP Vice-Chair

Action: For election

14.3.5. Antimicrobial Advice ad hoc Expert Group (AMEG)

Scope: Revised AMEG scientific advice for public consultation on the preliminary risk profiling and overview of comments received during the public consultation

Action: For adoption

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

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

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

Action: For information

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Preparedness of the system and capacity increase

Action: For information

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)*

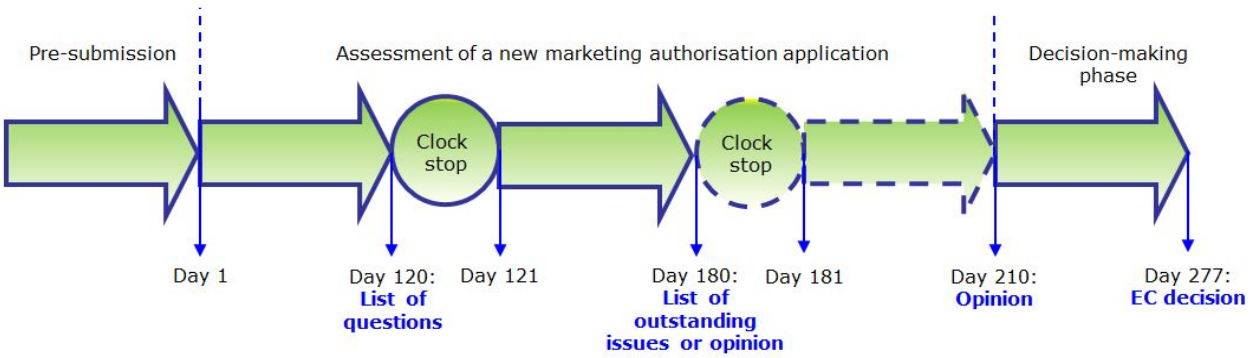
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures (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 June 2019
EMA/CHMP/355069/2019

Annex to 24-27 June 2019 CHMP Agenda

Pre-submission and post-authorisations issues

Temporary visiting address Spark building ● Orlyplein 24 ● 1043 DP Amsterdam ● The Netherlands
For deliveries refer to www.ema.europa.eu/how-to-find-us
Send us a question via www.ema.europa.eu/contacts **Telephone** +31(0)88 781 6000

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

Final Outcome of Rapporteurship allocation for June 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

Evoltra - clofarabine -
EMEA/H/C/000613/S/0063
Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Firdapse - amifampridine -
EMEA/H/C/001032/S/0064, Orphan
BioMarin International Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Kolbam - cholic acid -
EMEA/H/C/002081/S/0029, Orphan
Retrophin Europe Ltd, Rapporteur: Constantinos Markopoulos, PRAC Rapporteur: Agni Kapou
Request for Supplementary Information adopted on 26.04.2019.

Lamzede - velmanase alfa -
EMEA/H/C/003922/S/0004, Orphan
Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jan Neuhauser

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Otezla - apremilast - EMEA/H/C/003746/R/0027
Celgene Europe BV, Rapporteur: Peter Kiely, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Eva A. Segovia

Vargatef - nintedanib - EMEA/H/C/002569/R/0025
Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Agni Kapou
Request for Supplementary Information adopted on 26.04.2019.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

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
Request for Supplementary Information adopted on 29.05.2019.

Cosentyx - secukinumab - EMEA/H/C/003729/R/0050
Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Eva A. Segovia

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
Request for Supplementary Information adopted on 29.05.2019.

Duavive - estrogens conjugated / bazedoxifene - EMEA/H/C/002314/R/0021
Pfizer Europe MA EEIG, Rapporteur: Martina Weise, Co-Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber

Firdapse - amifampridine - EMEA/H/C/001032/R/0062, Orphan

BioMarin International Limited, Rapporteur: Kristina Dunder, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Ulla Wändel Liminga

Lynparza - olaparib - EMEA/H/C/003726/R/0029

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

Rasagiline ratiopharm - rasagiline - EMEA/H/C/003957/R/0014

Teva B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Ana Sofia Diniz Martins

Rixubis - nonacog gamma - EMEA/H/C/003771/R/0029

Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski

Trevicta - paliperidone - EMEA/H/C/004066/R/0022

Janssen-Cilag International NV, Informed Consent of Xeplion, Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga

Trulicity - dulaglutide - EMEA/H/C/002825/R/0036

Eli Lilly Nederland B.V., Rapporteur: Martina Weise, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Amelia Cupelli
Request for Supplementary Information adopted on 26.04.2019.

B.2.3. Renewals of Conditional Marketing Authorisations

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

MolMed S.p.A, Rapporteur: Carla Herberts, Co-Rapporteur: Sol Ruiz, CHMP Coordinator: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski
Request for Supplementary Information adopted on 24.05.2019.

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 11-14 June 2019 PRAC:

Rivaroxaban – XARELTO, RUNAPLAX - Signal of premature ending of the GALILEO study in patients who have received an artificial heart valve through a transcatheter aortic valve replacement (TAVR)
PRAC recommendation on a variation: **For Adoption**

Secukinumab – COSENTYX – Signal of dermatitis exfoliative generalised
PRAC recommendation on a variation: **For Adoption**

Temozolomide – TEMODAL- Signal of drug reaction with eosinophilia and systemic symptoms (DRESS)
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 June 2019 meeting:

EMEA/H/C/PSUSA/00001267/201810
(eslicarbazepine acetate)
CAPS:
Zebinix (EMEA/H/C/000988) (eslicarbazepine acetate), Bial - Portela & Cª, S.A., Rapporteur: Martina Weise
NAPS:
ESLICARBAZEPINE ACETAAT G.L. - G.L. PHARMA GMBH
PRAC Rapporteur: Martin Huber, “From: 21/10/2015 To: 21/10/2018”

EMEA/H/C/PSUSA/00002014/201810
(methotrexate)
CAPS:
Jylamvo (EMEA/H/C/003756) (methotrexate), Therakind (Europe) Limited, Rapporteur: Bruno Sepodes
Nordimet (EMEA/H/C/003983) (methotrexate), Nordic Group B.V., Rapporteur: Bruno Sepodes
NAPS:
VELOS - DIFA COOPER S.P.A
, PRAC Rapporteur: Martin Huber, “01 Jul 2017 - 31 Oct 2018”

EMEA/H/C/PSUSA/00002697/201810
(sevelamer)
CAPS:
Renagel (EMEA/H/C/000254) (sevelamer), Genzyme Europe BV, Rapporteur: Outi Mäki-Ikola
Renvela (EMEA/H/C/000993) (sevelamer carbonate), Genzyme Europe BV, Rapporteur: Bart Van der Schueren
Sevelamer carbonate Winthrop (EMEA/H/C/003971) (sevelamer carbonate), Genzyme Europe BV, Rapporteur: Bart Van der Schueren
NAPS:
NAPs - EU
PRAC Rapporteur: Laurence de Fays, "31-Oct-2017 – 30-Oct-2018"

EMEA/H/C/PSUSA/00010134/201812
(sofosbuvir)
CAPS:
Sovaldi (EMEA/H/C/002798) (sofosbuvir), Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, "06/12/2017 To: 05/12/2018"

EMEA/H/C/PSUSA/00010180/201811
(cabozantinib)
CAPS:
CABOMETYX (EMEA/H/C/004163) (cabozantinib), Ipsen Pharma, Rapporteur: Greg Markey
Cometriq (EMEA/H/C/002640) (cabozantinib), Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Period Covered From: 29/11/2017 To: 28/11/2018"

EMEA/H/C/PSUSA/00010301/201811
(ibrutinib)
CAPS:
Imbruvica (EMEA/H/C/003791) (ibrutinib), Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "11/11/2017 To: 11/11/2018"

EMEA/H/C/PSUSA/00010307/201811
(aclidinium bromide / formoterol fumarate dihydrate)
CAPS:
Brimica Genuair (EMEA/H/C/003969) (aclidinium / formoterol fumarate dihydrate), AstraZeneca AB, Rapporteur: Nithyanandan Nagercoil

Duaklir Genuair (EMEA/H/C/003745) (aclidinium / formoterol fumarate dihydrate), AstraZeneca AB, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Adam Przybylkowski, “Period Covered From: 20/11/2017 To: 19/11/2018”	
EMEA/H/C/PSUSA/00010595/201811 (nusinersen) CAPS: **Spinraza** (EMEA/H/C/004312) (nusinersen), Biogen Netherlands B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ulla Wändel Liminga, “From: 30/05/2018 To: 30/11/2018”	
EMEA/H/C/PSUSA/00010614/201812 (pentosan polysulfate sodium (for centrally authorised product)) CAPS: **elmiron** (EMEA/H/C/004246) (pentosan polysulfate sodium), bene-Arzneimittel GmbH, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Ana Sofia Diniz Martins, “01/06/2018 To: 01/12/2018”	
EMEA/H/C/PSUSA/00010644/201811 (atezolizumab) CAPS: **Tecentriq** (EMEA/H/C/004143) (atezolizumab), Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Period Covered From: 17/05/2018 To: 17/11/2018”	
EMEA/H/C/PSUSA/00010699/201811 (erenumab) CAPS: **Aimovig** (EMEA/H/C/004447) (erenumab), Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Kirsti Villikka, “Period Covered From: 17/05/2018 To: 16/11/2018”	

B.4. EPARs / WPARs

Cufence - trientine dihydrochloride - EMEA/H/C/004111, Orphan Univar BV, treatment of Wilson's disease., 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.
Doxolipad - doxorubicin hydrochloride - EMEA/H/C/004110 TLC Biopharmaceuticals B.V., treatment of breast	For information only. Comments can be sent to the EPL in case necessary.

and ovarian cancer, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	
LysaKare - L-lysine hydrochloride / L-arginine hydrochloride - EMEA/H/C/004541 Advanced Accelerator Applications, reduction of renal radiation exposure during Peptide-Receptor Radionuclide Therapy (PRRT) with lutetium (177Lu) oxodotreotide, Well-established use application (Article 10a of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Posaconazole Accord - posaconazole - EMEA/H/C/005005 Accord Healthcare S.L.U., treatment of fungal infections, Generic, Generic of Noxafil, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Posaconazole AHCL - posaconazole - EMEA/H/C/005028 Accord Healthcare S.L.U., treatment of fungal infections in adults, Generic, Generic of Noxafil, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Xyndari - glutamine - EMEA/H/C/004734, Orphan Emmaus Medical Europe Ltd., treatment of sickle cell disease, Known active substance (Article 8(3) of Directive No 2001/83/EC)	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

Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0066, Orphan Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik	
BeneFIX - nonacog alfa - EMEA/H/C/000139/II/0160 Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 06.06.2019.	Request for supplementary information adopted with a specific timetable.
Benlysta - belimumab - EMEA/H/C/002015/II/0068	

GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 26.04.2019.	
Flixabi - infliximab - EMEA/H/C/004020/II/0038 Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 20.06.2019. Request for Supplementary Information adopted on 02.05.2019, 14.03.2019.	Positive Opinion adopted by consensus on 20.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0003 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz Request for Supplementary Information adopted on 14.03.2019.	
Hemoblast - thrombin - EMEA/H/D/002769/II/0006/G BSI Group, Rapporteur: Daniela Melchiorri Opinion adopted on 14.06.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Hulio - adalimumab - EMEA/H/C/004429/II/0010/G Mylan S.A.S, Rapporteur: Bart Van der Schueren Request for Supplementary Information adopted on 06.06.2019.	Request for supplementary information adopted with a specific timetable.
Ilumetri - tildrakizumab - EMEA/H/C/004514/II/0005/G Almirall S.A, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 26.04.2019.	
Keppra - levetiracetam - EMEA/H/C/000277/II/0178/G UCB Pharma S.A., Rapporteur: Koenraad Norga Request for Supplementary Information adopted on 14.06.2019.	Request for supplementary information adopted with a specific timetable.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0073 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 29.05.2019.	
Kovaltry - octocog alfa - EMEA/H/C/003825/II/0023 Bayer AG, Rapporteur: Kristina Dunder	
Matever - levetiracetam -	Positive Opinion adopted by consensus on

EMEA/H/C/002024/II/0032 Pharmathen S.A., Generic, Generic of Keppra, Rapporteur: Ondřej Slanař Opinion adopted on 14.06.2019. Request for Supplementary Information adopted on 14.02.2019.	14.06.2019. 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.	
NovoSeven - eptacog alfa (activated) - EMEA/H/C/000074/II/0106 Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 06.06.2019, 07.03.2019, 20.09.2018.	Request for supplementary information adopted with a specific timetable.
Nulojix - belatacept - EMEA/H/C/002098/II/0059/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson Opinion adopted on 20.06.2019.	Positive Opinion adopted by consensus on 20.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ogivri - trastuzumab - EMEA/H/C/004916/II/0006/G Mylan S.A.S, Rapporteur: Koenraad Norga Opinion adopted on 14.06.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ovitrelle - choriogonadotropin alfa - EMEA/H/C/000320/II/0078 Merck Europe B.V., Rapporteur: Paula Boudewina van Hennik Opinion adopted on 06.06.2019.	Positive Opinion adopted by consensus on 06.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0029/G CSL Behring GmbH, Rapporteur: Kristina Dunder Opinion adopted on 06.06.2019. Request for Supplementary Information adopted on 02.05.2019.	Positive Opinion adopted by consensus on 06.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Thyrogen - thyrotropin alfa - EMEA/H/C/000220/II/0104/G Genzyme Europe BV, Rapporteur: Peter Kiely Request for Supplementary Information adopted on 14.06.2019.	Request for supplementary information adopted with a specific timetable.
Vizarsin - sildenafil - EMEA/H/C/001076/II/0029 KRKA, d.d., Novo mesto, Generic, Generic of	

Viagra, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 28.02.2019, 22.11.2018.	
Zessly - infliximab - EMEA/H/C/004647/II/0007 Sandoz GmbH, Rapporteur: Bjorg Bolstad Opinion adopted on 14.06.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1519/G **HyQvia-EMEA/H/C/002491/WS1519/0047/G** **Kiovig-EMEA/H/C/000628/WS1519/0089/G** Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 14.06.2019. Request for Supplementary Information adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.06.2019. 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.	
WS1620 **Humalog-EMEA/H/C/000088/WS1620/0175** **Liprolog-EMEA/H/C/000393/WS1620/0136** Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 14.06.2019.	Request for supplementary information adopted with a specific timetable.
WS1625/G **Blitzima-EMEA/H/C/004723/WS1625/0025/G** **Ritemvia-EMEA/H/C/004725/WS1625/0025/G** **Truxima-EMEA/H/C/004112/WS1625/0028/G** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz Opinion adopted on 06.06.2019.	Positive Opinion adopted by consensus on 06.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Hexacima-EMEA/H/C/002702/WS1592/0089/G	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP

Hexaxim-EMEA/H/W/002495/WS1592/0094/G **Hexyon-EMEA/H/C/002796/WS1592/0093/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 14.06.2019.	Members were in agreement with the CHMP recommendation.

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

Aclasta - zoledronic acid - EMEA/H/C/000595/II/0072 Novartis Europharm Limited, Rapporteur: Kristina Dunder, "Update of sections 4.2 and 5.1 upon request of the CHMP following assessment of P46/036 based on final results from study ZOL446H2337; this is a randomised, double-blind, placebo-controlled efficacy and safety study of intravenous zoledronic acid administered twice yearly compared to placebo in children with glucocorticoid-induced osteoporosis (GIO) which was part of the main clinical measure of the Aclasta Paediatric Investigational plan (PIP). In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 26.04.2019.	
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 29.05.2019, 28.03.2019, 13.12.2018, 04.10.2018.	
Advagraf - tacrolimus -	Request for supplementary information adopted

EMEA/H/C/000712/II/0054 Astellas Pharma Europe B.V., Rapporteur: Jayne Crowe, “Update of section 4.2 of the SmPC to include a more clear statement for physicians regarding the potential risk of uncontrolled substitution between different tacrolimus formulations, even with those where BE has been proven, in order to minimise the risk of under or over exposure to tacrolimus.” Request for Supplementary Information adopted on 14.06.2019.	with a specific timetable.
Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0151 Amgen Europe B.V., Rapporteur: Martina Weise, “Submission of the final analysis of clinical study report (CSR, 10 May 2018) for Study 20110226 to fulfill the post-marketing authorization measure (category 3 pharmacovigilance activity in the Aranesp EU Risk Management Plan (RMP). Study 20110226 is a phase 3, multicenter, randomized, double-blind, parallel group study - START-CKD: Strategies Using Darbepoetin alfa to Avoid Transfusions in Chronic Kidney.” Request for Supplementary Information adopted on 04.04.2019.	
Biktarvy - bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449/II/0008/G Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, “Update of section 4.5 of the SmPC in order to remove the recommendation for caution when methadone is co-administered with Biktarvy based on final results from study AD-141-2321, an in vitro assessment of human Cytochrome P450 inhibition potential of GS-943389 (the sulfate metabolite, M20, of bictegravir). The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to remove reference to boceprevir in sections 4.4 and 4.5 of the SmPC and in the Package Leaflet as it is no longer available in the EU; as well as to introduce some minor editorial corrections throughout the SmPC, Annex II and Package Leaflet. Submission of the final report from study AD-141-2322, an in vitro assessment of the inhibition potential of GS-943389 against human P-gp and BCRP transporters.” Request for Supplementary Information adopted	

on 31.01.2019.

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.”

Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0075

UCB Pharma S.A., Rapporteur: Kristina Dunder, “Update of section 4.1 of the SmPC to add more clarity to the axial spondyloarthritis (axSpA) indication statement in particular with regard to the terms radiographic versus non-radiographic axSpA and update of sections 4.8 and 5.1 of the SmPC to reflect the availability of additional safety information from the phase 3 clinical study designed to evaluate the safety and efficacy of certolizumab in subjects with active axSpA without X-ray evidence of ankylosing spondylitis and objective signs of inflammation (AS0006)” Request for Supplementary Information adopted on 28.03.2019.

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.” Request for Supplementary Information adopted on 16.05.2019.

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."	
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."	
ELOCTA - efmoroctocog alfa - EMEA/H/C/003964/II/0030 Swedish Orphan Biovitrum AB (publ), Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2 and 4.8 of the SmPC in order to remove the class wording that no data are available in previously untreated patients and update the frequency category for blood and lymphatic system disorders in previously untreated patients following interim results from study 997HA306, this is an ongoing open-label, single-arm, multicentre study evaluating the safety and efficacy of rFVIIIFc in paediatric previously untreated patients with severe haemophilia A when used according to local standard of care; the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to delete the non-mandatory list of local representatives." Opinion adopted on 06.06.2019. Request for Supplementary Information adopted on 04.04.2019, 31.01.2019.	Positive Opinion adopted by consensus on 06.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0046 Merck Sharp & Dohme B.V., Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.3, 4.4 and 4.9 of the SmPC in order to revise the current text regarding Ovarian Hyperstimulation	Request for supplementary information adopted with a specific timetable.

Syndrome (OHSS) to add clarity and remove clinical advice describing specific clinical interventions for reducing OHSS that have become outdated, based on post-marketing data and literature review. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder to include some editorial changes to the Package Leaflet." Request for Supplementary Information adopted on 14.06.2019.	
EXJADE - deferasirox - EMEA/H/C/000670/II/0064 Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "To update the Risk Management Plan (RMP) version 16.0 for Exjade (deferasirox, EMEA/H/C/000670), covering all formulations (dispersible tablets, film-coated tablets and granules). With this update, the MAH introduces the alignment with requirements of the new RMP template (as per the revised Good Pharmacovigilance Practices (GVP) Module V Rev.2) and consequential removal of the food interaction and drug-drug interactions (DDI) from the list of important identified risks. In addition, "drug reaction with eosinophilia and systemic symptoms" (DRESS) has been reclassified from important potential risk to important identified risk. The reclassification of DRESS was agreed with the PRAC during a previous procedure (EMEA/H/C/PSUSA/00000939/201710). Additional minor changes are have been also implemented in the RMP. With this variation, the Health Care Professional (HCP) guide is also updated." Opinion adopted on 14.06.2019. Request for Supplementary Information adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Exviera - dasabuvir - EMEA/H/C/003837/II/0044 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Update of section 4.3 of the SmPC to contraindicate the concomitant use with apalutamide, a strong CYP3A inducer, as well as to update section 4.5 of the SmPC on the interaction with apalutamide. The Package Leaflet is updated accordingly. In	Positive Opinion adopted by consensus on 06.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

addition, the MAH took the opportunity to implement minor editorial changes." Opinion adopted on 06.06.2019.	
IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0027, Orphan CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.4 of the SmPC to update the warning with regards to inhibitor development. Section 4.8 of the SmPC and the PL have been updated accordingly." Request for Supplementary Information adopted on 14.06.2019.	Request for supplementary information adopted with a specific timetable.
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 an 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 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.	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0074 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Submission of the final CSR version 03 for KEYNOTE-013 summarising final data from the rrcHL cohort." Request for Supplementary Information adopted on 14.06.2019.	Request for supplementary information adopted with a specific timetable.
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 cut-off 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)."	
Kyprolis - carfilzomib - EMEA/H/C/003790/II/0031, Orphan Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 to add a once-weekly dose regimen for carfilzomib (Kyprolis) at 20/70 mg/m^2 in combination with dexamethasone (Kd) for the treatment of the currently indicated patient population. The MAH took the opportunity to implement editorial changes to the SmPC and Patient Information Leaflet (PIL) due to the revised excipients guideline (EMA/CHMP/302620/2017). The PIL is updated accordingly." Request for Supplementary Information adopted on 28.02.2019, 15.11.2018.	See agenda item 9.1
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."	
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."	See agenda item 9.1
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)."	
Repatha - evolocumab - EMEA/H/C/003766/II/0031 Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC based on the final results from study 20110271 (TAUSSIG) listed as a category 3 study in the RMP, submitted in order to fulfil MEA 003 and article 46 of Regulation EC No 1901/2006; this is a multicenter, open-label study to assess the long-term safety, tolerability and efficacy of AMG 145 (evolocumab) on LDL-C in adult and adolescent subjects with severe familial hypercholesterolemic (FH), including subjects with homozygous familial hypercholesterolemia (HoFH). In addition, the Marketing authorisation holder (MAH) took the opportunity to make a correction to the Labelling." Request for Supplementary Information adopted on 28.03.2019.	
Saxenda - liraglutide - EMEA/H/C/003780/II/0023 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information regarding hypoglycaemia in patients with type 2 diabetes mellitus treated with insulin based on the final results from the Phase 3b clinical trial NN8022-4272 (SCALE Insulin), undertaken to investigate the effect and safety of liraglutide 3.0 mg in subjects with overweight or obesity and type 2 diabetes mellitus treated with basal insulin. The Package Leaflet is updated accordingly." Opinion adopted on 14.06.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Sprycel - dasatinib - EMEA/H/C/000709/II/0064 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Sinan B. Sarac, "Submission of results from existing and new PK analyses together with the review of the literature data on the dasatinib PK profile in fasted conditions to assess implications arising for the recommendation for administration, as requested by the CHMP." Request for Supplementary Information adopted	

on 28.03.2019, 15.11.2018.	
Sutent - sunitinib - EMEA/H/C/000687/II/0074 Pfizer Europe MA EEIG, Rapporteur: Daniela Melchiorri, “Submission of the final analyses of the overall survival data, and the additional biomarker analyses collected from study A6181202 (multi-centre, single-arm, open-label, Phase 4 clinical trial of sunitinib in patients with progressive, advanced/metastatic, well-differentiated, unresectable pancreatic neuroendocrine tumours (pNET)).” Opinion adopted on 14.06.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Taltz - ixekizumab - EMEA/H/C/003943/II/0026/G Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, “Type II- C.I.4 -Update of section 5.1 of the SmPC based on results of study RHCF - a 52-Week Multicenter, Randomized, Open-Label, Parallel-Group Study Evaluating the Efficacy and Safety of Ixekizumab versus Adalimumab in Patients with Psoriatic Arthritis Who Are Biologic Disease-Modifying Anti-Rheumatic Drug Naïve. Type II- C.I.4 -Update of section 4.5 of the SmPC based on results of study RHBU – a study evaluating of the effect of ixekizumab on the pharmacokinetics of cytochrome P450 substrates in patients with moderate-to-severe plaque psoriasis.” Request for Supplementary Information adopted on 14.06.2019.	Request for supplementary information adopted with a specific timetable.
Thyrogen - thyrotropin alfa - EMEA/H/C/000220/II/0102 Genzyme Europe BV, Rapporteur: Peter Kiely, “Update of sections 4.4 and 5.1 of the SmPC in order to update the safety information with HiLo and ESTIMABL1 long term follow-up data study results as well as fulfill FUM35. Additionally, the sodium content provision wording in the Package Leaflet is aligned to the Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal products for human use" (SANTE-2017-11668). Few editorial changes are also made and the name of an excipient in the German translation is also corrected.” Request for Supplementary Information adopted on 26.04.2019.	

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.	
Victoza - liraglutide - EMEA/H/C/001026/II/0050 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.2 and 5.1 of the SmPC, based on the phase 3b study NN2211-4315 (LIRA-ADD2SGLT2i), to include data on liraglutide vs placebo as add-on to SGLT2 inhibitors (+/- metformin) in subjects with type 2 diabetes mellitus. The Package Leaflet has been updated accordingly.” Request for Supplementary Information adopted on 26.04.2019.	
Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/II/0053 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, “Update of section 4.3 of the SmPC to contraindicate the concomitant use with lomitapide, a CYP3A4 substrate, and apalutamide, a strong CYP3A inducer, as well as update of section 4.5 of the SmPC on the potential interactions with apalutamide, encorafenib, ibrutinib and lomitapide. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes.” Opinion adopted on 06.06.2019.	Positive Opinion adopted by consensus on 06.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xeloda - capecitabine - EMEA/H/C/000316/II/0083 Roche Registration GmbH, Rapporteur: Janet Koenig, “Update of section 4.6 of the SmPC in order to add advice on post treatment contraception period and wash out period before initiation of breastfeeding. The Package leaflet is updated accordingly.” Request for Supplementary Information adopted on 26.04.2019.	
XGEVA - denosumab -	Request for supplementary information adopted

EMEA/H/C/002173/II/0069 Amgen Europe B.V., Rapporteur: Kristina Dunder, “Update of SmPC sections 4.2, 4.8, 5.1 and 5.2 based on the final analysis from study 20062004; a phase 2, open-label, single-group study to evaluate the safety and pharmacokinetics of denosumab in adult and adolescent subjects with giant cell tumour of bone (GCTB). The final CSR for study 20062004 was previously assessed by CHMP as part of procedure P46 027 and the finalisation of the study addresses the final PIP measure. Further, section 4.8 of the SmPC is being updated to include the new ADR ‘alopecia’ with a frequency of ‘common’, upon request by PRAC following the assessment of PSUSA/00009119/201809. In addition, the MAH took the opportunity to update the description of ONJ incidence in section 4.8 of the SmPC in order to express events per 100 patient years without a percentage sign. The Package Leaflet has been updated accordingly.” Request for Supplementary Information adopted on 14.06.2019.	with a specific timetable.
WS1511/G **Advagraf-EMEA/H/C/000712/WS1511/0052/G** **Modigraf-EMEA/H/C/000954/WS1511/0031/G** Astellas Pharma Europe B.V., Lead Rapporteur: Jayne Crowe, “Update of sections 4.5 and 4.8 of the SmPC to add the drug-drug interaction with letemovir and to add the febrile neutropenia with frequency unknown, based on the cumulative review of the MAH safety database. Update of section 4.6 of the SmPC to add the information on pregnancy and lactation following the cumulative review of the cases reported in the MAH global safety database, published literature and the transplantation pregnancy exposure registry. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor editorial changes throughout the PI and to implement the wording from the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'.” Request for Supplementary Information adopted on 14.06.2019, 14.03.2019.	Request for supplementary information adopted with a specific timetable.
WS1598	Positive Opinion adopted by consensus on

Cymbalta-EMEA/H/C/000572/WS1598/0079 **Duloxetine Lilly-EMEA/H/C/004000/WS1598/0016** **Xeristar-EMEA/H/C/000573/WS1598/0082** **Yentreve-EMEA/H/C/000545/WS1598/0064** Eli Lilly Nederland B.V., Duplicate, Duplicate of Ariclaim, Yentreve, Lead Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 5.1 to reflect on the data obtained from the paediatric study HMGW, submitted the final report for the paediatric study HMGW, a Phase 3b, Randomised, Double-Blind, Placebo-Controlled, Clinical Trial of Duloxetine in adolescent Juvenile Primary Fibromyalgia Syndrome (JPFS) population." Opinion adopted on 14.06.2019.	14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1607 **Kisplyx-EMEA/H/C/004224/WS1607/0023** **Lenvima-EMEA/H/C/003727/WS1607/0025** 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.	
WS1613 **Epclusa-EMEA/H/C/004210/WS1613/0039** **Vosevi-EMEA/H/C/004350/WS1613/0029** Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to add new information regarding co-administration with atorvastatin, based on final results from study GS-US-342-4034. Study GS-US-342-4034 was a phase 1 study to evaluate the effect of sofosbuvir/velpatasvir fixed dose combination on the pharmacokinetics of atorvastatin. The Package Leaflet is updated accordingly. In addition, the Worksharing Applicant took the opportunity to amend Annex II of the Product Information with regards to the due date for	Request for supplementary information adopted with a specific timetable.

submission of study DAA-PASS. This study is designed to evaluate the recurrence of hepatocellular carcinoma and the date has been postponed from Q2 2021 to Q2 2023, as approved in the framework of WS1476. Furthermore, the MAH implemented minor editorial updates throughout the Product Information." Request for Supplementary Information adopted on 20.06.2019.	
WS1617 **Filgrastim** **Hexal-EMEA/H/C/000918/WS1617/0050** **Zarzio-EMEA/H/C/000917/WS1617/0051** Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 6.6 of the SmPC in order to remove the latex warning based on company and post marketing data. The Package Leaflet is updated accordingly." Opinion adopted on 14.06.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
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.”	

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 29.05.2019, 28.02.2019, 20.09.2018.	See agenda item 9.1
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."	
Brinavess - vernakalant - EMEA/H/C/001215/II/0035 Correvio, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information following updates to the Company Core Safety Datasheet (CCDS) based on the results of an integrated safety analysis performed on data of existing clinical studies with a stronger emphasis on treatment-related ADRs and an incidence rate above one percent. The Package Leaflet was updated accordingly. The RMP version 7.0 has also been submitted and incorporates the results from the new safety analysis. In addition the results from completed observational Cohort SPECTRUM study (A Prospective Observational Registry Study to Characterise Normal Conditions of Use, Dosing and Safety Following Administration of Vernakalant IV Sterile Concentrate: PASS Protocol 6621-049) currently under assessment within Brinavess II/34 were included in the updated RMP. In addition, the Marketing authorisation holder (MAH) took the opportunity to update sections 4.2, 4.4, 4.6, 4.7, 4.8, 5.1, 5.2, 5.3, 6.4 of the SmPC, Annex II, Labelling sections 3 and 5, Package Leaflet sections 2, 4, 5 and 6 to include editorial changes, to correct typographical errors and to bring the PI in line with the latest QRD template version 10 and well as to update statements related to the excipients in the SmPC and Package Leaflet in line with the EC Guideline on "Excipients in the Labelling and Package Leaflet of medicinal products for human use" of March 2018 and the EMA Annex to the EC Guideline of October 2017 (SANTE-2017-11668)." Request for Supplementary Information adopted on 14.06.2019.	Request for supplementary information adopted with a specific timetable.
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, GRECO), 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 29.05.2019, 28.02.2019.	
Flebogamma DIF - human normal immunoglobulin - EMEA/H/C/000781/II/0059/G Instituto Grifols, S.A., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 4.8 of the SmPC for Flebogamma DIF 100 mg/ml in order to update the safety information based on the final results from study IG0601: A multi-center, prospective, open-label, clinical trial to assess the safety and the efficacy of a new intravenous immune globulin (IGIV3I Grifols 10%) in patients with idiopathic (immune) thrombocytopenic purpura. The Package Leaflet is updated accordingly. Update of section 4.8 of the SmPC to revise the adverse drug reactions for both strengths based on all completed studies previously submitted. The Package Leaflet is updated accordingly. Update of SmPC according to the Guideline on core SmPC for human normal immunoglobulin for intravenous administration (IVIg) which came into effect on 01 January 2019. With this submission, the MAH proposes the following changes in alignment with the guideline: - Inclusion of Chronic inflammatory demyelinating polyneuropathy (CIDP) and Multifocal motor neuropathy (MMN) as new therapeutic indications - Modification of Secondary immunodeficiencies (SID) therapeutic indication definition. The Package Leaflet is updated accordingly. The RMP version 7.0 has also been submitted."	

Request for Supplementary Information adopted on 26.04.2019.	
IBRANCE - palbociclib - EMEA/H/C/003853/II/0019/G Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark, "Update of section 4.8 of the SmPC in order to include ILD/pneumonitis as ADRs based on a safety cumulative review together with reclassification of the risk from potential to identified in the RMP (version 1.6). The Package Leaflet is updated accordingly. The MAH has also submitted the updated RMP version 1.6 in order to remove long term use from missing information in the list of safety concerns. In addition, the MAH is proposing to change the due date for submission of the final CSR of study A5481027 listed as a Category 3 study in the RMP." Request for Supplementary Information adopted on 14.06.2019.	Request for supplementary information adopted with a specific timetable.
Iclusig - ponatinib - EMEA/H/C/002695/II/0051, Orphan Incyte Biosciences Distribution B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of the RMP to version 19, including deletion of previously agreed safety concerns. These deletions are proposed in line with the guideline on Good Pharmacovigilance Practices (GVP) Module V on RMP (revision 2 - dated on 31 March 2017). Other updates include: review of the categorisation of the posterior reversible encephalopathy syndrome (PRES) risk in the RMP in line with the request from PSUSA/00010128/201712; correction of the category (from Category 3 to 1) of the study AP24534-14-203, an imposed Annex II condition; revision of the due date for the submission of this study report to August 2021, as described in the Iclusig PI, and as agreed as part of procedure EMEA/H/C/002695/ANX/016." Request for Supplementary Information adopted on 14.06.2019.	Request for supplementary information adopted with a specific timetable.
Inovelon - rufinamide - EMEA/H/C/000660/II/0052, Orphan Eisai GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of section 4.2 of the SmPC in order to include an additional method of administration via feeding	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

tube for Inovelon oral suspension. This fulfills the CHMP recommendation to evaluate the feasibility of administrating the rufinamide oral suspension via an enteral feeding tube adopted with variation II/45. The RMP version 11 has been submitted." Opinion adopted on 14.06.2019.	
Intuniv - guanfacine - EMEA/H/C/003759/II/0015 Shire Pharmaceuticals Ireland Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Maria del Pilar Rayon, "Update of section 4.5 of the SmPC in order to remove the statement on potential drug interactions with drugs that inhibit OCT1 based on final results from study V8953M-SPD503; this is a non-clinical study (Transporter Interaction - OCT1 inhibition); The RMP version 3.0 has also been submitted." Opinion adopted on 14.06.2019. Request for Supplementary Information adopted on 11.04.2019, 14.02.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kisqali - ribociclib - EMEA/H/C/004213/II/0003/G Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark, "C.I.4: Update of section 5.2 of the SmPC in order to reflect on results from study CLEE011A2109: A Phase I, open label, multi-centre, parallel cohort, single dose study to evaluate the pharmacokinetics of LEE011 in healthy subjects with normal hepatic function and subjects with impaired hepatic function; C.I.4: Update of sections 4.2 and 5.2 of the SmPC in order to reflect on results from study CLEE011A2116-Part I: A phase I, open label, multicentre, parallel-group, single dose two-staged study to evaluate the pharmacokinetics and safety of a single 400 mg oral dose of LEE011 in subjects with varying degrees of impaired renal function compared to matched healthy volunteers with normal renal function. The RMP version 2.0 has also been submitted." Request for Supplementary Information adopted on 17.01.2019, 06.09.2018.	
Mircera - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/II/0068	Request for supplementary information adopted with a specific timetable.

Roche Registration GmbH, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, “Submission of the final report from study BH21260 listed as a category 3 study in the RMP (MEA008.5). This is a randomized, controlled, open-label, multicenter, parallel-group study to assess all-cause mortality and cardiovascular morbidity in patients with chronic kidney disease on dialysis and those not on renal replacement therapy under treatment with Mircera or reference ESAs. The RMP (version 12.0) is updated accordingly and transitioned to the new EU RMP template in line with the revised Good Pharmacovigilance Practice (GVP) Module V (Revision 2) guideline.” Request for Supplementary Information adopted on 14.06.2019, 17.01.2019, 04.10.2018.	
Movymia - teriparatide - EMEA/H/C/004368/II/0010 STADA Arzneimittel AG, Duplicate, Duplicate of Terrosa, Rapporteur: Milena Stain, PRAC Rapporteur: Ronan Grimes, “Submission of the final clinical study report from Study RGB1023O31; a Phase III, multi-centre, randomised, active-controlled, parallel-group, comparative efficacy/safety study. An updated RMP version 1.4 was agreed during the procedure.” Opinion adopted on 14.06.2019. Request for Supplementary Information adopted on 11.04.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Signifor - pasireotide - EMEA/H/C/002052/II/0041/G, Orphan Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, “Update of section 4.8 of the SmPC based on the final CSR from Study CSOM230B2219; a multi-center, randomized, open-label, Phase IV study to investigate the management of pasireotide-induced hyperglycemia with incretin based therapy or insulin in adult patients with Cushing’s disease or acromegaly (listed as a category 3 study in the RMP). A revised RMP version 7.0, updated in line with the revised GVP Module V, including changes to the safety concerns, was provided as part of the application.” Request for Supplementary Information adopted on 14.06.2019.	Request for supplementary information adopted with a specific timetable.

Spinraza - nusinersen -
EMEA/H/C/004312/II/0014, Orphan
Biogen Netherlands B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ulla Wändel Liminga, "C.I.13: Submission of the final report from Phase 2 Study SM202 (EMBRACE or CS7) listed as a category 3 study in the RMP. This is a Phase 2, randomized, double-blind, sham-procedure-controlled study to assess the safety and tolerability and explore the efficacy of ISIS 396443 (BIIB058) administered intrathecally in subjects with spinal muscular atrophy who are not eligible to participate in the clinical studies ISIS 396443-CS3B or ISIS 396443-CS4 due to age at screening and/or SMN2 copy number.
An updated RMP version 10.1 has also been submitted."

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."

Tecentriq - atezolizumab -
EMEA/H/C/004143/II/0022
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of sections 4.2 and 5.2 of the SmPC in order to add 2 dosing regimens, 840 mg every 2 weeks and 1680 mg every 4 weeks administered as an IV infusion for the approved indications, based on results of population pharmacokinetics modelling and simulation analyses (report No. 1085557) and supported by exposure-response analyses (report No. 1087176). The package leaflet is updated accordingly.
An updated RMP is also provided in order to reflect the proposed new dosing regimens, and to align the indication statement for metastatic urothelial carcinoma with the SmPC.

Moreover, the due date for submission of RMP commitments and an Annex II condition are proposed to be updated." Request for Supplementary Information adopted on 26.04.2019.	
Terrosa - teriparatide - EMEA/H/C/003916/II/0009 Gedeon Richter Plc., Rapporteur: Milena Stain, PRAC Rapporteur: Ronan Grimes, "Submission of the final clinical study report from Study RGB1023O31; a Phase III, multi-centre, randomised, active-controlled, parallel-group, comparative efficacy/safety study. An updated RMP version 1.4 was agreed during the procedure." Opinion adopted on 14.06.2019. Request for Supplementary Information adopted on 11.04.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Truberzi - eluxadoline - EMEA/H/C/004098/II/0009/G Allergan Pharmaceuticals International Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Adam Przybylkowski, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update the safety information based on results from PK study ELX-PK-01 listed as a category 3 study in the RMP; this is a Single-dose, Open-label, Pharmacokinetic study of Eluxadoline in Healthy Subjects with normal Renal Function and Patients with Renal Impairment. Update of sections 4.4 and 4.8 of the SmPC following Company Core Data Sheet (CCDS) update based on review of clinical safety data and post- marketing safety data. Section 4.3 has been updated to add clarification in line with section 4.4. and section 5.1 has been updated to add Pharmacotherapeutic Group and ATC code. The RMP version 3.0 has also been submitted. The Package Leaflet is updated accordingly. In addition, the MAH also took the opportunity to change "eluxadoline" to "Truberzi" when referring to the medicinal product throughout the SmPC." Request for Supplementary Information adopted on 28.03.2019.	
Uptravi - selexipag - EMEA/H/C/003774/II/0022 Janssen-Cilag International N.V., Rapporteur: Martina Weise, PRAC Rapporteur: Adrien Inoubli, "Update of sections 4.2, 4.4 and 4.5 of the SmPC	

in order to update the safety information based on the final results from study AC-065-117 a listed category 3 study in the RMP which is a clinical pharmacology drug-drug interaction (DDI) study, evaluating the effect of clopidogrel a moderate inhibitor of CYP2C8, on the pharmacokinetics of selexipag and its active metabolite ACT-333679. The package leaflet is updated accordingly. The RMP version 6.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct minor discrepancies in the SmPC." Request for Supplementary Information adopted on 11.04.2019, 14.02.2019.	
Vimpat - lacosamide - EMEA/H/C/000863/II/0073/G UCB Pharma S.A., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.2, 4.4, 4.5 and 4.8 of the SmPC in order to include new safety information on cardiac arrhythmias based on safety signal assessment report (SSAR). In addition, the MAH took the opportunity to correct the frequency of the adverse event 'coordination abnormal' in section 4.8 of the SmPC from 'common' to 'uncommon' as the frequency of this ADR was erroneously classified as 'common' due to rounded ADR percentages in the initial SmPC. The Package Leaflet is updated accordingly. The RMP version 13.1 has also been submitted." Opinion adopted on 14.06.2019. Request for Supplementary Information adopted on 11.04.2019, 14.02.2019, 04.10.2018.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xolair - omalizumab - EMEA/H/C/000606/II/0093 Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of section 4.6 of the SmPC based on the data from the Xolair Pregnancy Registry (EXPECT) and final study report Q2952g listed as a category 3 study in the RMP; this is an observational study to evaluate pregnancy outcomes and estimate the incidence of spontaneous fetal loss in pregnant women exposed to omalizumab prenatally and to explore the potential risk to newborn infants exposed via breast milk. The Package Leaflet is proposed to be updated accordingly.	

The RMP version 14.0 has also been submitted." Request for Supplementary Information adopted on 28.03.2019, 13.12.2018.	
Yervoy - ipilimumab - EMEA/H/C/002213/II/0064 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of section 4.8 of the SmPC in order to update the safety information following final results from study CA184143 (A Multi-National, Prospective, Observational Study in Patients with Unresectable or Metastatic Melanoma) listed as a category 3 study in the RMP (MEA017.11); The RMP has been updated accordingly (submitted version 26.0). In addition, the Marketing authorisation holder (MAH) took the opportunity to update the RMP in regards to already assessed MEA 036.1 concerning protocol synopsis on the extension of the Dutch Melanoma Treatment Registry (DMTR) to paediatric melanoma patients treated with ipilimumab. Furthermore the MAH took the opportunity to request a 6-month shift in the dates associated to the next implementation steps of the DMTR extension (Registration of paediatric patients in the DMTR register and final CSR submission). Editorial changes have also been included in section 5.1 of the SmPC to provide more clarity on whether studies relate to melanoma or RCC and to monotherapy or combination therapy with nivolumab." Request for Supplementary Information adopted on 14.06.2019, 14.03.2019.	Request for supplementary information adopted with a specific timetable.
Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0043 Pfizer Ireland Pharmaceuticals, Rapporteur: Alar Irs, PRAC Rapporteur: Maia Uusküla, "Update of section 4.2 of the SmPC in order to provide dosing recommendations for a high-dose regimen of ceftaroline fosamil in paediatric patients from 2 months to less than18 years of age for the treatment of complicated skin and soft tissue infections (cSSTI) for which Staphylococcus aureus is known or suspected of having minimum inhibitory concentrations (MIC) of 2 or 4 mg/L based on final study report of extrapolation study PMAR-EQDD-C266b-DP4-826. The RMP version 18.0 has also been submitted." Request for Supplementary Information adopted	

on 28.03.2019.	
WS1518 **Epclusa-EMEA/H/C/004210/WS1518/0034** **Harvoni-EMEA/H/C/003850/WS1518/0077** **Sovaldi-EMEA/H/C/002798/WS1518/0055** **Vosevi-EMEA/H/C/004350/WS1518/0025** Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC (Epclusa, Harvoni), sections 4.2, 4.4, 5.1 and 5.2 (Sovaldi) and 4.2, 4.8 and 5.2 (Vosevi) in order to add new information regarding the use of the sofosbuvir-containing products in patients with renal impairment, based on final results from studies GS-US-342-4062, GS-US-337-4063 and GS-US-334-0154, listed as a category 3 study in the RMP and study GS-US-338-1125. Study GS-US-342-4062 was a phase 2, multi-centre, open-label study to evaluate the efficacy and safety of sofosbuvir/velpatasvir for 12 weeks in subjects with chronic HCV infection who are on dialysis for end stage renal disease. Study GS-US-337-4063 was a phase 2, multi-centre, open-label study to evaluate the efficacy and safety of ledipasvir/sofosbuvir in subjects with genotype 1, 4, 5 and 6 chronic HCV infection who are on dialysis for end stage renal disease. Study GS-US-334-0154 was a phase 2b, open label study of 200 mg or 400 mg Sofosbuvir+ribavirin for 24 weeks in Genotype 1 or 3 HCV infected subjects with renal insufficiency. Study GS-US-338-1125 was a phase 1, open-label, parallel-group, single-dose study to evaluate the pharmacokinetics of voxilaprevir in subjects with normal renal function and severe renal impairment. The Package Leaflet is updated accordingly. The RMPs have also been submitted for each of the products in this work-sharing procedure." Request for Supplementary Information adopted on 14.06.2019, 11.04.2019.	Request for supplementary information adopted with a specific timetable.

B.5.4. PRAC assessed procedures

PRAC Led	Positive Opinion adopted by consensus on

Adasuve - loxapine - EMEA/H/C/002400/II/0030 Ferrer Internacional s.a., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the category 3 final report from Drug Utilization study AMDC-204-403 EU (A Multinational Retrospective Medical Record Review to Evaluate Utilization Patterns of Adasuve-Staccato loxapine for inhalation in agitated persons in routine clinical care). In addition, the MAH also submitted the second report with results of the healthcare professional survey on the effectiveness of the additional risk minimisation measures in Annex 7 of the RMP submitted with this variation." Opinion adopted on 14.06.2019. Request for Supplementary Information adopted on 11.04.2019.	14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Betmiga - mirabegron - EMEA/H/C/002388/II/0030** Astellas Pharma Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of the final report of the Drug Utilization Study of mirabegron using real-word healthcare databases from the NL, ES, UK and FI (study 178-PV-002), as agreed via MEA 009.2." Opinion adopted on 14.06.2019. Request for Supplementary Information adopted on 17.01.2019, 04.10.2018.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
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." Opinion adopted on 14.06.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Request for Supplementary Information adopted on 14.03.2019.	
PRAC Led **Cotellic - cobimetinib - EMEA/H/C/003960/II/0016** Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 4 in order to align with the current GVP Rev 2. Additionally, in line with the request from PRAC in the AR dated 31 Oct 2018, the agreed wording is implemented." Request for Supplementary Information adopted on 14.06.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Edurant - rilpivirine - EMEA/H/C/002264/II/0034** Janssen-Cilag International NV, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 8.1 in order to remove 'bleeding disorders' as an important potential risk as agreed by PRAC during procedure PSUSA/00009282/201805. In addition, the MAH took the opportunity to remove some of the safety concerns and remove/reclassify additional pharmacovigilance activities (Category 4) in line with the revision 2 of the RMP template." Opinion adopted on 14.06.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Hulio - adalimumab - EMEA/H/C/004429/II/0009** Mylan S.A.S, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 3.0 in order to do the following changes: As part of Post-Authorization Measures (category 3 according to the RMP), the applicant has to submit the study protocol on a longitudinal observational study of patients with rheumatoid arthritis treated with biologic and other new advanced targeted therapies by 31 March 2019 (Ref No.MEA/PRO 002). The applicant now proposes to use a different registry (RABBIT) than the previously agreed BSRBR-RA and to update the study milestones in the	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

pharmacovigilance plan. Furthermore, the submitted RMP consolidates updates approved in two other variations (procedures EMEA/H/C/004429/II/0004 and EMEA/H/C/004429/IB/0007)." Opinion adopted on 14.06.2019.	
PRAC Led **Kiovig - human normal immunoglobulin - EMEA/H/C/000628/II/0091** Baxter AG, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 9.0 in order to include the new indication chronic inflammatory demyelinating polyradiculoneuropathy [CIDP] and update the list of safety concerns (implementation of new specifications from GCP Module V (Rev 2)." Request for Supplementary Information adopted on 14.06.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Kisplyx - lenvatinib - EMEA/H/C/004224/II/0024** Eisai GmbH, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Bjorg Bolstad, "Submission of an updated RMP version 11.1 in order to update the study design for Study E7080-G000-218 (MEA 007) from double-blind to open label as requested by the CHMP from post authorisation measure MEA 06.1. In addition the MAH is taking the opportunity to introduce minor administrative changes to the RMP." Request for Supplementary Information adopted on 14.06.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Otezla - apremilast - EMEA/H/C/003746/II/0023** Celgene Europe BV, Rapporteur: Peter Kiely, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of an updated RMP version 11.4 in order to reclassify and/or rename the known safety concerns associated with the use of apremilast in accordance with the new Guideline on GVP Module V. In addition, the RMP is converted to the RMP template Revision 2. The MAH also took the opportunity to update the milestones of the pharmacovigilance plan of	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

ongoing category 3 studies included in the RMP." Opinion adopted on 14.06.2019. Request for Supplementary Information adopted on 14.03.2019, 31.10.2018.	
PRAC Led **Ozurdex - dexamethasone - EMEA/H/C/001140/II/0035** Allergan Pharmaceuticals Ireland, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "C.I.13: Submission of the final report from study CMO-EPI-EYE-0522 listed as a category 3 study in the RMP. This is an observational, cross-sectional study conducted in France, Germany, Spain, and the UK having as primary objective the assessment of the effectiveness of the educational material provided to the treating physicians." Request for Supplementary Information adopted on 14.06.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Remicade - infliximab - EMEA/H/C/000240/II/0218** Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final study report on Remicade for the RABBIT Cohort 2 portion of the registry. Rheumatoide Arthritis - Beobachtung der Biologika-Therapie (RABBIT) is a German RA registry established as a prospective observational cohort study on the long-term safety and effectiveness of biologic disease-modifying anti-rheumatic drugs in patients with RA. RMP (v19) was updated with the conclusion of the study. The MAH also revised the list of safety concerns in the RMP as requested in the assessment of LEG 156." Opinion adopted on 14.06.2019. Request for Supplementary Information adopted on 11.04.2019, 17.01.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Revlimid - lenalidomide - EMEA/H/C/000717/II/0110, Orphan** Celgene Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau,	Request for supplementary information adopted with a specific timetable.

"Submission of the final results of the CC-5013-PASS-001 study report dated 2 Nov 2018, for the non-interventional post-authorisation safety study (PASS) of patients treated with lenalidomide." Request for Supplementary Information adopted on 14.06.2019.	
PRAC Led **Simponi - golimumab - EMEA/H/C/000992/II/0085** Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from study (CNTO148ART4002) listed as a category 3 study in the RMP. This is an observational phase 4 study using the Optum Research Database (ORD) to estimate the long-term safety profile in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) who are initiating Simponi treatment and/or other types of biologic and non-biologic treatments. In addition, the RMP (version 20.0) is updated to reflect the final study report from study CNTO148ART4002 and to revise the list of safety concerns in accordance with the GVP Module V guideline (rev. 2). The Annexes II and IIIA of the product information are updated to remove congestive heart failure and to add breakthrough infection after administration of live vaccine in infants exposed to golimumab in utero from the patient reminder card and labelling. In addition, the MAH took the opportunity to make some editorial changes in the SmPC." Opinion adopted on 14.06.2019. Request for Supplementary Information adopted on 11.04.2019, 17.01.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
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 **Xadago - safinamide - EMEA/H/C/002396/II/0031**	Request for supplementary information adopted with a specific timetable.

Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, “Submission of an updated RMP version 6.0 in order to implement RMP rev 2 template and introduce changes to pre-clinical, clinical and post-marketing exposure information and update the due date of DUS Z7219N02 from July 2019 to 28 February 2020 .” Request for Supplementary Information adopted on 14.06.2019.	
PRAC Led **Zaltrap - aflibercept - EMEA/H/C/002532/II/0051** sanofi-aventis groupe, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Filip Josephson, “Submission of the final report from study OBS13597 / OZONE listed as a category 3 study in the RMP. This is a prospective international observational cohort non-comparative study describing the safety and effectiveness of Zaltrap administered in combination with Folfiri for the treatment of patients with metastatic colorectal cancer in current clinical practice: A Post-Authorisation Safety Study (PASS). The RMP (final version 4.1) is updated accordingly and also adapted to revision 2 of the RMP template including revision of the List of Safety Concerns according to GVP module V Rev 2” Opinion adopted on 14.06.2019. Request for Supplementary Information adopted on 14.03.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1568** **Relvar Ellipta-EMEA/H/C/002673/WS1568/0043** **Revinty Ellipta-EMEA/H/C/002745/WS1568/0041** GlaxoSmithKline (Ireland) Limited, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, “Submission of the final report from study HZC102972 listed as a category 3 study in the RMP. This is a post-authorisation safety study to further characterise the important potential risk of decreased bone mineral density (BMD) and associated fractures with FF/VI in the treatment of chronic obstructive pulmonary disease (COPD)	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

by evaluating the effect of the inhaled corticosteroid fluticasone furoate (FF) on bone mineral density by comparing fluticasone furoate (FF)/vilanterol (VI) treatment with VI treatment in subjects with moderate COPD." Opinion adopted on 14.06.2019. Request for Supplementary Information adopted on 11.04.2019.	
PRAC Led **WS1596** **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 new manufacturing process." Opinion adopted on 14.06.2019. Request for Supplementary Information adopted on 16.05.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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." Request for Supplementary Information adopted on 24.05.2019.
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, "The MAH has submitted a prospective process validation study using batches manufactured with a well-controlled process and to collect quality data from a sufficient number of batches to demonstrate consistency, quality and genetic stability of the cells in the finished product which was a condition to the Marketing Authorisation."
YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0006, Orphan, ATMP Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus Request for Supplementary Information adopted on 17.04.2019.
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.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

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

WS1541 **Abasaglar-EMEA/H/C/002835/WS1541/0025** **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.	
WS1571 **Keppra-EMEA/H/C/000277/WS1571/0174** UCB Pharma S.A., Lead Rapporteur: Koenraad Norga Opinion adopted on 20.06.2019. Request for Supplementary Information adopted on 26.04.2019.	Positive Opinion adopted by consensus on 20.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1584 **Nuwiq-EMEA/H/C/002813/WS1584/0029** **Vihuma-EMEA/H/C/004459/WS1584/0011** Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 20.06.2019. Request for Supplementary Information adopted on 26.04.2019.	Positive Opinion adopted by consensus on 20.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1594 **Infanrix hexa-EMEA/H/C/000296/WS1594/0257** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 20.06.2019.	Positive Opinion adopted by consensus on 20.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1610/G **Silodyx-EMEA/H/C/001209/WS1610/0034/G** **Urorec-EMEA/H/C/001092/WS1610/0037/G** Recordati Ireland Ltd, Lead Rapporteur: Daniela Melchiorri, Lead PRAC Rapporteur: Amelia Cupelli, “To align the annexes and RMP of Urorec and Silodyx with the changes approved for the new, recently authorised product Silodosin Recordati, as listed below: • combined SmPC for both strengths 4mg and 8mg hard capsules • updates to QRD template version 10 • Deletion of the additional risk minimisation activities about IFIS from Annex II of the Product Information, in accordance with the outcome of the PSUSA procedure and RMP version 11.5 In addition, in order to have the same approved RMP for the mentioned medicinal products; it is submitted for Urorec and Silodyx the RMP version	

11.5 that has been approved for Silodosin Recordati (EMEA/H/C/004964)."	
WS1619 **Cymbalta-EMEA/H/C/000572/WS1619/0080** **Duloxetine Lilly-EMEA/H/C/004000/WS1619/0017** **Xeristar-EMEA/H/C/000573/WS1619/0083** **Yentreve-EMEA/H/C/000545/WS1619/0065** Eli Lilly Nederland B.V., Lead Rapporteur: Maria Concepcion Prieto Yerro Opinion adopted on 06.06.2019.	Positive Opinion adopted by consensus on 06.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1622/G **Thymanax-EMEA/H/C/000916/WS1622/0042/G** **Valdoxan-EMEA/H/C/000915/WS1622/0044/G** Les Laboratoires Servier, Lead Rapporteur: Bjorg Bolstad Opinion adopted on 14.06.2019.	Positive Opinion adopted by consensus on 14.06.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1628 **Aflunov-EMEA/H/C/002094/WS1628/0051** **Foclivia-EMEA/H/C/001208/WS1628/0046** Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 20.06.2019.	Request for supplementary information adopted with a specific timetable.
WS1633/G **Blitzima-EMEA/H/C/004723/WS1633/0026/G** **Ritemvia-EMEA/H/C/004725/WS1633/0026/G** **Truxima-EMEA/H/C/004112/WS1633/0029/G** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz, "Update of section 5.1 of the SmPC to reflect the final results of the PRIMA study (MO18264), a study in Patients with Advanced Follicular Lymphoma Evaluating the Benefit of Maintenance Therapy with Rituximab after Induction of Response with Chemotherapy plus Rituximab in Comparison with No Maintenance Therapy. The annexes are also updated to comply with the CHMP guideline on excipients regarding the	

sodium content. Extension of indication to include the maintenance of remission of polyangiitis (Wegener's) (GPA) and microscopic polyangiitis (MPA); as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package leaflet is updated accordingly. In addition, the MAH took the opportunity to implement a terminology change in Annex II. Extension of indication to include the treatment of patients with moderate to severe pemphigus vulgaris (PV); as a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.8 and 5.1 of the SmPC are updated. Data from a phase III, randomized, controlled, multicenter, open-label study (Study ML22196) evaluating rituximab treatment plus short-term, low dose prednisone treatment compared to long-term, standard dose prednisone treatment as first-line treatment in patients with moderate to severe pemphigus had been provided. The Package leaflet is updated accordingly. Minor corrections are also proposed for the sake of accuracy and clarity.”

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

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

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

apixaban - EMEA/H/C/005358 prevention of venous thromboembolic events (VTE)
crizanlizumab - EMEA/H/C/004874, Orphan Novartis Europharm Limited, Treatment of sickle cell disease
dasatinib - EMEA/H/C/005317 treatment of leukaemia
bupivacaine - EMEA/H/C/004586 Indicated for prolonged acute pain management and reduction in need for opioids in adults compared to immediate-release bupivacaine.
insulin aspart - EMEA/H/C/005033 treatment of diabetes mellitus
obiltoxaximab - EMEA/H/C/005169,

Orphan
SFL Regulatory Services GmbH, treatment of inhalational anthrax due to Bacillus anthracis

doxorubicin - EMEA/H/C/005320
treatment of breast cancer, ovarian cancer, progressive multiple myeloma and AIDS-related Kaposi's sarcoma

idebenone - EMEA/H/C/005123, Orphan
Santhera Pharmaceuticals (Deutschland) GmbH, treatment of respiratory dysfunction in patients with Duchenne muscular dystrophy (DMD) not using glucocorticoids

lefamulin - EMEA/H/C/005048
treatment of community-acquired pneumonia (CAP)

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

Sovaldi - sofosbuvir - EMEA/H/C/002798/X/0059/G
Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, “Extension application to introduce a new strength (200 mg film-coated tablets) and a new pharmaceutical form (oral granules) associated with new strengths (150 and 200 mg). The new presentations are indicated in combination with other medicinal products for the treatment of chronic hepatitis C (CHC) in patients aged 3 to <12 years. The extension application is grouped with a type II variation (C.I.6.a) to include paediatric use in patients aged 3 to < 12 years who weigh greater than or equal to 35 kg to the existing presentations of 400 mg film-coated tablets.
The RMP (version 8.3) is updated in accordance. In addition, the MAH took the opportunity to implement minor linguistic corrections throughout the Product Information.”

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

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

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

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

IKERVIS - ciclosporin -
EMEA/H/C/002066/R/0017
Santen Oy, Rapporteur: Peter Kiely, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Jan Neuhauser

Orbactiv - oritavancin -
EMEA/H/C/003785/R/0027
Menarini International Operations Luxembourg S.A., Rapporteur: Janet Koenig, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Adam Przybylkowski

Sivextro - tedizolid phosphate -
EMEA/H/C/002846/R/0031
Merck Sharp & Dohme B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Maria del Pilar Rayon

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

Alunbrig - brigatinib -
EMEA/H/C/004248/II/0003
Takeda Pharma A/S, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Extension of indication to include first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously untreated with an ALK inhibitor for Alunbrig.
The addition of a new indication is supported by data from Study 301 (AP26113-13-301; ALTA 1L), a phase 3, randomized, open label, comparative, multicenter, international phase 3 study.
As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package leaflet and

labelling are updated in accordance. The RMP version 5.1 has also been submitted. Minor editorial corrections are also proposed."
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

ECALTA - anidulafungin - EMEA/H/C/000788/II/0040
Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, "Extension of the approved indication "treatment of invasive candidiasis (ICC)" to include paediatric patients aged from 1 month to less than 18 years of age; consequently, sections 4.1, 4.2, 4.4, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated in order to add paediatric dosing instructions, warnings and precautions, clinical, and non-clinical information. The Package Leaflet is updated accordingly consequent to the revisions to the SmPC. In addition, the Marketing Authorisation Holder (MAH) has taken the opportunity to update the information in the SmPC and Package Leaflet in line with the current excipient's guideline for fructose.
The RMP Version number 13.0 dated 08 March 2019 which includes GVP module V rev 2 changes has also been submitted."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0069, Orphan
Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik

AJOVY - fremanezumab - EMEA/H/C/004833/II/0002
TEVA GmbH, Rapporteur: Jan Mueller-Berghaus

Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0007
Seqirus Netherlands B.V., Rapporteur: Sol Ruiz

Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0093
AstraZeneca AB, Rapporteur: Bart Van der Schueren

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

B.6.10. CHMP-PRAC assessed procedures

B.6.11. PRAC assessed procedures

B.6.12. CHMP-CAT assessed procedures

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

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WS1635
Ryzodeg-EMEA/H/C/002499/WS1635/0033
Tresiba-EMEA/H/C/002498/WS1635/0039
Xultophy-EMEA/H/C/002647/WS1635/0031
Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder

WS1640
PegIntron-EMEA/H/C/000280/WS1640/0138
ViraferonPeg-EMEA/H/C/000329/WS1640/0131
Merck Sharp & Dohme B.V., Lead Rapporteur: Filip Josephson

WS1641
Corlentor-EMEA/H/C/000598/WS1641/0053
Ivabradine Anpharm-EMEA/H/C/004187/WS1641/0013
Procoralan-EMEA/H/C/000597/WS1641/0052
Les Laboratoires Servier, Duplicate, Duplicate of Procoralan, Lead Rapporteur: Johann Lodewijk Hillege

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WS1646
Fluenz Tetra-EMEA/H/C/002617/WS1646/0091
Pandemic influenza vaccine H5N1 AstraZeneca-EMEA/H/C/003963/WS1646/0024
AstraZeneca AB, Lead Rapporteur: Bart Van der Schueren

WS1650

Olanzapine Glenmark-EMEA/H/C/001085/WS1650/0031
Olanzapine Glenmark Europe-EMEA/H/C/001086/WS1650/0028
Olazax-EMEA/H/C/001087/WS1650/0024
Olazax Disperzi-EMEA/H/C/001088/WS1650/0025
Glenmark Arzneimittel GmbH, Generic, Generic of Olansek (SRD), Zyprexa, Zyprexa Velotab, Lead Rapporteur: Alexandre Moreau, “To updated section 4.8 of the SmPC to add "stuttering", section 5.2 of the SmPC to include new section with a sub heading 'Hepatic Impairment' and text related to smoking in line with PI text of the reference product. The PL has been updated accordingly. In addition the MAH has taken the opportunity to align the annexes with minor linguistic changes in line with the reference product.”

WS1657
Advate-EMEA/H/C/000520/WS1657/0101
ADYNOVI-EMEA/H/C/004195/WS1657/0006
Baxter AG, 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 24-27 June 2019 CHMP plenary:

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

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