29 April 2020
EMA/CHMP/228836/2020
Human Medicines Division

Committee for medicinal products for human use (CHMP)

Agenda for the meeting on 28-30 April 2020

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

28 April 2020, 08:30 – 19:30, room 1C/ virtual meeting

29 April 2020, 08:30 – 19:30, room 1C/ virtual meeting

30 April 2020, 08:30 – 19:30, room 1C/ virtual meeting

Separate meeting for Scientific Advice topics

04 May 2020, 14:00 – 16:00, virtual meeting

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 27-30 April 2020. See April 2020 CHMP minutes (to be published post May 2020 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 27-30 April 2020

1.3. Adoption of the minutes

CHMP minutes for 23-26 March 2020

ORGAM minutes for 20 April 2020

Extraordinary CHMP meeting on compassionate use for remdesivir, 2 April 2020

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. erlotinib - EMEA/H/C/005071

treatment of lung and pancreatic cancers.

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday, 29 April 2020 at 11:00

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

2.1.2. fingolimod - EMEA/H/C/005282

treatment of multiple sclerosis.

Scope: Oral explanation

Action: Oral explanation to be held on Thursday, 30 April 2020 at 11:00

List of Outstanding Issues adopted on 27.02.2020. List of Questions adopted on 19.09.2019.

2.1.3. alpelisib - EMEA/H/C/004804

treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor2 (HER2)-negative, advanced breast cancer with a PIK3CA mutation in combination with fulvestrant after disease progression following an endocrine-based regimen.

Scope: Oral explanation,

List of experts for the SAG Oncology meeting adopted via written procedure on 14 April 2020, Report from SAG Oncology meeting held on 15 April 2020

Action: Oral explanation to be held on Wednesday, 29 April 2020 at 16:00

List of Outstanding Issues adopted on 27.02.2020, 19.09.2019. List of Questions adopted on 29.05.2019.

2.2. Re-examination procedure oral explanations

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

D&A PHARMA; for the treatment of alcohol dependence.

Scope: Oral explanation

Report from the ad-hoc expert group meeting held on 06 April 2020

Action: Oral explanation to be held on Tuesday, 28 April 2020 at 14:00

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

Participation of patient representative

See 3.5

2.3. Post-authorisation procedure oral explanations

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

Janssen-Cilag International NV

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

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

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

Oral explanation

Action: Oral explanation to be held on Wednesday, 29 April 2020 at 14:00

Request for Supplementary Information adopted on 27.02.2020, 14.11.2019.

See 5.1

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. cabazitaxel - EMEA/H/C/005178

treatment of adult patients with metastatic castration resistant prostate cancer previously treated with a docetaxel-containing regimen.

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.03.2020, 27.02.2020. List of Questions adopted on 19.09.2019.

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

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 27.02.2020. List of Questions adopted on 19.09.2019.

3.1.3. indacaterol / glycopyrronium / mometasone - EMEA/H/C/005061

treatment of asthma and to reduce asthma exacerbations.

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 30.01.2020. List of Questions adopted on 19.09.2019.

3.1.4. fingolimod - EMEA/H/C/005191

treatment of multiple sclerosis.

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 27.02.2020. List of Questions adopted on 19.09.2019.

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

treatment of diabetes mellitus.

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 27.02.2020. List of Questions adopted on 17.10.2019.

3.1.6. paliperidone - EMEA/H/C/005486

treatment of schizophrenia.

Scope: Opinion

Action: For adoption

3.1.7. luspatercept - Orphan - EMEA/H/C/004444

Celgene Europe BV; treatment of adult patients with very low- to intermediate-risk myelodysplastic syndromes (MDS) - associated anaemia and the treatment of adult patients with beta-thalassaemia (β-thalassaemia)-associated anaemia who require RBC transfusions.

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 27.02.2020. List of Questions adopted on 19.09.2019.

3.1.8. indacaterol / glycopyrronium / mometasone - EMEA/H/C/005518

treatment of asthma and to reduce asthma exacerbations.

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 30.01.2020.

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

3.2.1. amikacin - Orphan - EMEA/H/C/005264

Insmed Netherlands B.V.; treatment of lung infection as part of combination antibacterial drug regiment in adults.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 14.11.2019.

3.2.2. avapritinib - Orphan - EMEA/H/C/005208

Blueprint Medicines (Netherlands) B.V.; treatment of gastrointestinal stromal tumours.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 14.11.2019.

3.2.3. crizanlizumab - Orphan - EMEA/H/C/004874

Novartis Europharm Limited; treatment of sickle cell disease.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 17.10.2019.

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

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

Scope: List of outstanding issues,

List of experts for the ad-hoc expert group meeting adopted via written procedure on 14 April 2020, Report from ad-hoc expert group meeting held 21 April 2020

Action: For adoption

List of Outstanding Issues adopted on 27.02.2020. List of Questions adopted on 27.06.2019.

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

Accelerated assessment

is indicated for active immunisation for prevention of disease caused by Ebola virus.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 25.02.2020.

3.2.6. idebenone - Orphan - EMEA/H/C/005123

Santhera Pharmaceuticals (Deutschland) GmbH; treatment of respiratory dysfunction in patients with Duchenne muscular dystrophy (DMD) not using glucocorticoids.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 17.10.2019.

3.2.7. teriparatide - EMEA/H/C/005233

treatment of osteoporosis.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 25.07.2019.

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

Accelerated assessment

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 25.02.2020.

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

for application into the surgical site to reduce post-operative pain.

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 27.02.2020. List of Questions adopted on 25.07.2019.

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

3.3.1. remimazolam - EMEA/H/C/005246

indicated for procedural sedation.

Scope: List of questions

Action: For adoption

3.3.2. belantamab mafodotin - Orphan - EMEA/H/C/004935

Accelerated assessment

GlaxoSmithKline (Ireland) Limited; treatment of patients with relapsed or refractory multiple myeloma.

Scope: List of questions

Action: For adoption

3.3.3. duvelisib - Orphan - EMEA/H/C/005381

Verastem Europe GmbH; treatment of adult patients with relapsed or refractory chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL) and relapsed or refractory follicular lymphoma (FL).

Scope: List of questions

Action: For adoption

3.3.4. glucagon - EMEA/H/C/005391

for the treatment of severe hypoglycaemia in adults, adolescents, and children aged 2 years and over with diabetes mellitus.

Scope: List of questions

Action: For adoption

3.3.5. istradefylline - EMEA/H/C/005308

indicated as an adjunctive treatment to levodopa-based regimens in patients with Parkinson’s disease.

Scope: List of questions

Action: For adoption

3.3.6. azathioprine - EMEA/H/C/005055

indicated for the prophylaxis of transplant rejection, and an immunosuppressant antimetabolite, indicated in patients who are intolerant to glucocorticosteroids, and chronic inflammatory bowel disease (IBD) (Crohn’s disease or ulcerative colitis), relapsing multiple sclerosis, generalised myasthenia gravis.

Scope: List of questions

Action: For adoption

3.3.7. moxetumomab pasudotox - Orphan - EMEA/H/C/005322

AstraZeneca AB; relapsed or refractory hairy cell leukaemia (HCL) after receiving at least two prior systemic therapies.

Scope: List of questions

Action: For adoption

3.3.8. pemigatinib - Orphan - EMEA/H/C/005266

Incyte Biosciences Distribution B.V.; treatment of locally advanced or metastatic cholangiocarcinoma.

Scope: List of questions

Action: For adoption

3.3.9. netarsudil / latanoprost - EMEA/H/C/005107

reduction of elevated intraocular pressure.

Scope: List of questions

Action: For adoption

3.3.10. valoctocogene roxaparvovec - Orphan - ATMP - EMEA/H/C/004749

Accelerated assessment

BioMarin International Limited; treatment of haemophilia A.

Scope: List of questions

Action: For information

3.3.11. fostemsavir - EMEA/H/C/005011

Accelerated assessment

indicated, in combination with other antiretrovirals, for the treatment of adults with multidrug resistant HIV-1 infection for whom it is otherwise not possible to construct a suppressive anti-viral regimen due to resistance, intolerance or safety considerations.

Scope: List of questions

Action: For adoption

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

3.4.1. aripiprazole - EMEA/H/C/005062

treatment of schizophrenia, or of moderate to severe manic episodes in bipolar I disorder with sensor to measure medication adherence

Scope: Letter from the applicant dated 15 April 2020 requesting an extension of clock-stop to respond to the list of outstanding issues adopted in March 2020.

Action: For adoption

List of Outstanding Issues adopted on 26.03.2020. List of Questions adopted on 25.07.2019.

3.4.2. abiraterone acetate - EMEA/H/C/005408

treatment of metastatic prostate cancer.

Scope: Letter from the applicant dated 03 April 2020 requesting an extension of clock-stop to respond to the list of questions adopted in January 2020.

Action: For adoption

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

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

Scope: Letter from the applicant dated 01 April 2020 requesting an extension of clock-stop to respond to the list of outstanding issues adopted in March 2020.

Action: For adoption

List of Outstanding Issues adopted on 26.03.2020, 25.06.2019. List of Questions adopted on 24.04.2019.

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

Vertex Pharmaceuticals (Ireland) Limited; treatment of cystic fibrosis.

Scope: Letters from third parties, CHMP response letters

Action: For adoption

3.4.5. selinexor - Orphan - EMEA/H/C/005127

Karyopharm Europe GmbH; treatment of patients with relapsed refractory multiple myeloma (RRMM).

Scope: Letter from the applicant dated 20 April 2020 requesting an extension of clock-stop to respond to the list of outstanding issues adopted in January 2020 – adopted via written procedure on 23 April 2020

Action: For information

List of Outstanding Issues adopted on 30.01.2020, 19.09.2019. List of Questions adopted on 24.04.2019.

3.4.6. plazomicin - EMEA/H/C/004457

treatment of complicated urinary tract infection (cUTI), including pyelonephritis; treatment

of bloodstream infection (BSI); treatment of infections due to Enterobacteriaceae

Scope: Letter from the applicant dated 23 April 2020 requesting an extension of clock-stop to respond to the list of outstanding issues adopted in November 2019.

Action: For adoption

List of Outstanding Issues adopted on 14.11.2019, 25.07.2019. List of Questions adopted on 28.02.2019.

3.4.7. Zeposia - ozanimod - EMEA/H/C/004835

Celgene Europe BV; treatment of multiple sclerosis.

Scope: Revised opinion documents adopted via written procedure on 09 April 2020.

Action: For information

Opinion adopted on 26.03.2020. List of Outstanding Issues adopted on 12.12.2019. List of Questions adopted on 25.07.2019.

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

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

D&A PHARMA; treatment of alcohol dependence.

Scope: Oral explanation

Report from the ad-hoc expert group meeting scheduled on 06 April 2020

Action: For adoption

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

See 2.2

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

Janssen-Cilag International NV

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

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

Action: For adoption

List of Outstanding Issues adopted on 26.03.2020. List of Questions adopted on 12.12.2019.

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

Gilead Sciences Ireland UC

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

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

Action: For adoption

List of Outstanding Issues adopted on 27.02.2020. List of Questions adopted on 17.10.2019.

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

Gilead Sciences Ireland UC

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

Scope: "Extension application to introduce a new strength (200 mg film-coated tablets) and a new pharmaceutical form (oral granules) associated with new strengths (150 and 200 mg). The new presentations are indicated in combination with other medicinal products for the treatment of chronic hepatitis C (CHC) in patients aged 3 to <12 years. The extension

application is grouped with a type II variation (C.I.6.a) to include paediatric use in patients aged 3 to < 12 years who weigh greater than or equal to 35 kg to the existing presentations of 400 mg film-coated tablets. The RMP (version 8.3) is updated in accordance. In addition, the MAH took the opportunity to implement minor linguistic corrections throughout the Product Information."

Action: For adoption

List of Outstanding Issues adopted on 27.02.2020. List of Questions adopted on 17.10.2019.

4.1.4. Suboxone - buprenorphine / naloxone - EMEA/H/C/000697/X/0042

Indivior Europe Limited

Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber

Scope: "Extension application to introduce a new pharmaceutical form (sublingual film) associated with four new strengths (2/0.5, 4/1, 8/2, and 16/4 mg) and a new route of administration (either sublingual or buccal administration)."

Action: For adoption

List of Outstanding Issues adopted on 27.02.2020. List of Questions adopted on 25.07.2019.

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

No items

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

4.3.1. Sirturo - bedaquiline - Orphan - EMEA/H/C/002614/X/0036/G

Janssen-Cilag International NV

Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add a new strength (20 mg tablets) grouped with a type II variation (C.I.6) to extend the existing SIRTURO indication to include paediatric patients aged from 5 years to less than 18 years of age and weighing more than 15 kg, based on the results of the Week 24 analysis of Cohort 2 (paediatric subjects aged ≥5 to <12 years) of Study TMC207-C211. Sections 4.1, 4.2, 4.4, 4.8, 5.1, and 5.2 and the Product Leaflet are updated to support the extended indication. The RMP (version 4.4) is updated in accordance."

Action: For adoption

4.3.2. Ultomiris - ravulizumab - EMEA/H/C/004954/X/0004/G

Alexion Europe SAS

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Agnes Gyurasics

Scope: "Extension application to add a new strength (1100 mg in 11 ml vial, concentration 100 mg/ml) for Ultomiris concentrate for solution for infusion, grouped with a Type II application (B.II.z) for a new presentation (300 mg in 3 ml vial, concentration 100 mg/ml) including changes in the active substance concentration, excipients composition and concentrations, and minor differences in the last two steps of the manufacturing process."

Action: For adoption

4.3.3. Xarelto - rivaroxaban - EMEA/H/C/000944/X/0074/G

Bayer AG

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to introduce a new pharmaceutical form, granules for oral suspension, 1 mg/ml. Extension of indication to include treatment of venous thromboembolism (VTE) and prevention of VTE recurrence in term neonates, infants and toddlers, children, and adolescents aged less than 18 years following initiation of standard anticoagulation treatment for Xarelto 15 and 20 mg tablets. As a consequence, sections 4.2, 4.4, 4.5, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated accordingly. In addition, sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC is updated for all other dose strengths (2.5/10 and 15/20 mg initiation packs) of Xarelto and corresponding sections of the Package Leaflet. Section 4.4 has been updated with regards to sodium content according to Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (SANTE-2017-11668). The RMP version 12.1 has also been submitted."

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

Obvius Investment B.V

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

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

Action: For adoption

Request for Supplementary Information adopted on 27.02.2020, 17.10.2019.

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

Otsuka Novel Products GmbH

Rapporteur: Koenraad Norga, PRAC Rapporteur: Laurence de Fays

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

Action: For adoption

Request for Supplementary Information adopted on 27.02.2020.

5.1.3. Dupixent - dupilumab - EMEA/H/C/004390/II/0027

sanofi-aventis groupe

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

Scope: "Extension of indication to include atopic dermatitis patients from 6 years to 11 years. Consequently, the sections 4.1, 4.2, 4.8, 5.1 and 5.2 are updated. The PL is updated accordingly."

Action: For adoption

5.1.4. Ecalta - anidulafungin - EMEA/H/C/000788/II/0040

Pfizer Europe MA EEIG

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "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."

Action: For adoption

Request for Supplementary Information adopted on 30.01.2020, 19.09.2019.

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

Eisai GmbH

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

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

Action: For adoption

Request for Supplementary Information adopted on 12.12.2019.

5.1.6. Imbruvica - ibrutinib - Orphan - EMEA/H/C/003791/II/0059

Janssen-Cilag International NV

Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication in chronic lymphocytic leukaemia (CLL) to add combination with rituximab as follows: In combination with rituximab or obinutuzumab for the treatment of adult patients with previously untreated CLL.

This extension of the approved CLL indication is based on results from the Phase 3 Eastern Cooperative Oncology Group-American College of Radiology Imaging Network (ECOG ACRIN) Study E1912 (also referred to as PCYC-1126e-CA). The SmPC is revised to include information related to the new indication. The PL has been revised accordingly. Minor editorial changes have been implemented in Annex II and Annex IIIA. An updated RMP has been submitted."

Action: For adoption

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

Janssen-Cilag International NV

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

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

Oral explanation

Action: For adoption

Request for Supplementary Information adopted on 27.02.2020, 14.11.2019.

See 2.3

5.1.8. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/II/0082

Vertex Pharmaceuticals (Ireland) Limited

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

Scope: "Extension of indication to include new population for Kalydeco 150 mg tables to extend the use to patients with cystic fibrosis (CF) aged 6 years and older and weighing 25 kg or more who have an R117H mutation in the CFTR gene and for Kalydeco granules 75 mg and 50 mg, to add patients with CF aged 12 months and older and weighing 7 kg to less than 25 kg who have an R117H mutation in the CFTR gene. This is based on a clinical trial and literature data, and post-marketing experience with Kalydeco. As a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 8.5 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 30.01.2020.

5.1.9. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0057

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication to include 1st line treatment of locally advanced or metastatic non-small cell lung cancer tumours expressing PD-L1 with a ≥ 1% tumour proportion score (TPS), based on data from study KEYNOTE-042; an international, randomized, open-label Phase 3 study investigating KEYTRUDA monotherapy compared to

standard of care platinum-based chemotherapy in patients with locally advanced or metastatic PD-L1 positive (TPS ≥ 1%) NSCLC, and on supportive data from the final planned analysis of KEYNOTE-024; a Phase 3 randomized open-label study of KEYTRUDA monotherapy compared to platinum-based chemotherapy in metastatic NSCLC with PD-L1 TPS ≥50%. As a result, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC have been updated. An updated RMP version 18.1 was provided as part of the application."

Action: For adoption

Request for Supplementary Information adopted on 27.02.2020, 19.09.2019, 28.03.2019, 18.10.2018.

5.1.10. Lynparza - olaparib - EMEA/H/C/003726/II/0033

AstraZeneca AB

Rapporteur: Alexandre Moreau, Co-Rapporteur: Koenraad Norga, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to support the use of Lynparza tablets (100 mg and 150 mg) for the maintenance treatment of gBRCAm metastatic pancreatic cancer based on the results from the pivotal Phase 3 study, POLO; as a consequence, sections 4.1, 4.2, 4.8, 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 section 4.8 for lynparza hard capsules (50 mg) to revise list of ADR based on the pooled safety data analysis. The RMP version 18 has also been submitted. Furthermore, the PI is brought in line with the latest guideline regarding the sodium content. The MAH also took the occasion to include some minor editorial changes in the PI.",

Report from the SAG Oncology meeting held on 03 April 2020.

Action: For adoption

Request for Supplementary Information adopted on 30.01.2020, 17.10.2019.

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

Nordic Group B.V.

Rapporteur: Bruno Sepodes, PRAC Rapporteur: Martin Huber

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

Action: For adoption

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

Novo Nordisk A/S

Rapporteur: Jean-Michel Race, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension of indication to include treatment of bleeding episodes in patients with congenital factor XIII A-subunit deficiency as well as minor surgery based on the results of study NN1841-3868 and the PRO-RBDD registry. As a consequence, sections 4.1, 4.2, 4.4, 4.6, 5.1, 5.2 of the SmPC and the RMP version 15 have been submitted. Annex IID and the package leaflet have been updated accordingly. Furthermore, the PI is brought in line with the latest QRD template version. Minor editorial updates have also been made." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)."

Action: For adoption

5.1.13. Opdivo - nivolumab - EMEA/H/C/003985/II/0080

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC) after prior fluoropyrimidine- and platinum-based chemotherapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 16.0 of the RMP has also been submitted."

Action: For adoption

5.1.14. Remsima - infliximab - EMEA/H/C/002576/II/0082

Celltrion Healthcare Hungary Kft.

Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension of indication to add Crohn's disease, ulcerative colitis, ankylosing spondylitis, psoriatic arthritis and psoriasis to the Remsima SC pharmaceutical form to be in line with the IV formulation."

Action: For adoption

5.1.15. Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0022

GlaxoSmithkline Biologicals SA

Rapporteur: Christophe Focke, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sonja Hrabcik

Scope: "Extension of indication to include a new population for Shingrix: adults 18 years of age or older at increased risk of Herpes Zoster supported by the clinical studies ZOSTER-002 (MEA 001), ZOSTER-039 (MEA 002), ZOSTER-041 (MEA 003), ZOSTER-028 (MEA 004), ZOSTER-001 and ZOSTER-015. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated in order to delete a warning and to add new safety and efficacy information. The Package Leaflet is updated in accordance. The RMP version 2.1 has also been submitted."

Action: For adoption

5.1.16. Spravato - esketamine - EMEA/H/C/004535/II/0001/G

Janssen-Cilag International N.V.

Rapporteur: Martina Weise, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kirsti Villikka

Scope: "C.I.6(a): Extension of indication to include a new indication for Spravato for the rapid reduction of depressive symptoms in adult patients with a moderate to severe depressive episode of MDD who have current suicidal ideation with intent. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 the SmPC are updated. The RMP version 2.1 has also been submitted.
B.II.e.5.a.2: Addition of a new pack size corresponding to 4 weeks of treatment in the new indication.
The Package Leaflet and labelling are updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to clarify the wording in Annex II.D."

Action: For adoption

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

Eli Lilly Nederland B.V.

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

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

Action: For adoption

Request for Supplementary Information adopted on 26.03.2020, 12.12.2019.

5.1.18. Taltz - ixekizumab - EMEA/H/C/003943/II/0031

Eli Lilly Nederland B.V.

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

Scope: "Extension of indication to include the treatment of moderate to severe plaque psoriasis in children from the age of 6 years and adolescents who are candidates for systemic therapy for Taltz; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated with new safety and efficacy information. The Package Leaflet is updated in accordance. In addition, the marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 7.1 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 30.01.2020.

5.1.19. Ultomiris - ravulizumab - EMEA/H/C/004954/II/0002

Alexion Europe SAS

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension of indication to include the treatment of patients with atypical hemolytic uremic syndrome (aHUS) for Ultomiris; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, Annex II.D is proposed to be updated to include the risk of thrombotic microangiopathy (TMA) with the new indication in the educational materials. The RMP version 1.6 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 26.03.2020, 14.11.2019.

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

Janssen-Cilag International NV

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

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

Action: For adoption

Request for Supplementary Information adopted on 27.02.2020, 14.11.2019.

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

Novartis Europharm Limited

Rapporteur: Janet Koenig

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

10.1."

Action: For adoption

Request for Supplementary Information adopted on 12.12.2019.

5.1.22. WS1695
Braftovi - encorafenib - EMEA/H/C/004580/WS1695/0008

Pierre Fabre Medicament

Lead Rapporteur: Janet Koenig

Scope: "Extension of indication to include encorafenib in combination with cetuximab, for the treatment of adult patients with metastatic colorectal cancer (CRC) with a BRAF V600E mutation, who have received prior systemic therapy, as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 2.0 has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.1." 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 30.01.2020.

5.1.23. WS1769
Iscover - clopidogrel - EMEA/H/C/000175/WS1769/0140
Plavix - clopidogrel - EMEA/H/C/000174/WS1769/0138

sanofi-aventis groupe

Lead Rapporteur: Bruno Sepodes, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of indication to include adult patients with high risk Transient Ischemic Attack (TIA) (ABCD2 score ≥4) or minor Ischemic Stroke (IS) (NIHSS ≤3) within 24 hours of either the TIA or IS event. The new indication is based on the results of two double-blind, randomised, placebo-controlled phase III trials (studies POINT & CHANCE). As a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated, the PL is updated accordingly. Version 1.0 of the RMP has also been submitted."

Action: For adoption

5.1.24. WS1782
Lacosamide UCB - lacosamide - EMEA/H/C/005243/WS1782/0006
Vimpat - lacosamide - EMEA/H/C/000863/WS1782/0088

UCB Pharma S.A.

Lead Rapporteur: Filip Josephson, Lead Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include the treatment as adjunctive therapy of primary generalised tonic-clonic seizures in adults, adolescents and children from 4 years of age with idiopathic generalised epilepsy for Lacosamide UCB and Vimpat; consequently, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in

accordance. The RMP version 15.0 has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.1. The MAH also takes the opportunity to align the PI of Lacosamide UCB with the PI of Vimpat and to implement some corrections in BG, CS, DA, FR, DE, HU, PL and ES."

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

8.1.1. setmelanotide - Orphan - H0005089

TMC Pharma (EU) Limited; Setmelanotide is indicated for the treatment of obesity and the control of hunger associated with deficiencies in the leptin-melanocortin pathway in patients 6 years of age or older.

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

Action: For adoption

8.2. Priority Medicines (PRIME)

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

8.2.1. List of applications received

Action: For information

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

9. Post-authorisation issues

9.1. Post-authorisation issues

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

Ablynx NV

Rapporteur: Filip Josephson

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

Opinion

Action: For adoption

9.1.2. Helixate NexGen (SRD)- octocog alfa- EMEA/H/C/000276

Bayer AG

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Filip Josephson

Scope: Withdrawal of marketing authorisation

Action: For information

9.1.3. Polivy - polatuzumab vedotin - Orphan - EMEA/H/C/004870

Roche Registration GmbH; treatment of mature B cell lymphomas

Rapporteur: Alexandre Moreau, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Annika Folin

Scope: DHPC and communication plan to provide information concerning the exceptional release of one batch with different stopper cap colour, adopted via written procedure on 22 April 2020

Action: For information

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

Opinion adopted on 14.11.2019. List of Outstanding Issues adopted on 19.09.2019, 25.07.2019, 25.06.2019. List of Questions adopted on 24.04.2019.

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

Grunenthal GmbH

Rapporteur: Bruno Sepodes

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

Opinion

Action: For adoption

Request for Supplementary Information adopted on 12.12.2019.

9.1.5. Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0063

Biogen Netherlands B.V.

Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber

Scope: "Update of sections 4.4 and 4.8 of the SmPC to reflect PML in the setting of mild lymphopenia based on data submitted in the ongoing PSUSA/00010143/201903. The Package Leaflet is updated accordingly. Additionally, the Product Information has been updated in line with QRD template (version 10.1).",

CHMP request for PRAC advice

Action: For adoption

Request for Supplementary Information adopted on 30.01.2020, 19.09.2019.

9.1.6. WS1587/G Abasaglar-EMEA/H/C/002835/WS1587/0028/G Humalog-EMEA/H/C/000088/WS1587/0178/G

Eli Lilly Nederland B.V.

Lead Rapporteur: Kristina Dunder

Scope: "Type II variation. Type IAIN B."

Action: For adoption

Request for Supplementary Information adopted on 14.11.2019, 19.09.2019

10. Referral procedures

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

10.1.1. Picato - ingenol mebutate - EMEA/H/A-20/1489

MAH: LEO Laboratories Ltd

PRAC Rapporteur: Adam Przybylkowski; PRAC Co-Rapporteur: Adrien Inoubli

Scope: Opinion

Action: For adoption

Review of the benefit-risk balance following notification by the European Commission (EC) of a referral under Article 20 of Regulation (EC) No 726/2004, based on pharmacovigilance data.

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

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

MAHs: various

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

Scope: Discussion/Opinion (TBC)

Action: For adoption

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

No items

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

10.4.1. Carbamazepine – EMEA/H/A-29(4)/1497

MAH: Laboratorios Tillomed Spain S.L.U

Referral Rapporteur: Martina Weise, Referral Co-Rapporteur: Tomas Radimersky

Scope: Opinion

Action: For adoption

Summary: Disagreements regarding the bioequivalence acceptance criteria for Cmax of carbamazepine. The objecting MS is of the opinion that bioequivalence has not been demonstrated between the test and the reference product.

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. Fluorouracil and related substances: capecitabine - CAPECITABINE ACCORD (CAP); CAPECITABINE MEDAC (CAP); CAPECITABINE TEVA (CAP); ECANSYA (CAP); XELODA (CAP); NAP flucytosine (NAP); 5-fluorouracil (5-FU) (NAP); tegafur (NAP); tegafur, gimeracil, oteracil – TEYSUNO (CAP) - EMEA/H/A-31/1481

MAHs: Accord Healthcare Limited (Capecitabine Accord), Krka, d.d., Novo mesto (Ecansya), Medac Gesellschaft fur klinische Spezialpraparate mbH (Capecitabine medac), Nordic Group B.V. (Teysuno), Roche Registration GmbH (Xeloda), Teva B.V. (Capecitabine Teva), various

PRAC Rapporteur: Jean-Michel Dogné; PRAC Co-rapporteur: Martin Huber

Scope: DHPC for 5-Fluorouracil (i.v.), capecitabine and tegafur containing products on pre-treatment testing to identify DPD-deficient patients at increased risk of severe toxicity. DHPC for Flucytosine on updated recommendations for the use in patients with dihydropyrimidine dehydrogenase (DPD) deficiency

Opinion

Action: For adoption

Review of the benefit-risk balance following notification by France of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

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

MAHs: various

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

Scope: Opinion

Action: For adoption

Tests performed in a random selection of ranitidine API batches and finished products available in the EU have shown levels of NDMA which raise concerns.
European Commission triggered on 12 September 2019 a referral procedure under Article 31 of Directive 2001/83/EC to evaluate the relevance of these findings, the potential root causes and their impact on the benefit-risk balance of medicinal products containing ranitidine.

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

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

April 2020 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

Action: For information

13.2. Innovation Task Force briefing meetings

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

No items

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on 14-17 April 2020

Action: For information

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for April 2020

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 22-24 April 2020
Action: For information

14.2.3. Paediatric Committee (PDCO)

PIPs reaching D30 at April 2020 PDCO

Action: For information

Report from the PDCO meeting held on 28-30 April 2020

Action: For information

14.2.4. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 21-23 April 2020
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 28-30 April 2020

Action: For information

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

14.3.1. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP April 2020 meeting to CHMP for adoption:

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

Action: For adoption

Election of new BWP vice chair

The second term of vice chair Nanna Aaby Kruse will expire in April 2020.

Action: For election

Response letter to request from third party

Action: For adoption

Follow up from April 2020 ORGAM meeting

14.3.2. Blood Products Working Party (BPWP)

Chair: TBC/Karri Penttila

Election of new BPWP chair

The first term of chair Jacqueline Kerr expired in March 2020.

Action: For election

14.3.3. Quality Working Party (QWP)

Chair: Blanka Hirschlerova

Election of new QWP vice chair

Previous vice chair Blanka Hirschlerova has now become the chair of QWP.

Action: For election

Nomination of new member and alternate to QWP

Action: For adoption

14.3.4. Scientific Advice Working Party (SAWP)

Chair: Anja Schiel

Report from the SAWP meeting held on 14-17 April 2020. 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.

Separate CHMP meeting on SAWP topics to be held remotely on 04 May 2020 from 14:00 to 16:00

Action: For information

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Update on COVID-19

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)*

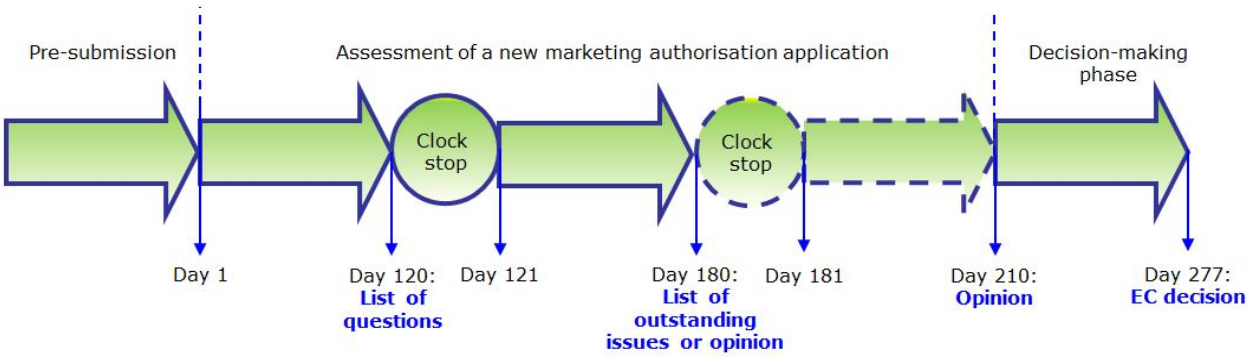
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

29 April 2020
EMA/CHMP/231225/2020

Annex to 28-30 April 2020 CHMP Agenda

Pre-submission and post-authorisations issues

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A. PRE-SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for April 2020: **For adoption**

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

Final outcome of Rapporteurship allocation for April 2020: **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

Obizur - susoctocog alfa - EMEA/H/C/002792/S/0028
Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski
Request for Supplementary Information adopted on 27.02.2020.

Orphacol - cholic acid - EMEA/H/C/001250/S/0033, Orphan
Laboratoires CTRS, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Sofia Trantza
Request for Supplementary Information adopted on 27.02.2020.

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

Vyndaqel - tafamidis - EMEA/H/C/002294/S/0055, Orphan
Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Ghania Chamouni

Request for Supplementary Information adopted on 26.03.2020.

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Nucala - mepolizumab - EMEA/H/C/003860/R/0031
GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Brigitte Keller-Stanislawski

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

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Aripiprazole Sandoz - aripiprazole - EMEA/H/C/004008/R/0014
Sandoz GmbH, Generic, Generic of Abilify, Rapporteur: John Joseph Borg, PRAC Rapporteur: Ana Sofia Diniz Martins
Request for Supplementary Information adopted on 26.03.2020.

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

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

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

Intuniv - guanfacine - EMEA/H/C/003759/R/0022

Shire Pharmaceuticals Ireland Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Maria del Pilar Rayon
Request for Supplementary Information adopted on 26.03.2020.

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

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

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

Pregabalin Accord - pregabalin - EMEA/H/C/004024/R/0015
Accord Healthcare S.L.U., Generic, Generic of Lyrica, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Liana Gross-Martirosyan
Request for Supplementary Information adopted on 26.03.2020.

Pregabalin Sandoz - pregabalin - EMEA/H/C/004010/R/0012
Sandoz GmbH, Generic, Generic of Lyrica, Rapporteur: Tomas Radimersky, PRAC Rapporteur: Liana Gross-Martirosyan
Request for Supplementary Information adopted on 30.01.2020.

Pregabalin Sandoz GmbH - pregabalin - EMEA/H/C/004070/R/0013
Sandoz GmbH, Generic, Duplicate, Generic of Lyrica, Duplicate of Pregabalin Sandoz, Rapporteur: Tomas Radimersky, PRAC Rapporteur: Liana Gross-Martirosyan
Request for Supplementary Information adopted on 30.01.2020.

RAVICTI - glycerol phenylbutyrate - EMEA/H/C/003822/R/0034, Orphan

Immedica Pharma AB, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Ilaria Baldelli

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

B.2.3. Renewals of Conditional Marketing Authorisations

Translarna - ataluren - EMEA/H/C/002720/R/0057, Orphan
PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Liana Gross-Martirosyan

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 14-17 April 2020
PRAC:

Signal of erroneous assay results for levels of anti-factor Xa activity with use of andexanet alfa:

ONDEXXYA - andexanet alfa

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Maria Concepcion Prieto Yerro

PRAC recommendation on a variation / DHPC

Action: For adoption

Signal of DRESS (Drug reaction with eosinophilia and systemic symptoms):

ZYDELIG – idelalisib

Rapporteur: Filip Josephson, Co-Rapporteur: Paula Boudewina van Hennik

PRAC recommendation on a variation

Action: For adoption

Signal of cutaneous amyloidosis:

FIASP, NOVOMIX, NOVORAPID, RYZODEG, TRESIBA, XULTOPHY, LEVEMIR, SULIQUA, APIDRA, ACTRAPHANE, ACTRAPID, INSULATARD, INSUMAN, MIXTARD, PROTAPHANE, HUMALOG, INSULIN LISPRO SANOFI, LIPROLOG - insulins

Rapporteurs: various

PRAC recommendation on a variation

Action: For adoption

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its April 2020 meeting:

EMEA/H/C/PSUSA/00002919/201910
(thalidomide)
CAPS:
Thalidomide Celgene (EMEA/H/C/000823) (thalidomide), Celgene Europe BV, Rapporteur: Alexandre Moreau
NAPS:
NAP - EU
PRAC Rapporteur: Ghania Chamouni, "Period Covered From: 10/10/2018 To: 09/10/2019"

EMEA/H/C/PSUSA/00010052/201909
(vortioxetine)
CAPS:
Brintellix (EMEA/H/C/002717) (vortioxetine), H. Lundbeck A/S, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Laurence de Fays, "Period Covered From: 29/09/2018 To: 29/09/2019"

EMEA/H/C/PSUSA/00010055/201909
(alemtuzumab)
CAPS:
Lemtrada (EMEA/H/C/003718) (alemtuzumab), Sanofi Belgium, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, "Period Covered From: 12/09/2018 To: 12/09/2019"

EMEA/H/C/PSUSA/00010366/201909
(naltrexone / bupropion)
CAPS:
Mysimba (EMEA/H/C/003687) (naltrexone hydrochloride / bupropion hydrochloride), Orexigen Therapeutics Ireland Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber, "Period Covered From:

09/09/2018 To: 09/09/2019”

EMEA/H/C/PSUSA/00010480/201909
(dexamethasone (centrally authorised product indicated in symptomatic multiple myeloma))
CAPS:
Neofordex (EMEA/H/C/004071) (dexamethasone), Laboratoires CTRS, Rapporteur: Ondřej Slanař, PRAC Rapporteur: Ghania Chamouni, “Period Covered From: 15/09/2018 To: 15/09/2019”

EMEA/H/C/PSUSA/00010490/201909
(pitolisant)
CAPS:
Wakix (EMEA/H/C/002616) (pitolisant), BIOPROJET PHARMA, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Kirsti Villikka, “From: 30/09/2018 To: 30/09/2019”

EMEA/H/C/PSUSA/00010585/201908
(budesonide / formoterol)
CAPS:
BiResp Spiromax (EMEA/H/C/003890) (budesonide / formoterol), Teva Pharma B.V., Rapporteur: John Joseph Borg
DuoResp Spiromax (EMEA/H/C/002348) (budesonide / formoterol), Teva Pharma B.V., Rapporteur: John Joseph Borg
NAPS:
NAP - EU
PRAC Rapporteur: Hans Christian Siersted, “Period Covered From: 24/08/2016 To: 24/08/2019”

EMEA/H/C/PSUSA/00010645/201909
(dupilumab)
CAPS:
Dupixent (EMEA/H/C/004390) (dupilumab), sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Kimmo Jaakkola, “Period Covered From: 28/03/2019 To: 28/09/2019”

EMEA/H/C/PSUSA/00010655/201909
(niraparib)
CAPS:
Zejula (EMEA/H/C/004249) (niraparib), GlaxoSmithKline (Ireland) Limited, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Jan Neuhauser, “From: 25/03/2019 To: 25/09/2019”

EMEA/H/C/PSUSA/00010758/201909

(fremanezumab) CAPS: **AJOVY** (EMEA/H/C/004833) (fremanezumab), TEVA GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Kirsti Villikka, "Period Covered From: 13/03/2019 To: 13/09/2019"	
EMEA/H/C/PSUSA/00010780/201909 (cemiplimab) CAPS: **LIBTAYO** (EMEA/H/C/004844) (cemiplimab), Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Menno van der Elst, "Period Covered From: 26/03/2019 To: 26/09/2019"	

B.4. EPARs / WPARs

Fluad Tetra - influenza vaccine (surface antigen, inactivated) - EMEA/H/C/004993, Article 28 Seqirus Netherlands B.V., Active immunisation against influenza in the elderly (65 years of age and older) and in children 6 months to less than 6 years of age., 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.
Nepexto - etanercept - EMEA/H/C/004711 Mylan IRE Healthcare Limited, Rheumatoid arthritis, Juvenile idiopathic arthritis, Psoriatic arthritis, Axial spondyloarthritis, Ankylosing spondylitis, Non-radiographic axial spondyloarthritis, Plaque psoriasis, Paediatric plaque psoriasis, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Pretomanid FGK - pretomanid - EMEA/H/C/005167, Orphan FGK Representative Service GmbH, treatment of tuberculosis, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
SARCLISA - isatuximab - EMEA/H/C/004977, Orphan sanofi-aventis groupe, For the treatment of patients with multiple myeloma (MM), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Zeposia - ozanimod - EMEA/H/C/004835 Celgene Europe BV, Treatment of multiple sclerosis, New active substance (Article 8(3) of	For information only. Comments can be sent to the PL in case necessary.

Directive No 2001/83/EC)	
Zolgensma - onasemnogene abeparvovec - EMEA/H/C/004750, Orphan, ATMP AveXis EU Limited, treatment of treatment of spinal muscular atroophy (SMA), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Adenuric - febuxostat - EMEA/H/C/000777/II/0056 Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 13.02.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Advate - octocog alfa - EMEA/H/C/000520/II/0107 Takeda Manufacturing Austria AG, Rapporteur: Jan Mueller-Berghaus	
BeneFIX - nonacog alfa - EMEA/H/C/000139/II/0161/G Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 17.04.2020, 20.02.2020, 05.12.2019.	Request for supplementary information adopted with a specific timetable.
Brineura - cerliponase alfa - EMEA/H/C/004065/II/0019, Orphan BioMarin International Limited, Rapporteur: Martina Weise Opinion adopted on 02.04.2020. Request for Supplementary Information adopted on 06.02.2020.	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cinacalcet Mylan - cinacalcet - EMEA/H/C/004014/II/0009 Mylan S.A.S, Generic, Generic of Mimpara, Rapporteur: Tomas Radimersky	
Cometriq - cabozantinib - EMEA/H/C/002640/II/0037, Orphan Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik	Positive Opinion adopted by consensus on 23.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 23.04.2020. Request for Supplementary Information adopted on 12.03.2020.	
CooperSurgical Inc ART Media - human albumin solution - EMEA/H/D/002307/II/0006/G BSI Group, Rapporteur: Kristina Dunder Opinion adopted on 02.04.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Dupixent - dupilumab - EMEA/H/C/004390/II/0024/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 23.01.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Entyvio - vedolizumab - EMEA/H/C/002782/II/0048 Takeda Pharma A/S, Rapporteur: Daniela Melchiorri	
HyQvia - human normal immunoglobulin - EMEA/H/C/002491/II/0055 Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 17.04.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0037, Orphan CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 02.04.2020, 30.01.2020.	Request for supplementary information adopted with a specific timetable.
Kineret - anakinra - EMEA/H/C/000363/II/0072 Swedish Orphan Biovitrum AB (publ), Rapporteur: Mark Ainsworth Opinion adopted on 02.04.2020. Request for Supplementary Information adopted on 30.01.2020.	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kiovig - human normal immunoglobulin - EMEA/H/C/000628/II/0098 Takeda Manufacturing Austria AG, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 17.04.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Mepsevii - vestronidase alfa - EMEA/H/C/004438/II/0013/G, Orphan	Request for supplementary information adopted with a specific timetable.

Ultragenyx Germany GmbH, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 17.04.2020.	
Obizur - susoctocog alfa - EMEA/H/C/002792/II/0027 Baxalta Innovations GmbH, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 26.03.2020.	
Ogivri - trastuzumab - EMEA/H/C/004916/II/0011/G Mylan S.A.S, Rapporteur: Koenraad Norga Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 12.03.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ogivri - trastuzumab - EMEA/H/C/004916/II/0013 Mylan S.A.S, Rapporteur: Koenraad Norga Opinion adopted on 17.04.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0007 Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 17.04.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0010/G Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 17.04.2020.	Request for supplementary information adopted with a specific timetable.
Orencia - abatacept - EMEA/H/C/000701/II/0137/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 17.04.2020.	Request for supplementary information adopted with a specific timetable.
Pelmeg - pegfilgrastim - EMEA/H/C/004700/II/0006/G Mundipharma Corporation (Ireland) Limited, Rapporteur: Koenraad Norga	
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0155 CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 02.04.2020. Request for Supplementary Information adopted on 30.01.2020.	
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0157/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 17.04.2020.	Request for supplementary information adopted with a specific timetable.
Puregon - follitropin beta - EMEA/H/C/000086/II/0106/G Merck Sharp & Dohme B.V., Rapporteur: Peter Kiely Request for Supplementary Information adopted on 02.04.2020.	Request for supplementary information adopted with a specific timetable.
Ritonavir Mylan - ritonavir - EMEA/H/C/004549/II/0007/G Mylan S.A.S, Generic, Generic of Norvir, Rapporteur: John Joseph Borg Request for Supplementary Information adopted on 17.04.2020.	Request for supplementary information adopted with a specific timetable.
RoActemra - tocilizumab - EMEA/H/C/000955/II/0093/G Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 13.02.2020.	
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0026 GlaxoSmithkline Biologicals SA, Rapporteur: Christophe Focke Opinion adopted on 17.04.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0027/G GlaxoSmithkline Biologicals SA, Rapporteur: Christophe Focke Opinion adopted on 23.04.2020.	Positive Opinion adopted by consensus on 23.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Skilarence - dimethyl fumarate - EMEA/H/C/002157/II/0019 Almirall S.A, Rapporteur: Janet Koenig Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 13.02.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

SonoVue - sulphur hexafluoride - EMEA/H/C/000303/II/0039/G Bracco International B.V., Rapporteur: Alexandre Moreau Opinion adopted on 02.04.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0055 MCM Vaccine B.V., Rapporteur: Christophe Focke Opinion adopted on 02.04.2020.	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xadago - safinamide - EMEA/H/C/002396/II/0034 Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 02.04.2020, 16.01.2020.	Request for supplementary information adopted with a specific timetable.
Zaltrap - aflibercept - EMEA/H/C/002532/II/0055/G sanofi-aventis groupe, Rapporteur: Filip Josephson Opinion adopted on 02.04.2020.	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ziextenzo - pegfilgrastim - EMEA/H/C/004802/II/0005/G Sandoz GmbH, Rapporteur: Andrea Laslop Opinion adopted on 02.04.2020. Request for Supplementary Information adopted on 06.02.2020.	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1587/G **Abasaglar-EMEA/H/C/002835/WS1587/0028/G** **Humalog-EMEA/H/C/000088/WS1587/0178/G** Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 14.11.2019, 19.09.2019.	See agenda 9.1
WS1700/G **Humalog-EMEA/H/C/000088/WS1700/0180/G** **Liprolog-EMEA/H/C/000393/WS1700/0141/G** Eli Lilly Nederland B.V., Informed Consent of	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Humalog, Lead Rapporteur: Kristina Dunder Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 24.10.2019.	
WS1736/G **Elebrato Ellipta-EMEA/H/C/004781/ WS1736/0015/G** **Temybric Ellipta-EMEA/H/C/005254/ WS1736/0003/G** **Trelegy Ellipta-EMEA/H/C/004363/ WS1736/0013/G** GlaxoSmithKline Trading Services Limited, Lead Rapporteur: Peter Kiely Request for Supplementary Information adopted on 17.04.2020.	Request for supplementary information adopted with a specific timetable.
WS1786 **Hexacima-EMEA/H/C/002702/ WS1786/0097** **Hexaxim-EMEA/H/W/002495/ WS1786/0102** **Hexyon-EMEA/H/C/002796/ WS1786/0101** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus	
WS1804/G **HBVAXPRO-EMEA/H/C/000373/WS1804/ 0068/G** **Vaxelis-EMEA/H/C/003982/WS1804/ 0058/G** MCM Vaccine B.V., Lead Rapporteur: Jan Mueller-Berghaus	

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

AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0028 sanofi-aventis groupe, Rapporteur: Martina Weise, "To update section 4.6 of the SmPC with additional information in relation to human experience of use of teriflunomide during pregnancy, from an analysis of the data recorded in the global safety database and available sources (clinical trial cases, registries and cohort studies, literature and post-marketing pregnancy reports). The MAH also took the opportunity to update sections 2 and 4.4 of the SmPC to align with the updated annex of the guideline excipients with regards to sodium.	Request for supplementary information adopted with a specific timetable.

The Labelling and Package Leaflet are updated accordingly." Request for Supplementary Information adopted on 17.04.2020.	
Avamys - fluticasone furoate - EMEA/H/C/000770/II/0040 GlaxoSmithKline (Ireland) Limited, Rapporteur: Ewa Balkowiec Iskra, "Update of section 4.8 of the SmPC in order to add bronchospasm with a frequency 'not known' and dyspnoea with a frequency 'common' to the list of adverse drug reactions based on post-marketing experience and clinical trial reports. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet." Opinion adopted on 02.04.2020. Request for Supplementary Information adopted on 06.02.2020.	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Bosulif - bosutinib - EMEA/H/C/002373/II/0041 Pfizer Europe MA EEIG, Rapporteur: Janet Koenig, "Update of section 5.2 of the SmPC in order to update the population PK model and the exposure-response model with additional PK and safety data from the recently completed Phase 2 study (B1871048) following a commitment within variation EMEA/H/C/002373/II/0036. In addition, a pooled safety data analysis has been performed to assess the clinical impact of reduced clearance in Asian population. The MAH takes also the opportunity to make editorial changes on the Package Leaflet."	
Bridion - sugammadex - EMEA/H/C/000885/II/0036 Merck Sharp & Dohme B.V., Rapporteur: Outi Mäki-Ikola, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC with information on morbidly obese patients (based on study report P146MK8616 - a phase 4 randomized, active-comparator controlled trial to study the efficacy and safety of sugammadex (MK-8616) for the reversal of neuromuscular blockade induced by either rocuronium bromide or vecuronium bromide in morbidly obese subjects) and information related to the excipient sodium in accordance with the revised Annex to the EC guideline on excipients (section 4.4). The	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Patient Leaflet is updated accordingly. The MAH also took the opportunity to include the changes related to the new EMA QRD template version 10.1 and to implement some editorial changes." Opinion adopted on 02.04.2020.	
Brintellix - vortioxetine - EMEA/H/C/002717/II/0025 H. Lundbeck A/S, Rapporteur: Bart Van der Schueren, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC to reflect the outcomes of the paediatric clinical study 12710A (a paediatric efficacy and safety study in adolescent MDD patients) and the study 12708A (paediatric pharmacokinetics and tolerability study in children and adolescent patients with DSM-IV diagnosis of depressive and anxiety disorder). In addition, the MAH took the opportunity to propose minor amendments to the labelling and to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 17.04.2020.	Request for supplementary information adopted with a specific timetable.
Cablivi - caplacizumab - EMEA/H/C/004426/II/0021, Orphan Ablynx NV, Rapporteur: Filip Josephson, "Submission of the results of the study ALX-0681-MS-01, a Modelling/Simulation study performed for the paediatric population as part of the approved Paediatric Investigation Plan (EMEA-001157-PIP-01-11-M02) for Cablivi" Request for Supplementary Information adopted on 27.02.2020.	
CABOMETYX - cabozantinib - EMEA/H/C/004163/II/0012 Ipsen Pharma, Rapporteur: Bjorg Bolstad, "Update of section 4.4 of the SmPC to include the risk of Osteonecrosis as a warning. Update of section 4.8 of the SmPC based on the Company Core Safety Information: - to remove Anaemia, Oral pain and Dry mouth from the list of adverse reactions (ADRs), - to add Dysphagia and Hyperkeratosis to the existing ADR, - to replace Peripheral sensory neuropathy by Peripheral neuropathy in order to reflect the broader medical concept and to add DVT (Deep vein thrombosis) to the existing ADR venous thrombosis in order to alert prescribers	

to the most frequently reported type of venous thrombosis. Changes to the frequency categorisation of some ADRs are also proposed based on new pooled data. The Package Leaflet is updated accordingly. The MAH took the opportunity to align the product Information with the QRDv10.1 and update the local representative information of Hungary." Request for Supplementary Information adopted on 26.03.2020, 23.01.2020.	
Cometriq - cabozantinib - EMEA/H/C/002640/II/0035, Orphan Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.2 to introduce a clarification in alignment with Cabometyx; update of section 4.4 of the SmPC to include the addition of the risk of diarrhoea and additional test to the existing risks of thromboembolic events, haemorrhage, wound complications and RPLS (Reversible posterior leukoencephalopathy syndrome). Update of section 4.8 of the SmPC, based on the Company Core Safety Information, to remove oropharyngeal pain from the list of adverse reactions (ADRs) and to add DVT (Deep vein thrombosis) to the existing ADR venous thrombosis in order to alert prescribers to the most frequently reported type of venous thrombosis. Changes to the frequency categorisation of some ADRs are also proposed based on new pooled data. The Package Leaflet is updated accordingly. The MAH took the opportunity to align the Product Information with the QRDv10.1 and update the local representative information of Hungary." Request for Supplementary Information adopted on 26.03.2020, 23.01.2020.	
Evicel - human fibrinogen / human thrombin - EMEA/H/C/000898/II/0078 Omrix Biopharmaceuticals N. V., Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information following the final results from study 400-12-006 listed as in the paediatric investigation plan; this is a prospective, randomized, controlled study evaluating Evicel (fibrin sealant) as an adjunct to hemostasis during abdominal, retroperitoneal, pelvic or thoracic (non-Cardiac) surgery in pediatric patients. The Package Leaflet is updated accordingly."	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 02.04.2020. Request for Supplementary Information adopted on 30.01.2020.	
Faslodex - fulvestrant - EMEA/H/C/000540/II/0068 AstraZeneca AB, Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information based on the results from study Phase 3 Study A5481023 (PALOMA-3) a randomized controlled study of fulvestrant and palbociclib combination. In addition, the MAH took the opportunity to make a number of editorial changes to the PI to comply with the new QRD template v10.1 and the addition of the respective strength and pharmaceutical form to the corresponding Marketing Authorisation Number." Opinion adopted on 02.04.2020.	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0037/G MSD Vaccins, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC based on the 2nd interim report from studies V503-002-20 (MEA 005) and V503-021 (MEA 004) listed as a category 3 in the RMP and on final results from study V501-015-21-01 (qHPV); these are effectiveness and immunogenicity long-term follow-up (LTFU) studies from the 9-valent HPV and 4-valent HPV (qHPV) vaccines programs in women 16-26YOA. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.1. In addition, one linguistic comment received from the Czech NCA on the PI during procedure EMEA/H/C/003852/II/033 will be implemented as well."	
Gliolan - 5-aminolevulinic acid - EMEA/H/C/000744/II/0018/G medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Bruno Sepodes, "To update section 4.4 of the SmPC to add a warning (false positive and false negative fluorescence) following an analysis of the MAHs safety database.	Request for supplementary information adopted with a specific timetable.

To update section 4.2 of the SmPC to exclude re-administration if surgery is delayed by less than 12 hours." Request for Supplementary Information adopted on 17.04.2020.	
Herceptin - trastuzumab - EMEA/H/C/000278/II/0160 Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.7 of the SmPC in order to add "dizziness and somnolence" to the recommendations on the effects on the patient's ability to drive and use machines. Update of section 4.8 of the SmPC to remove Herpes zoster, Erysipelas, Cellulitis Common, Sepsis, Thinking abnormal, Ataxia, Paresis, Brain oedema, Pericarditis, Bradycardia and Hepatic failure as adverse drug reactions. An update of the frequencies of adverse reactions is proposed in accordance to a change in the company core datasheet (CDS) for Herceptin: Anaphylactic reaction and Anaphylactic shock is changed to frequency Rare, Wheezing is changed to frequency Uncommon, Pneumonitis is changed to frequency Uncommon and Palpitation is changed to frequency Common. The MAH is taking the opportunity to update section 2 of the Herceptin PL to ensure compliance with the guidance on Excipients in the Labelling and Package Leaflet of medicinal products for Human Use (SANTE 2017-11668). The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 17.04.2020.	Request for supplementary information adopted with a specific timetable.
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0058, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of sections 4.5, 4.6 and 5.2 of the SmPC following the results from study CLL1017 (MEA 012.2). The PL is updated accordingly. In addition, the MAH took the opportunity to update the PI to the latest QRD template v10.1." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 13.02.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Imnovid - pomalidomide - EMEA/H/C/002682/II/0036/G, Orphan	

Celgene Europe BV, Rapporteur: Jorge Camarero Jiménez, "Group of two type II variations to update sections 4.2, 4.4 and 4.8 of the SmPC and section 4 of the PL with information on anaphylaxis and section 4.8 of SmPC with hypothyroidism ADR following a safety review. This group also includes a Type IB Variation to update section 6.6 of the SmPC in order to include recommendations to minimize the risk of unintended occupational exposures in healthcare professionals. The MAH has also proposed minor updates to section 4.4 of the SmPC and Annex IID regarding the educational materials, prescribing and dispensing restrictions in order to provide more clarity about the recommended maximum duration of treatment." Request for Supplementary Information adopted on 16.01.2020, 12.09.2019.	
Kisqali - ribociclib - EMEA/H/C/004213/II/0022 Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC based on updated efficacy and safety data from study CLEE011F2301 (MONALEESA-3), a randomised double-blind, placebo-controlled, multicentre phase III clinical study in the treatment of men and postmenopausal women with hormone receptor positive, HER2-negative advanced breast cancer who had received no or only one line of prior endocrine treatment, in combination with fulvestrant versus fulvestrant alone. The Package leaflet is updated accordingly." Opinion adopted on 23.04.2020. Request for Supplementary Information adopted on 13.02.2020.	Positive Opinion adopted by consensus on 23.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kyprolis - carfilzomib - EMEA/H/C/003790/II/0043, Orphan Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of section 4.8 of the SmPC in order to include cardiomyopathy as a new adverse drug reaction with uncommon frequency following a signal evaluation triggered by a request from the Therapeutic Goods Administration (TGA) Australian authority. The RMP version 11.0 has also been submitted. In addition, the MAH took the opportunity to make some minor editorial changes to the PI."	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 17.04.2020.	
LIBTAYO - cemiplimab - EMEA/H/C/004844/II/0007 Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Sinan B. Sarac, Co-Rapporteur: Tuomo Lapveteläinen, "C.I.4, Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning and add new ADRs with frequency uncommon, regarding new safety information in the post marketing setting on the terms "Transplant rejection", "Graft Versus Host Disease (GVHD)" and "Myositis". The MAH took the opportunity to provide minor corrections to the efficacy data in the SmPC from study R2810-ONC-1540 (primary analysis for group 2 and 3 dated 09 Jul 2019), based on errors that were revealed in two patient's data following the completion of the MA. The Package Leaflet is updated accordingly. The MAH also took the opportunity to introduce editorial changes in the PI."	
Lorviqua - lorlatinib - EMEA/H/C/004646/II/0002 Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, "Update of sections 4.5 and 5.2 of the SmPC in order to further reflect the induction potential of lorlatinib on CYP2C9, P-gp, CYP2B6 and UGT1A1 substrates based on the results from the drug-drug interaction sub-study of B7461001. Furthermore, the Marketing authorisation holder (MAH) corrected information regarding ADRs in section 4.8 of the SmPC and added clarification regarding linearity/non-linearity of lorlatinib PK in section 5.2 of the SmPC. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1." Opinion adopted on 02.04.2020. Request for Supplementary Information adopted on 12.12.2019.	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Lymphoseek - tilmanocept - EMEA/H/C/002085/II/0019 Norgine B.V., Rapporteur: Peter Kiely, "To update SmPC sections 4.2, 4.4, 4.8 in order to correct the radiation dose for patients with hepatic and renal impairment, and section 12 in order to change the labelling-activity that can be added to the vial. In addition, the Marketing authorisation holder (MAH) took the opportunity	

to bring the PI in line with the latest QRD template version 10.1." Request for Supplementary Information adopted on 30.01.2020.	
Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0027 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Jean-Michel Race, "Submission of the final clinical study report from study M16-133, this is a phase 3b, single Arm, open label, multicenter study aimed to evaluate the efficacy and safety of glecaprevir (GLE)/pibrentasvir (PIB) in treatment of naïve adults with chronic Hepatitis C Virus (HCV) Genotypes 1 – 6 infection and aspartate aminotransferase to platelet ratio index (APRI) ≤ 1." Request for Supplementary Information adopted on 16.01.2020, 24.10.2019.	
Nivestim - filgrastim - EMEA/H/C/001142/II/0061 Pfizer Europe MA EEIG, Rapporteur: Outi Mäki-Ikola, "Update of section 6.5 of the SmPC to add a statement on the content of a derivative of natural rubber latex in the needle cover formulation. Section 6 of the Package Leaflet was updated accordingly." Request for Supplementary Information adopted on 06.02.2020.	
Opsumit - macitentan - EMEA/H/C/002697/II/0035/G, Orphan Janssen-Cilag International N.V., Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 4.5 of the SmPC in order to update the drug-drug interaction information of macitentan with Breast cancer resistance protein (BCRP) substrate drugs based on final results from studies AC-055-122 and AC-055-123; these are single-center, open-label, one-sequence, two-treatment studies investigating the effect of macitentan at steady state on the pharmacokinetics of rosuvastatin and riociguat respectively in healthy male subjects. In addition, a minor editorial change was introduced in section 5.1." Opinion adopted on 17.04.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Perjeta – pertuzumab – EMEA/H/C/002547/II/0047 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Submission of the final report from	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

study W020698 (CLEOPATRA), a phase III, randomized, double blind, placebo-controlled clinical trial to evaluate the efficacy and safety of pertuzumab + trastuzumab + docetaxel vs placebo + trastuzumab + docetaxel in previously untreated HER2-positive metastatic breast cancer." Opinion adopted on 02.04.2020. Request for Supplementary Information adopted on 06.02.2020.	recommendation.
Perjeta – pertuzumab – EMEA/H/C/002547/II/0048 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to add safety information in elderly patients based on a safety review. Sections 4.2 and 4.4 of the SmPC and the Package leaflet have been updated accordingly. In addition, the MAH took the opportunity to make minor amendments to section 4.7 of the SmPC and to update the PL in accordance with the excipient guideline and in line with the SmPC." Opinion adopted on 17.04.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Qutenza – capsaicin – EMEA/H/C/000909/II/0048 Grunenthal GmbH, Rapporteur: Bruno Sepodes, "Update of sections 4.2 and 5.1 of the SmPC in order to amend the posology based on PACE and STRIDE studies. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 27.02.2020, 12.12.2019.	
Revlimid – lenalidomide – EMEA/H/C/000717/II/0112/G Celgene Europe BV, Rapporteur: Alexandre Moreau, "Group of variations including one type II to update sections 4.2, 4.4 and 4.8 of the SmPC and section 4 of the PL with anaphylaxis following a safety review and a Type IB to update section 6.6 of the SmPC in order to include recommendations to minimize the risk of unintended occupational exposures in healthcare professionals. The MAH has also proposed minor updates to section 4.4 of the SmPC and Annex IID regarding the educational materials, prescribing and dispensing restrictions in order to provide more clarity about the recommended maximum duration of treatment. Finally the MAH took the opportunity	

to make editorial changes throughout the product information." Request for Supplementary Information adopted on 16.01.2020, 12.09.2019.	
Shingrix – herpes zoster vaccine (recombinant, adjuvanted) – EMEA/H/C/004336/II/0021 GlaxoSmithkline Biologicals SA, Rapporteur: Christophe Focke, "C.I.13: Submission of the final report from studyZoster-063, listed as a category 3 study in the RMP version 2.0. The study was conducted to investigate the impact of reactogenicity on health-related quality of life in subjects ≥50 YOA following Shingrix vaccination." Opinion adopted on 02.04.2020. Request for Supplementary Information adopted on 13.02.2020.	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Skyrizi – risankizumab – EMEA/H/C/004759/II/0008 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Peter Kiely, "Update of section 5.1 'Pharmacodynamic Properties' of the SmPC. The amendment pertains to the addition of information on retreatment after withdrawal of risankizumab to the summary of the IMMhance clinical study (M15-992). No change to the Package leaflet is introduced." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 13.02.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
TAGRISSO – osimertinib – EMEA/H/C/004124/II/0032 AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.4 and 4.8 of the SmPC in order to include erythema multiforme as an adverse drug reaction following the review of the MAH internal safety data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity of this procedure to add the event frequency of Stevens-Johnson syndrome to align with the approved text in the SmPC." Opinion adopted on 02.04.2020. Request for Supplementary Information adopted on 13.02.2020.	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tecentriq – atezolizumab – EMEA/H/C/004143/II/0030 Roche Registration GmbH, Rapporteur: Sinan B.	

Sarac, "Update of section 4.8 of the SmPC to reflect the outcome of anti-drug antibody (ADA) analyses conducted across studies POPLAR, OAK, Impower 150, Impower 130, IMPower 131, Impower 132, Imvigor 211, Immotion 151, Impower 133 and Impassion 130, further to the CHMP recommendation." Request for Supplementary Information adopted on 05.12.2019.	
Tecentriq – atezolizumab – EMEA/H/C/004143/II/0040 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC to include the adverse drug reactions (ADRs) hyperthyroidism with a "common" frequency and hypertension with a "very common" frequency for atezolizumab used in combination with chemotherapy, as identified in study Imvigor130. The MAH took the opportunity of this variation to add preferred terms (PTs) to the footnotes to the ADR table in section 4.8 of the SmPC. The package leaflet is proposed to be updated accordingly." Opinion adopted on 17.04.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Thalidomide Celgene – thalidomide – EMEA/H/C/000823/II/0061/G Celgene Europe BV, Rapporteur: Alexandre Moreau, "Group of variations including one type II to update sections 4.2, 4.4 and 4.8 of the SmPC and section 4 of the PL with anaphylaxis following a safety review and a Type IB to update section 6.6 of the SmPC in order to include recommendations to minimize the risk of unintended occupational exposures in healthcare professionals. The MAH has also proposed minor updates to section 4.4 of the SmPC and Annex IID regarding the educational materials, prescribing and dispensing restrictions in order to provide more clarity." Request for Supplementary Information adopted on 16.01.2020, 12.09.2019.	
Tygacil – tigecycline – EMEA/H/C/000644/II/0111 Pfizer Europe MA EEIG, Rapporteur: Jorge Camarero Jiménez, "Update of section 4.5 of the SmPC in order to add drug interaction information regarding the concomitant use of tigecycline and calcineurin inhibitors, based on pharmacovigilance data; the Package Leaflet is	

updated accordingly." Request for Supplementary Information adopted on 12.03.2020.	
VITRAKVI – larotrectinib – EMEA/H/C/004919/II/0001 Bayer AG, Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to remove the warning related to drug-drug interactions between larotrectinib and CYP2 substrates based on the results of study PH-40955 investigating the inductive potential of Larotrectinib on the expression of cytochrome P450 (CYP) enzymes. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 13.02.2020.	
Xaluprine – mercaptopurine – EMEA/H/C/002022/II/0022, Orphan Nova Laboratories Ireland Limited, Rapporteur: Filip Josephson, "Update of sections 4.4, 4.8 and 4.9 of the SmPC to add further information on hepatic toxicity. The MAH took the opportunity to implement minor editoral changes to the SmPC and PIL." Request for Supplementary Information adopted on 26.03.2020, 13.02.2020, 21.11.2019, 12.09.2019.	
Xyrem – sodium oxybate – EMEA/H/C/000593/II/0088 UCB Pharma S.A., Rapporteur: Bruno Sepodes, "Update of sections 4.4. and 4.8 of the SmPC in order to update the safety information to add choking sensation; the Package Leaflet is updated accordingly." Opinion adopted on 02.04.2020.	Positive Opinion adopted by consensus on 02.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zebinix – eslicarbazepine acetate – EMEA/H/C/000988/II/0074 Bial – Portela & Cª, S.A., Rapporteur: Martina Weise, "Update of sections 4.2 and 5.2 of the SmPC in order to add the possibility to crush the tablets for patients unable to swallow whole tablets based on final results from study SEP093-155; this is an interventional study to investigate and compare the relative bioavailability and bioequivalence of a crushed tablet and an intact tablet of eslicarbazepine acetate (ESL) (800 mg); The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

representatives in the PL." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 13.02.2020.	
Zoely – nomegestrol acetate / estradiol – EMEA/H/C/001213/II/0050 Theramex Ireland Limited, Rapporteur: Jean-Michel Race, "Update of sections 4.3 and 4.4 of the SmPC in order to add a new contraindication and a new warning regarding meningioma, upon request by PRAC following the assessment of Post-authorisation measure "LEG 014". The Package Leaflet is being updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in the Netherlands and Portugal in the Package Leaflet." Request for Supplementary Information adopted on 26.03.2020, 12.12.2019, 14.11.2019, 19.09.2019.	
WS1718 **Eviplera-** **EMEA/H/C/002312/WS1718/0101** **Odefsey-** **EMEA/H/C/004156/WS1718/0045** Gilead Sciences Ireland UC, Lead Rapporteur: Bruno Sepodes, "Update of section 4.6 of the Eviplera and Odefsey SmPCs in order to reflect rilpivirine data from the Antiretroviral Pregnancy Registry (APR) Interim Report issued in December 2019. The Eviplera Package Leaflet is updated in accordance. Furthermore, section 4.6 of the SmPC was updated to harmonise the text for breast-feeding with the already agreed text for rilpivirine, sections 4.4, 4.5 and 4.8 of the SmPC regarding the drug-drug interaction with didanosine and section 4.8 of the SmPC was updated regarding lactic acidosis, as agreed by the PRAC in the Viread procedure EMEA/H/C/PSUSA/00002892/201903. Section 4.5 was also updated to remove the reference to simeprevir. In addition, the Worksharing applicant (WSA) took the opportunity to bring the PI in line with the latest QRD template version 10.1, make minor editorial changes and update the PI in line with the Annex to the European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use' (EMA/CHMP/302620/2017 Rev.1) regarding	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

sodium content, for both products." Opinion adopted on 17.04.2020.	

B.5.3. CHMP-PRAC assessed procedures

Baraclude – entecavir – EMEA/H/C/000623/II/0064 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect the completion of the two paediatric studies AI463028 (Evaluation of the pharmacokinetics, safety, tolerability and efficacy of Entecavir (ETV) in paediatric subjects with chronic hepatitis B virus (HBV) infection who are HbeAg-Positive) and AI463189 (A Comparative study of the antiviral efficacy and safety of ETV versus placebo in paediatric subjects with Chronic Hepatitis B Virus (HBV) infection who are HbeAg-Positive). Section 5.1 is also updated to reflect the outcome of study AI463080 (Randomized, observational study of ETV to assess long-term outcomes associated with nucleoside/nucleotide monotherapy for patients with Chronic HBV Infection: The REALM Study). Moreover, section 5.2 of the SmPC is also updated to remove information on the pharmacokinetics of entecavir in lamivudine-experienced paediatric patients, at the request of the CHMP; and section 5.3 to make reference to the clinical data in section 5.1 in respect to carcinogenicity. The RMP version 15 has also been approved, which implements Revision 2 of the EU-RMP template. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1 and to make minor editorial changes to the PI." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 13.02.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Bavencio – avelumab – EMEA/H/C/004338/II/0015 Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Hans Christian Siersted, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to change posology recommendations, amend an existing warning	

and add new ADRs with frequency uncommon regarding myasthenia gravis and myasthenic syndrome. The update results from an update of the Company Core Data Sheet (CCDS) based on the review of cases of myasthenia gravis/myasthenic syndrome. The Package Leaflet is updated accordingly. The RMP version 2.2 has also been submitted with the proposal to reclassify "Other immune-related events (myasthenic syndrome)" from an important potential risk to an important identified risk of "Other immune-related events (myasthenia gravis/myasthenic syndrome)""	
Cimzia – certolizumab pegol – EMEA/H/C/001037/II/0084/G UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information following the final results from studies PS0002 (CIMPASI-2), PS0003 (CIMPACT) and PS0005 (CIMPASI-1) listed as category 3 studies in the RMP; these are results from the open label treatment periods assessing the safety and efficacy of long term use of certolizumab pegol in psoriasis. The RMP version 16.0 has also been updated. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cimzia – certolizumab pegol – EMEA/H/C/001037/II/0087 UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.2, 4.8, 5.1 of the SmPC in order to introduce a change in posology for axial spondyloarthritis (axSpA) and to update the safety and efficacy information based on the results of the study AS0005 (C-OPTIMISE) listed as a category 3 study in the RMP; this is a multicentre, open-label (part A) followed by a randomised, double-blind, parallel-group, placebo-controlled study (part B) to evaluate maintenance of remission in subjects with active axSpA receiving either certolizumab pegol 200mg q2w or 200mg q4w as compared to placebo. The package leaflet is updated	

accordingly. The RMP version 17.0 has also been submitted to reflect the completion of study AS0005 and update to list of safety concerns. In addition, the interim study reports AS0006 and AS0007 have been submitted to include additional pooled safety data in the SmPC. Study AS0006 is a phase 3, multicentre, randomised, placebo-controlled, double-blind study to evaluate efficacy and safety of certolizumab pegol in subjects with active aSpA without x-ray evidence of ankylosing spondylitis and objective signs of inflammation. Study AS0007 is a multicentre, open-label study to assess the effects of certolizumab pegol on the reduction of anterior uveitis flares in aSpA subjects with a history of anterior uveitis (C-view)."	
Fabrazyme – agalsidase beta – EMEA/H/C/000370/II/0113 Genzyme Europe BV, PRAC Rapporteur: Liana Gross-Martirosyan, "Submission of the final report from study listed as a category 3 study in the RMP. This is a postauthorisation study (AGALSC08994) on Fabrazyme (agalsidase beta) home infusion educational materials effectiveness evaluation: a survey of healthcare providers and patients / caregivers. The RMP version 2 has also been submitted accordingly and to comply with the Good Pharmacovigilance Practice (GVP) Module V Rev. 2 template and information on study (AGAL02603) and the Fabry Registry/Pregnancy Sub-registry (AGAL 19211)." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 12.03.2020, 16.01.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Gazyvaro – obinutuzumab – EMEA/H/C/002799/II/0038, Orphan Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Annika Folin, "Submission of final CSR for study MO28543/GREEN to fulfil the post authorization commitment [MEA] 005, the RMP is updated with the deletion of the study under PhV plan, (initial RMP version 6.1 was updated during the procedure to RMP version 7 to reflect also the information on incidence rate of infusion-related reactions (IRR) from the Study MO29543)." Opinion adopted on 17.04.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Request for Supplementary Information adopted on 13.02.2020.

Herceptin – trastuzumab – EMEA/H/C/000278/II/0158

Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Submission of the final report from study BO29159 (MetaPHER) a post-authorization safety measure Category 3 Non-Imposed Post-Approval Safety Study (NI-PASS), following approval of the Herceptin SC line extension procedure EMEA/H/C/278/X/60 to generate and evaluate additional safety and tolerability data for the approved triplet regimen (Herceptin+Perjeta+docetaxel) in the advanced breast cancer setting. In addition, bioanalytical supportive studies are presented. An updated version of the Herceptin Risk Management Plan (version 21) has also been submitted."
Request for Supplementary Information adopted on 13.02.2020.

Kyntheum – brodalumab – EMEA/H/C/003959/II/0014

LEO Pharma A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia, "Update of section 4.4 and 4.8 of the SmPC and relevant sections of the PL to reflect a signal of anaphylactic reaction detected in the post marketing setting.
Minor updates have also been included throughout the product information."

Ocrevus – ocrelizumab – EMEA/H/C/004043/II/0017

Roche Registration GmbH, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Brigitte Keller-Stanislawski, "To update sections 4.2, 4.8 and 5.1 of the SmPC to add the option of a shorter infusion for second and subsequent doses of Ocrevus (2 hours, compared to the approved 3.5 hours infusion) based on the primary analysis of a therapeutic use substudy, MA30143 Shorter Infusion Substudy (Ensemble Plus). The Package Leaflet is updated accordingly. The RMP has been updated (ver. 4.0) with regards to the inclusion of shorter infusion duration (Part I Product Overview), the clinical trial exposure (Part II Module SIII) and the identified risk of infusion-related reactions (Part II Module SVII)."

Ondexxya – andexanet alfa – EMEA/H/C/004108/II/0009/G Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "C.I.4, C.I.3, C.I.6 (non-EoI) Update of section 5.2 of the SmPC in order to update pharmacokinetic information based on results from study CSR 19-514 (PK Comparability) and CSR 16-508 (Japanese Ethnicity Study) listed as a specific obligation in the Annex II. Annex II was proposed to be updated accordingly. The RMP version 2.1 has also been submitted."	
Orkambi – lumacaftor / ivacaftor – EMEA/H/C/003954/II/0055 Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Rhea Fitzgerald, "Update of SmPC section 4.8 following results of safety study in children. Additionally, the applicant took the opportunity to update the SmPC in line with the latest version of the QRD template v10.1. The PL is updated accordingly. In addition, the RMP is updated and version 7,1 is submitted." Request for Supplementary Information adopted on 17.04.2020.	Request for supplementary information adopted with a specific timetable.
Palynziq – pegvaliase – EMEA/H/C/004744/II/0007/G, Orphan BioMarin International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, "Update of sections 4.4, 4.8 and 5.1 of the SmPC based on final results from studies 1655-003, a long-term extension of a Phase 2, open-label, dose-finding study and 165-302 a Phase 3, randomised, double-blind, placebo-controlled, four-arm, discontinuation study which are listed in the RMP as category 3 studies. The RMP version 2.0 has also been submitted. In addition, the SmPC was amended with minor editorial changes." Request for Supplementary Information adopted on 17.04.2020.	Request for supplementary information adopted with a specific timetable.
Sancuso – granisetron – EMEA/H/C/002296/II/0056/G Kyowa Kirin Holdings B.V., Rapporteur: Simona Stankeviciute, PRAC Rapporteur: Rugile Pilviniene, "Update of the SmPC section 5.2. to add pharmacokinetic information concluded	

from a completed paediatric PK study, 392MD/44/C. The RMP has been updated accordingly. The RMP has also been updated to implement RMP template EMA/PRAC/613102/2015 Rev 2 and includes the addition or deletion of safety concerns ((identified risks, potential risks, missing information) not previously assessed or requested by a competent authority. The MAH took the opportunity to update the Pregnancy information in section 4.6 of Annex I to align with the QRD statements provided in the QRD product information template. Minor QRD updates have also been made to the English language annex in line with version 10.1 of the QRD template." Request for Supplementary Information adopted on 12.12.2019.	
Zometa – zoledronic acid – EMEA/H/C/000336/II/0091 Novartis Europharm Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, "Update of sections 4.4 and 5.1 of the SmPC in order to update the safety information on ONJ based on final results from study CZOL446EUS122 listed as a category 3 study in the RMP; this is a non-interventional, prospective, observational, multicentre cohort study to assess the incidence of ONJ in cancer patients with bone metastases starting zoledronic acid treatment. The RMP version 12 has also been submitted. The requested variation proposed amendments to the Summary of Product Characteristics and to the Risk Management Plan (RMP)." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1664 **Keppra-EMEA/H/C/000277/WS1664/0187** UCB Pharma S.A., Lead Rapporteur: Koenraad Norga, Lead PRAC Rapporteur: Laurence de Fays, "Update of section 4.2 of the SmPC to recommend the same dosing for monotherapy and adjunctive therapy based on data from modelling and simulation project. The Package Leaflet is updated accordingly. The RMP version 9.0 has also been submitted. The MAH took the opportunity to move Braille to another box section and to review and adapt the	

German PI according to the current QRD template.”	
WS1704 **Alimta-EMEA/H/C/000564/WS1704/0058** **Pemetrexed Lilly-EMEA/H/C/004114/WS1704/0010** Eli Lilly Nederland B.V., Lead Rapporteur: Alexandre Moreau, Lead PRAC Rapporteur: Ghania Chamouni, “Worksharing to update section 4.8 of the SmPC as requested by CHMP following the assessment of the PSUR covering the period between 05 February 2015 and 04 February 2018. To comply with SmPC guideline and latest QRD update, the Alimta and Pemetrexed Lilly SmPCs are updated combining multiple tables of ADRs into two tables: one for the ADRs reported in the pivotal registration trials and one for ADRs from the postmarketing period (both clinical trials and spontaneous reporting), organized by SOC with the respective frequency categories. The Package Leaflet is updated accordingly. In addition an updated RMP version 6.1 has been submitted to implement the revised GVP Module V (Rev 2) format as requested by CHMP following the assessment of the PSUR covering the period between 05 February 2015 and 04 February 2018.” Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 20.02.2020, 28.11.2019.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.4. PRAC assessed procedures

PRAC Led **BeneFIX – nonacog alfa – EMEA/H/C/000139/II/0163** Pfizer Europe MA EEIG, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, “Update of the RMP to remove LETE (Less than therapeutic effect) as an important identified risk. In addition, in the light of GVP Module V Revision 2,1 the MAH proposes to remove patient populations that were previously identified as Missing information.” Opinion adopted on 17.04.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **BLINCYTO – blinatumomab –**	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP

EMEA/H/C/003731/II/0034/G, Orphan Amgen Europe B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Eva Jirsová, PRAC-CHMP liaison: Ondřej Slanař, "Submission of the final reports from studies 20150163 and 20150228 assessed the effectiveness of Blincyto additional risk minimization measures for healthcare professionals (study 20150163) and patients/caregivers (study 20150228) listed as a category 3 post-authorization safety studies (PASS) in the Risk Management Plan (RMP)." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 16.01.2020.	Members were in agreement with the CHMP recommendation.
PRAC Led **Ceplene – histamine dihydrochloride – EMEA/H/C/000796/II/0040** Noventia Pharma Srl, Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, "Submission of an updated RMP version 8.1 in order to include the information about the termination of the non-interventional study (NIS) of category 3 Ceplene-3290 and of the PAES Ceplene Cohort Study 3306. -RMP has been adapted to the new RMP template (GVP V rev.2, mandatory since 31 March 2018). -The safety concerns (Part II Modules SVII and SVIII, Part V, Part VI) have been changed. A new important potential risk, named "Drug effect decreased as a consequence of drug interaction", has been added to the list of safety concerns. -Part III and Part IV have been updated to include information about the termination of the non-interventional study (NIS) of category 3 Ceplene-3290 and of the PAES Ceplene Cohort Study 3306. -updated information about the other ongoing studies included in the Pharmacovigilance Plan, "Ceplene-3292" and "Ceplene-3298", have been included in Part III and related parts/modules. -Details about the Marketing Authorization Holder have been updated accordingly upon implementation of transfer from previous Marketing Authorisation Holder, Meda AB, (positive decision received 08 December 2017)" Request for Supplementary Information adopted on 17.04.2020.	Request for supplementary information adopted with a specific timetable.

PRAC Led **Docetaxel Zentiva – docetaxel – EMEA/H/C/000808/II/0061** Zentiva, k.s., Informed Consent of Taxotere, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 1.1 in order to revise the list of safety concerns in line with the GVP Module V Rev.2 and to complete Part II modules." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **EXJADE – deferasirox – EMEA/H/C/000670/II/0068** Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final report related to the Physician Survey (NO6987) conducted for Exjade to assess the impact of educational materials on the prescribers' awareness of doses and biological monitoring recommendations and to assess the awareness and appropriate use of both formulations (Dispersible Tablets and Film-Coated tablets). The updated RMP version 17.1 is submitted as well." Request for Supplementary Information adopted on 17.04.2020, 16.01.2020, 03.10.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Inflectra – infliximab – EMEA/H/C/002778/II/0079** Pfizer Europe MA EEIG, Duplicate, Duplicate of Remsima, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of the final clinical study report for C1231002 (PERSIST) study, an observational cohort study designed to evaluate real life drug persistence in biologic I rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis patients receiving CT-P13 or those switched to CT-P13 from stable treatment with Remicade (reference medicinal product)." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 28.11.2019.	
PRAC Led **Inflectra – infliximab – EMEA/H/C/002778/II/0080** Pfizer Europe MA EEIG, Duplicate, Duplicate of Remsima, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of the final clinical study report for C1231001 (CONNECT-IBD) study; a non-interventional study designated as a Post Authorisation Safety Study conducted voluntarily to capture data from real-world clinical practice to characterise the population and document drug utilisation patterns. In addition, available safety data and data on the effectiveness of CT-P13 in the context of standard of care utilisation of Remicade (reference medicinal product) was collected in patients with Crohn's disease or ulcerative colitis." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 28.11.2019.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Lemtrada – alemtuzumab – EMEA/H/C/003718/II/0031** Sanofi Belgium, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an update of the RMP (version 7.0) incorporating all amendments and additional activities defined in the Article 20 referral procedure (EMEA/H/A-20/1483/C/3718/0028)." Request for Supplementary Information adopted on 17.04.2020.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Ozurdex – dexamethasone – EMEA/H/C/001140/II/0037** Allergan Pharmaceuticals Ireland, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of an updated RMP version 9.0 (and 10.0 during the procedure) in order to reflect increased knowledge of the product and align to the new RMP template." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 16.01.2020.	
PRAC Led **Remsima – infliximab – EMEA/H/C/002576/II/0073** Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of the final clinical study report for C1231001 (CONNECT-IBD) study; a non-interventional study designated as a Post Authorisation Safety Study conducted voluntarily to capture data from real-world clinical practice to characterise the population and document drug utilisation patterns. In addition, available safety data and data on the effectiveness of CT-P13 in the context of standard of care utilisation of Remicade (reference medicinal product) was collected in patients with Crohn's disease or ulcerative colitis." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 28.11.2019.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Remsima – infliximab – EMEA/H/C/002576/II/0074** Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of the final clinical study report for C1231002 (PERSIST) study, an observational cohort study designed to evaluate real life drug persistence in biologic I rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis patients receiving CT-P13 or those switched to CT-P13 from stable treatment with Remicade (reference medicinal product)." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 28.11.2019.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Siklos – hydroxycarbamide – EMEA/H/C/000689/II/0045** Addmedica S.A.S., Rapporteur: Koenraad Norga, PRAC Rapporteur: Laurence de Fays, PRAC-CHMP liaison: Bart Van der Schueren, "Update of sections 4.2, 4.3, 4.4, 4.5, 4.6, 4.8 and 4.9 of the SmPC as a consequence of the final study results of the non-interventional	Request for supplementary information adopted with a specific timetable.

cohort study ESCORT-HU (European Sickle Cell Disease Cohort – Hydroxyurea) and harmonisation with other HU products. In addition, Annex II is amended to delete the paragraph about the treatment guide for physicians. The PIL is updated in accordance with the changes to the SmPC. The RMP is updated to reflect the finalisation of the ESCORT-HU study." Request for Supplementary Information adopted on 17.04.2020.	
PRAC Led **Spectrila – asparaginase – EMEA/H/C/002661/II/0017** medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Jan Neuhauser, PRAC-CHMP liaison: Andrea Laslop, "Update of the Risk Management Plan (version 12) for Spectrila in accordance with GVP Module V Rev 2 including the implementation of the new RMP template and the new definition of safety concerns. The QPPV and the Milestones / Timelines for the clinical study MC-Spectrila.1/ALL were updated in accordance to the newly applied DLP for this Risk Management Plan." Request for Supplementary Information adopted on 17.04.2020.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Taxotere – docetaxel – EMEA/H/C/000073/II/0134** Sanofi Mature IP, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 1.2 in order to revise the list of safety concerns in line with the GVP Module V Rev.2 and to complete Part II modules." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Taxotere – docetaxel – EMEA/H/C/000073/II/0136/G** Sanofi Mature IP, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Update of sections 4.4 and 4.8 of the SmPC to add a	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

warning and safety information about tumour lysis syndrome based on a cumulative safety review requested as part of the last PSUR; The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor corrections to the SmPC and update the list of local representatives in the Package Leaflet. Update of section 4.8 of the SmPC to add safety information about myositis based on cumulative safety review requested as part of the last PSUR; the Package Leaflet is updated accordingly." Opinion adopted on 17.04.2020.	
PRAC Led **Teysuno – tegafur / gimeracil / oteracil – EMEA/H/C/001242/II/0042** Nordic Group B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 9.1 in order to remove Category 3 MATEO study and associated evaluation of the effect of tumour Microsatellite Instability (MSI) status on Teysuno efficacy and safety in gastric cancer as obligations within the RMP. An update of the safety specifications (re-classifying and removing risks from the list of important safety concerns as outlined in PSUSA/2875/201801) is also included." Opinion adopted on 17.04.2020. Request for Supplementary Information adopted on 13.02.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1653** **Enbrel-EMEA/H/C/000262/WS1653/0230** **LIFMIOR-EMEA/H/C/004167/WS1653/0024** Pfizer Europe MA EEIG, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of the second 5-year report from the British Society for Rheumatology Biologics Register (BSRBR, also referred as study B1801309) listed as a category 3 study in the RMP. This is a prospective observational cohort study which investigates the long-term outcomes of patients with rheumatoid arthritis treated with etanercept with particular reference to safety."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 17.04.2020, 16.01.2020.	
PRAC Led **WS1773** **Exelon-EMEA/H/C/000169/WS1773/0128** **Prometax-EMEA/H/C/000255/WS1773/0128** Novartis Europharm Limited, Lead Rapporteur: Alexandre Moreau, Lead PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP v 10.0 to reflect the results of the Drug Utilisation Study CENA713D2409 (submitted and assessed in variation WS-1557, opinion adopted in July 2019) and to reassess all important risks in accordance of GVP revision 2. In addition, as requested by the PRAC following the assessment of the PSUSA/00002654/201901, some safety concerns have been removed." Opinion adopted on 17.04.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1775** **Renagel-EMEA/H/C/000254/WS1775/0114** **Renvela-EMEA/H/C/000993/WS1775/0051** **Sevelamer carbonate Winthrop-EMEA/H/C/003971/WS1775/0024** Genzyme Europe BV, Lead Rapporteur: Christophe Focke, Lead PRAC Rapporteur: Laurence de Fays, PRAC-CHMP liaison: Bart Van der Schueren, "Submission of an updated RMP version 10 in order to remove the important potential risk "sevelamer crystals associated with serious gastrointestinal disorders" from the list of safety concerns in the RMP of sevelamer hydrochloride/carbonate products, as agreed by the CHMP during the procedure for the renewal of the marketing authorization for Sevelamer Carbonate Winthrop (EMEA/H/C/003971/R/0022)." Opinion adopted on 17.04.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.5. CHMP-CAT assessed procedures

Imlygic – talimogene laherparepvec – EMEA/H/C/002771/II/0036, ATMP Amgen Europe B.V., Rapporteur: Olli Tenhunen,	

CHMP Coordinator: Tuomo Lapveteläinen, Request for Supplementary Information adopted on 21.02.2020.

Spherox – spheroids of human autologous matrix-associated chondrocytes – EMEA/H/C/002736/II/0015, ATMP

CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder, , "Update of section 4.8 and 5.1 of the SmPC following the 48-month follow up data for trial cod 16 HS 13, a study assessing the long-term efficacy and safety of Spherox."

Yescarta – axicabtagene ciloleucel – EMEA/H/C/004480/II/0015, Orphan, ATMP

Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus,
Request for Supplementary Information adopted on 21.02.2020.

B.5.6. CHMP-PRAC-CAT assessed procedures

Strimvelis – autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence – EMEA/H/C/003854/II/0024, Orphan, ATMP

Orchard Therapeutics (Netherlands) BV, Rapporteur: Sol Ruiz, CHMP Coordinator: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information following the completion of the STRIM-004 study, which is a non-interventional long term follow up of the subjects who received Strimvelis gene therapy. This study included paediatric patients and is listed as a category 3 study in the RMP. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor administrative changes in the PI."
Request for Supplementary Information adopted on 20.03.2020.

B.5.7. PRAC assessed ATMP procedures

B.5.8. Unclassified procedures and work-sharing procedures of type I variations

WS1770/G **Infanrix hexa-** **EMEA/H/C/000296/WS1770/0271/G** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke	
WS1789/G **AZILECT-EMEA/H/C/000574/WS1789/0086/G** **Rasagiline ratiopharm-EMEA/H/C/003957/WS1789/0018/G** Teva B.V., Lead Rapporteur: Bruno Sepodes Opinion adopted on 17.04.2020.	Positive Opinion adopted by consensus on 17.04.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Esmya – ulipristal acetate – EMEA/H/C/002041/II/0048 Gedeon Richter Plc., Rapporteur: Kristina Dunder, "Update of sections 4.4, 4.8 of the SmPC in order to add a warning and update the safety information based on a new case of liver transplantation following exposure to Esmya; the Package Leaflet and Labelling are updated accordingly" Withdrawal request submitted on 27.03.2020.	The MAH withdrew the procedure on 27.03.2020.
Esmya – ulipristal acetate – EMEA/H/C/002041/II/0048 Gedeon Richter Plc., Rapporteur: Kristina Dunder, "Update of sections 4.4, 4.8 of the SmPC in order to add a warning and update the safety information based on a new case of liver transplantation following exposure to Esmya; the Package Leaflet and Labelling are updated accordingly" Withdrawal request submitted on 27.03.2020.	The MAH withdrew the procedure on 27.03.2020.
Olanzapine Apotex - olanzapine - EMEA/H/C/001178/II/0037 Apotex Europe BV, Generic, Generic of Zyprexa, Rapporteur: John Joseph Borg, "Update of sections 4.8 and 4.4 in order to add information regarding the risk of metabolic syndrome with the use of olanzapine, based on review of the available data." Request for Supplementary Information adopted	The MAH withdrew the procedure on 22.04.2020.

on 16.01.2020.

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

Fulphila – pegfilgrastim – EMEA/H/C/004915/II/0005/G Mylan S.A.S, Rapporteur: Martina Weise Request for Supplementary Information adopted on 28.11.2019.	Request by the applicant for an extension of the clock stop to respond to the RSI adopted on 28.11.2019.
Kisqali – ribociclib – EMEA/H/C/004213/II/0018 Novartis Europharm Limited, Rapporteur: Filip Josephson "Update of section 5.2 of the SmPC to include updated information about the use of Kisqali in patients with mild or moderate renal impairment based on the results of Study CLEE011A2116 Part II and additional data from breast cancer patients with mild or moderate renal impairment." Request for Supplementary Information adopted on 14.11.2019.	Request by the applicant for an extension of the clock stop to respond to the RSI adopted on 14.11.2019.

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

lonafarnib - EMEA/H/C/005271, Orphan EigerBio Europe Limited, treatment of Hutchinson-Gilford Progeria Syndrome and Progeroid Laminopathies	**Accelerated review**
lumasiran - EMEA/H/C/005040, Orphan Alnylam Netherlands B.V., primary hyperoxaluria type 1 (PH1)	**Accelerated review**

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

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

abicipar pegol - EMEA/H/C/005103 treatment of neovascular (wet) age-related macular degeneration (AMD) List of Questions adopted on 14.11.2019.
arsenic trioxide - EMEA/H/C/005218 treatment of relapsed acute promyelocytic leukaemia (APL)

List of Questions adopted on 12.12.2019.

bevacizumab - EMEA/H/C/005181
Treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer.
First-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer.
First line treatment of patients with advanced and/or metastatic renal cell cancer.
List of Questions adopted on 30.01.2020.

acalabrutinib - EMEA/H/C/005299, Orphan
AstraZeneca AB, Treatment of adult patients with chronic lymphocytic leukaemia (CLL)/small lymphocytic lymphoma (SLL)
List of Questions adopted on 27.02.2020.

satralizumab - EMEA/H/C/004788, Orphan
Roche Registration GmbH, treatment of adult and adolescent patients from 12 years of age with neuromyelitis optica spectrum disorders (NMOSD)
List of Questions adopted on 10.12.2019.

fampridine - EMEA/H/C/005359
treatment of Multiple Sclerosis
List of Questions adopted on 12.12.2019.

filgotinib - EMEA/H/C/005113
treatment of adult patients with moderately to severely active rheumatoid arthritis
List of Questions adopted on 12.12.2019.

elexacaftor / tezacaftor / ivacaftor - EMEA/H/C/005269, Orphan
Vertex Pharmaceuticals (Ireland) Limited, treatment of cystic fibrosis
List of Questions adopted on 28.01.2020.

Ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005343
is indicated for active immunization for prevention of disease caused by Ebola virus
List of Questions adopted on 25.02.2020.

caffeine citrate - EMEA/H/C/005435
treatment of primary apnoea
List of Questions adopted on 27.02.2020.

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

immunotherapy (OIT) for patients aged 4 to 17 years with a confirmed diagnosis of peanut allergy
List of Questions adopted on 14.11.2019.

Pemetrexed Accord - pemetrexed - EMEA/H/C/004072/X/0010
Accord Healthcare S.L.U., Generic, Generic of Alimta, Rapporteur: John Joseph Borg, PRAC Rapporteur: Ghania Chamouni, "Extension application to introduce a new pharmaceutical form associated with new strength (25 mg/ml solution for infusion)"
List of Questions adopted on 30.01.2020.

rivaroxaban - EMEA/H/C/005279
prevention of atherothrombotic events
List of Questions adopted on 12.12.2019.

somapacitan - EMEA/H/C/005030, Orphan
Novo Nordisk A/S, indicated for the replacement of endogenous GH with growth hormone deficiency (AGHD).
List of Questions adopted on 30.01.2020.

deferiprone - EMEA/H/C/005004, Orphan
Apotex B.V., treatment of neurodegeneration with brain iron accumulation
List of Questions adopted on 19.09.2019.

Ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005337
is indicated for active immunization for prevention of disease caused by Ebola virus (Zaire ebolavirus species)
List of Questions adopted on 25.02.2020.

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

Chenodeoxycholic acid Leadiant - chenodeoxycholic acid - EMEA/H/C/004061/S/0014, Orphan
Leadiant GmbH, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Adam Przybylkowski

Elaprase - idursulfase - EMEA/H/C/000700/S/0087
Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan

Evoltra - clofarabine - EMEA/H/C/000613/S/0068

Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Firdapse - amifampridine - EMEA/H/C/001032/S/0066
BioMarin International Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Lamzede - velmanase alfa - EMEA/H/C/003922/S/0011, Orphan
Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jan Neuhauser

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

Armisarte - pemetrexed - EMEA/H/C/004109/R/0022
Actavis Group PTC ehf, Rapporteur: Alar Irs, PRAC Rapporteur: Ghania Chamouni

Bavencio - avelumab - EMEA/H/C/004338/R/0017
Merck Europe B.V., Rapporteur: Filip Josephson, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Hans Christian Siersted

Benepali - etanercept - EMEA/H/C/004007/R/0053
Samsung Bioepis NL B.V., Rapporteur: Andrea Laslop, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Eva A. Segovia

ELOCTA - efmoroctocog alfa - EMEA/H/C/003964/R/0036
Swedish Orphan Biovitrum AB (publ), Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Sol Ruiz, PRAC Rapporteur: Sonja Hrabcik

Jevtana - cabazitaxel - EMEA/H/C/002018/R/0042
sanofi-aventis groupe, Rapporteur: Alexandre Moreau, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ghania Chamouni

Kolbam - cholic acid - EMEA/H/C/002081/R/0034, Orphan
Retrophin Europe Ltd, Rapporteur: Konstantinos Markopoulos, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Agni Kapou

Lopinavir/Ritonavir Mylan - lopinavir / ritonavir - EMEA/H/C/004025/R/0014
Mylan S.A.S, Generic, Generic of Kaletra, Rapporteur: John Joseph Borg, PRAC Rapporteur: Adrien Inoubli

Pemetrexed Accord - pemetrexed - EMEA/H/C/004072/R/0012
Accord Healthcare S.L.U., Generic, Generic of Alimta, Rapporteur: John Joseph Borg, PRAC Rapporteur: Ghania Chamouni

Pemetrexed Hospira - pemetrexed - EMEA/H/C/003970/R/0022
Pfizer Europe MA EEIG, Generic, Generic of Alimta, Rapporteur: Alar Irs, PRAC Rapporteur: Ghania Chamouni

Rasagiline Mylan - rasagiline - EMEA/H/C/004064/R/0006
Mylan S.A.S, Generic, Generic of AZILECT, Rapporteur: Kolbeinn Gudmundsson, PRAC Rapporteur: Ana Sofia Diniz Martins

Spectrila - asparaginase - EMEA/H/C/002661/R/0018
medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Andrea Laslop, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Jan Neuhauser

Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/R/0065
MCM Vaccine B.V., Rapporteur: Christophe Focke, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Brigitte Keller-Stanislawski

VITRAKVI - larotrectinib - EMEA/H/C/004919/R/0006
Bayer AG, Rapporteur: Filip Josephson, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Rugile Pilviniene

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

B.6.7. Type II Variations scope of the Variations: Extension of indication

Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell

cultures - EMEA/H/C/004814/II/0013
Seqirus Netherlands B.V., Rapporteur: Sol Ruiz, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension of indication of prophylaxis of influenza, from the currently approved age range "adults and children from 9 years of age" to "adults and children from 2 years of age" for Flucelvax Tetra; 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. Version 2.1 of the RMP has also been submitted."

Prezista - darunavir - EMEA/H/C/000707/II/0107
Janssen-Cilag International NV, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, "Extension of indication for PREZISTA (darunavir) (800 mg) in combination with COBI (150 mg) for the treatment of HIV-1 infection in adolescents (aged 12 years and older with body weight at least 40 kg). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 of the SmPC and section 3 of the PL are being updated accordingly. The updated RMP version 27.1 has also been submitted."

Quofenix - delafloxacin - EMEA/H/C/004860/II/0003
A. Menarini Industrie Farmaceutiche Riunite s.r.l., Rapporteur: Janet Koenig, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Željana Margan Koletić, "Extension of indication to include treatment of Community Acquired Pneumonia (CAP) for Quofenix 450 mg tablets and 300 mg powder for concentrate for solution for infusion; 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. Version 2.0 of the RMP has also been submitted."

Recarbrio - imipenem / cilastatin / relebactam - EMEA/H/C/004808/II/0001
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Adam Przybylkowski, "Extension of indication to include the treatment of hospital-acquired pneumonia (HAP) including ventilator-associated pneumonia (VAP), with or without concurrent bacteraemia in adults for Recarbrio; as a

consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Furthermore, the Marketing authorisation holder (MAH) made editorial corrections and brought the PI in line with the latest QRD template version 10.1.
Version 1.1 of the RMP has also been submitted."

Tecentriq - atezolizumab - EMEA/H/C/004143/II/0042
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Extension of indication to include, in combination with platinum-based chemotherapy, first-line treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC) for Tecentriq; as a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated. Version 14.0 of the RMP has also been submitted."

WS1783
OPDIVO-
EMEA/H/C/003985/WS1783/0081
Yervoy-EMEA/H/C/002213/WS1783/0077
Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Jorge Camarero Jiménez, Lead PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension of indication to include first-line treatment of metastatic non small cell lung cancer in adults with no EGFR or ALK positive tumour mutations for combination of Odpivo and Yervoy; 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. Version 17.0 of the RMP for Opdivo and version 27.0 for Yervoy have also been submitted."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0075/G, Orphan
Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik

Afstyla - lonoctocog alfa - EMEA/H/C/004075/II/0033
CSL Behring GmbH, Rapporteur: Jan Mueller-

Berghaus

Bemfola - follitropin alfa - EMEA/H/C/002615/II/0025/G
Gedeon Richter Plc., Rapporteur: Paula Boudewina van Hennik

Buvidal - buprenorphine - EMEA/H/C/004651/II/0007/G
Camurus AB, Rapporteur: Peter Kiely

Caprelsa - vandetanib - EMEA/H/C/002315/II/0044/G
Genzyme Europe BV, Rapporteur: Alexandre Moreau

Cegfila - pegfilgrastim - EMEA/H/C/005312/II/0004/G
Mundipharma Corporation (Ireland) Limited, Rapporteur: Koenraad Norga

Emgality - galcanezumab - EMEA/H/C/004648/II/0013
Eli Lilly Nederland B.V., Rapporteur: Daniela Melchiorri

Emtricitabine/Tenofovir disoproxil Mylan - emtricitabine / tenofovir disoproxil - EMEA/H/C/004050/II/0013/G
Mylan S.A.S, Generic, Generic of Truvada, Rapporteur: Simona Stankeviciute

Emtricitabine/Tenofovir disoproxil Zentiva - emtricitabine / tenofovir disoproxil - EMEA/H/C/004137/II/0015
Zentiva k.s., Generic, Generic of Truvada, Rapporteur: Alar Irs

Entyvio - vedolizumab - EMEA/H/C/002782/II/0049
Takeda Pharma A/S, Rapporteur: Daniela Melchiorri

Grastofil - filgrastim - EMEA/H/C/002150/II/0029
Accord Healthcare S.L.U., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka

Grastofil - filgrastim - EMEA/H/C/002150/II/0031/G
Accord Healthcare S.L.U., Rapporteur: Outi Mäki-Ikola

IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0038, Orphan
CSL Behring GmbH, Rapporteur: Jan Mueller-

Berghaus

Kevzara - sarilumab - EMEA/H/C/004254/II/0022/G
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus

Mircera - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/II/0078/G
Roche Registration GmbH, Rapporteur: Maria Concepcion Prieto Yerro

Ogivri - trastuzumab - EMEA/H/C/004916/II/0016
Mylan S.A.S, Rapporteur: Koenraad Norga

Orencia - abatacept - EMEA/H/C/000701/II/0139
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola

Praluent - alirocumab - EMEA/H/C/003882/II/0056/G
sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege

Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0186/G
Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder

Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0160
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0040
CSL Behring GmbH, Rapporteur: Kristina Dunder

Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0030
GlaxoSmithkline Biologicals SA, Rapporteur: Christophe Focke

Soliris - eculizumab - EMEA/H/C/000791/II/0112, Orphan
Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez

TAKHZYRO - lanadelumab -

EMEA/H/C/004806/II/0014/G, Orphan
Shire Pharmaceuticals Ireland Limited,
Rapporteur: Kristina Dunder

Ultomiris - ravulizumab -
EMEA/H/C/004954/II/0005
Alexion Europe SAS, Rapporteur: Jorge
Camarero Jiménez

Victoza - liraglutide -
EMEA/H/C/001026/II/0057
Novo Nordisk A/S, Rapporteur: Johann Lodewijk
Hillege

Zevalin - ibritumomab tiuxetan -
EMEA/H/C/000547/II/0051/G
Ceft Biopharma s.r.o., Rapporteur: Sinan B.
Sarac

WS1784/G
Hexacima-EMEA/H/C/002702/WS1784/
0096/G
Hexaxim-EMEA/H/W/002495/WS1784/
0101/G
Hexyon-EMEA/H/C/002796/WS1784/
0100/G
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-
Berghaus

WS1797/G
Hexacima-EMEA/H/C/002702/WS1797/
0100/G
Hexaxim-EMEA/H/W/002495/WS1797/
0105/G
Hexyon-EMEA/H/C/002796/WS1797/
0104/G
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-
Berghaus

WS1799/G
Luveris-EMEA/H/C/000292/WS1799
/0085/G
Pergoveris-EMEA/H/C/000714/WS1799/
0067/G
Merck Europe B.V., Lead Rapporteur: Mark
Ainsworth

WS1819/G
Lantus-EMEA/H/C/000284/WS1819/
0119/G
Suliqua-EMEA/H/C/004243/WS1819/
0014/G
Toujeo-EMEA/H/C/000309/WS1819/
0112/G

Sanofi-Aventis Deutschland GmbH, Lead Rapporteur: Kristina Dunder

WS1821/G
Hexacima-EMEA/H/C/002702/WS1821/0101/G
Hexaxim-EMEA/H/W/002495/WS1821/0106/G
Hexyon-EMEA/H/C/002796/WS1821/0105/G
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

WS1802
Hexacima-EMEA/H/C/002702/WS1802/0098
Hexaxim-EMEA/H/W/002495/WS1802/0103
Hexyon-EMEA/H/C/002796/WS1802/0102
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

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

AJOVY - fremanezumab - EMEA/H/C/004833/II/0008/G
TEVA GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of section 5.1 of SmPC to include data from Study TV48125-CNS-30068 (FOCUS) - A Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Study with an Open-Label Period to Evaluate the Efficacy and Safety of Fremanezumab for the Prophylactic Treatment of Migraine in Patients with Inadequate Response to Prior Preventive Treatments."

Atripla - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/000797/II/0143/G
Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, "Grouped variation:
- C.I.3.z (Type IB): Update of sections 4.4, 4.5 and 4.8 of the SmPC regarding the drug-drug interaction with didanosine and of section 4.8 of the SmPC regarding lactic acidosis, as agreed by the PRAC in the Viread procedure EMEA/H/C/PSUSA/00002892/201903,
- C.I.3.z (Type IB): Update of section 4.5 of the SmPC to update the wording of the interaction between efavirenz and etonogestrel implants, as

agreed by the PRAC in the Sustiva procedure EMEA/H/C/PSUSA/00001200/201804, - C.I.4 (Type II): Update of section 4.5 of the SmPC to state that co-administration of glecaprevir/pibrentasvir with Atripla is not recommended; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the PI in line with the Annex to the European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use' (EMA/CHMP/302620/2017 Rev.1) regarding sodium content."	
BLINCYTO - blinatumomab - EMEA/H/C/003731/II/0036, Orphan Amgen Europe B.V., Rapporteur: Alexandre Moreau, "C.I.13: Submission of the final report from study MT103-211 classified as Category 3 Post-Authorization Safety Study (PASS) in the Risk Management Plan (RMP). This is an interventional clinical study (Open-label, Multicenter, Phase 2) to Evaluate Efficacy and Safety of the Bi-specific T cell Engager (BiTE) Antibody Blinatumomab in Adult Subjects with Relapsed/Refractory B-precursor Acute Lymphoblastic Leukemia (ALL). The objective of this PASS was to evaluate central nervous system (CNS) symptoms and explore predictive factors for CNS events associated with blinatumomab, based on an additional evaluation cohort that had been opened to help better understand CNS symptoms with blinatumomab."	
Cubicin - daptomycin - EMEA/H/C/000637/II/0075 Merck Sharp & Dohme B.V., Rapporteur: Bjorg Bolstad, "Update of sections 4.4 and 4.8 of the SmPC in order to include two new terms, tubulointerstitial nephritis (TIN) and drug reaction with eosinophilia and systemic symptoms (DRESS) to the Special warnings and precautions of the SmPC. TIN has also been added to the Adverse events section, based on a review of the cumulative postmarketing cases associated with the use of daptomycin. Wording has been added to the Product information with regard to the contents of sodium, implementing the guideline for excipients in the labelling and package leaflet of	

medicinal products for human use.
The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce QRD-related, spelling, formatting and spacing corrections."

Effentora - fentanyl - EMEA/H/C/000833/II/0054/G
Teva B.V., Rapporteur: Janet Koenig, "Update of the SmPC in line with the recent PSUSA evaluation outcome and to reflect the updated Company core safety information"

Elaprase - idursulfase - EMEA/H/C/000700/II/0086
Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.9 of the SmPC in order to include a warning on the risk of anaphylactoid reaction following overdose with elaprase."

Erleada - apalutamide - EMEA/H/C/004452/II/0006
Janssen-Cilag International N.V., Rapporteur: Jorge Camarero Jiménez, "Update of section 4.8 of the SmPC to add interstitial lung disease to the list of adverse drug reactions (ADRs) with frequency unknown based on a safety review; the Package Leaflet is updated accordingly. The MAH also took the opportunity to update the PI in line with the QRD template 10.1."

Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0116
Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 5.1 of the SmPC in order to change posology recommendations in adults, children and adolescents aged 8 years and older by removing the information on the lower dosing regimens that have been used in clinical studies and update the clinical information based on the review of published scientific literature including 3 observational studies in patients remaining on standard dose of Fabrazyme or switching to low-dose Fabrazyme (0.5 mg/kg every 2 weeks) or to the registered dose of agalsidase alfa (0.2 mg/kg every 2 weeks). In addition, the MAH took the opportunity to propose changes in the Product Information according to the QRD templates and current guidelines, including new warnings related to sodium excipient and

traceability of biological medicinal products."

Fotivda - tivozanib - EMEA/H/C/004131/II/0012
EUSA Pharma (Netherlands) B.V., Rapporteur: Bruno Sepodes, "Submission of AV-951-15-303 (TIVO-3) study (Phase 3 randomized, controlled, multi-centre, open-label study to compare tivozanib versus sorafenib in RCC patients who have failed 2 or 3 prior systemic regimens) in order to present the second interim OS analysis and to fulfil PAM LEG-003 procedure."

Infanrix hexa - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/000296/II/0275
GlaxoSmithkline Biologicals SA, Rapporteur: Christophe Focke, "Update of sections 4.8 and 5.1 of the SmPC in relation to the frequency of adverse reactions somnolence and fatigue and to update the safety and immunogenicity information in infants and toddlers born to mothers vaccinated with dTpa during pregnancy; based on data generated from DTPA-048 and DTPA-049; these are phase IV, open-label, non-randomised, multicentre studies aimed to provide immunological responses to Infanrix hexa in terms of seroprotection status for diphtheria (D), tetanus (T), HBs antigen, inactivated poliovirus (IPV) and Haemophilus influenzae type b (Hib) antigens (PRP) and in terms of vaccine or booster responses to the pertussis antigens, 1 month after the last dose of the primary vaccination or the booster dose.
The MAH took the opportunity to update the posology information in the package leaflet to align it with the SmPC.
In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.1."

Mepsevii - vestronidase alfa - EMEA/H/C/004438/II/0014, Orphan
Ultragenyx Germany GmbH, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8 and 5.1 of the SmPC following the assessment of final results from study UX003-CL202, a multicenter, multinational, open-label

treatment, extension of study UX003-CL301 in subjects with MPS VII, previously submitted under Article 46 of Regulation (EC) No 1901/2006; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the Product Information."	
Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0081 Genzyme Europe BV, Rapporteur: Alexandre Moreau, "Update of section 5.1 of the SmPC on long term efficacy of alglucosidase alfa on survival and other clinical outcome based on the review of published scientific literature. In addition, the MAH took the opportunity to update the Product Information to mention the change on contact details of local representatives for Italy and Malta and to add traceability statement as per QRD template version 10.1."	
Nerlynx - neratinib - EMEA/H/C/004030/II/0011/G Pierre Fabre Medicament, Rapporteur: Bruno Sepodes, "Update of sections 4.2, 4.3, 4.4, 4.5 and 5.2 of the SmPC in order to update the pharmacokinetics properties of neratinib and amend drug-drug interaction (DDI) information with CYP3A4/P-gp inducers and inhibitors based on two ADME studies (PUMA-NER-0105 and PUMA-NER-0102), a PBPK model report and in vitro studies; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor corrections to the PI and to bring the PI in line with the latest QRD template version 10. Update of sections 4.2, 4.3, 4.4, 4.5 and 5.2 of the SmPC in order to update DDI information with H2-receptor antagonists and add DDI information with loperamide based on two DDI studies (PUMA-NER-0104, PUMA-NER-0103); the Package Leaflet is updated accordingly."	
Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0011 Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, "C.I.4 Update of sections 4.4 and 4.5 of the SmPC in order to add a new warning on use of heparin after administration of andexanet based on spontaneous reports,	

medical literature
reports, clinical trials and In vitro data. The Package Leaflet is updated accordingly.
Additional editorial changes were proposed in Annex I and IIIB."

Ozempic - semaglutide - EMEA/H/C/004174/II/0014

Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 5.1 of the SmPC in order to include information on the use of semaglutide once weekly in combination with a SGLT-2 inhibitor, based on the final results from the SUSTAIN 9 study (study NN9535-4269); this is a 30-week, randomised, double-blind, placebo-controlled phase 3 trial investigating the efficacy and safety of semaglutide as add-on to treatment with an SGLT-2 inhibitor ± metformin or sulphonylurea (SU) in subjects with T2DM; the Package Leaflet is updated accordingly."

Reyataz - atazanavir / atazanavir sulfate - EMEA/H/C/000494/II/0129/G

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jean-Michel Race, "Grouped application:
- C.I.4 (Type IB) - Update of sections 4.3 and 4.5 of the SmPC to add a new contraindication and a new drug-drug interaction related to co-administration with lomiptapide, based on recommendations already approved for lomitapide; the Package Leaflet is updated accordingly.
- C.I.4 (Type II) - Update of section 4.5 of the SmPC to add a new drug-drug interaction related to co-administration with direct oral anticoagulants (DOACs), to align with wording approved for DOACs; the Package Leaflet is updated accordingly.
In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the PI in line with the Annex to the European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use' (EMA/CHMP/302620/2017 Rev.1) regarding sucrose content, remove boceprevir from section 4.5 of the SmPC and section 2 of the PL, bring the PI in line with the latest QRD template version 10.1 and update the list of local representatives in the Package Leaflet."

Rubraca - rucaparib -

EMEA/H/C/004272/II/0019/G
Clovis Oncology Ireland Limited, Rapporteur: Jorge Camarero Jiménez, "Submission of the final report from study CO-338-017 (ARIEL2), a Phase 2, open-label, study evaluating the efficacy and safety of rucaparib in patients with relapsed high-grade serous or endometrioid epithelial ovarian, fallopian tube, or primary peritoneal cancer.
Submission of the final report from study CO-338-010 (Study 10), a Phase 1/2, open-label study evaluating the safety, PK and efficacy of rucaparib in patients with relapsed platinum-sensitive high grade ovarian cancer."

Soliris - eculizumab - EMEA/H/C/000791/II/0113, Orphan
Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez, "Submission of a variation to update section 4.2 of the SmPC to include home-infusion as an alternative infusion setting for Soliris for all the approved indications (paroxysmal nocturnal hemoglobinuria, atypical hemolytic uremic syndrome, refractory generalized myasthenia gravis and neuromyelitis optica spectrum disorder).
The PL has been updated accordingly."

TAGRISSO - osimertinib - EMEA/H/C/004124/II/0036
AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, "Update of section 5.1 of the SmPC in order to update the information regarding overall survival (OS) based on the final results from study D5160C00003 (AURA3); this is a randomized study of osimertinib versus platinum-based doublet chemotherapy for patients with Locally advanced or metastatic non-small cell lung cancer whose disease has progressed with previous EGFR TKI. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1."

Talzenna - talazoparib - EMEA/H/C/004674/II/0004
Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to include the final OS results from Study 673-301 (C3441009, EMBRACA), a phase 3, open-label, randomised, multicenter study of talazoparib vs chemotherapy in patients with germline BRCA mutated HER-2 negative locally

advanced or metastatic breast cancer."

Tegsedi - inotersen - EMEA/H/C/004782/II/0011, Orphan
Akcea Therapeutics Ireland Limited, Rapporteur: Martina Weise, "Update of SmPC section 5.3 to reflect the results of rat carcinogenicity study."

Translarna - ataluren - EMEA/H/C/002720/II/0058, Orphan
PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "C.I.z Safety Efficacy and Pharmacovigilance - Other changes. Update of section 4.1 and 5.1 solely based on the interpretation of the recently published "Guide for Assessors of Centralised Applications on the wording of the therapeutic indication" (EMA/CHMP/483022/2019) ("EMA Assessor Guide")."

Tysabri - natalizumab - EMEA/H/C/000603/II/0117
Biogen Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, "C.I.4 Update of section 5.2 of the SmPC in order to update pharmacokinetic information based on an updated PK analysis from 11 studies (both IV and SC administration) and data with serial PK sampling as measured by and industry standard assay."

Veltassa - patiromer - EMEA/H/C/004180/II/0018
Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Jayne Crowe, "Update of section 5.1 of the SmPC in order to update efficacy information based on final results from Study RLY5016-207; this is a randomised, double-blind, placebo-controlled, parallel group study of patiromer to enable concomitant spironolactone treatment in patients with resistant hypertension and CKD."

Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/II/0057
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to add information on drug-drug interaction with fostamatinib. The Package Leaflet is updated accordingly."

Xagrid - anagrelide - EMEA/H/C/000480/II/0089
Shire Pharmaceuticals Ireland Limited,

Rapporteur: Alexandre Moreau, "C.I.4, Update of sections 4.5. and 5.2 of the SmPC in order to add drug-drug interaction information with omeprazole, and update pharmacokinetics, based on final results from clinical study SPD-422-113 a Drug-Drug interaction (DDI) study with Xagrid (anagrelide hydrochloride) assessing the effect of multiple doses omeprazole on anagrelide and 3-OH anagrelide exposure; The study was agreed as a commitment in variation EMEA/H/C/000480/II/0075"	
Zejula - niraparib - EMEA/H/C/004249/II/0020, Orphan GlaxoSmithKline (Ireland) Limited, Rapporteur: Bjorg Bolstad, "Update of section 4.8 of the SmPC in order to add hypersensitivity, psychiatric disorders and non-infectious penumonitis to the list of adverse drug reactions (ADRs) with the frequency unknown based on safety evaluations; the Package Leaflet is updated accordingly."	
Zejula - niraparib - EMEA/H/C/004249/II/0021, Orphan GlaxoSmithKline (Ireland) Limited, Rapporteur: Bjorg Bolstad, "Update of section 4.5 of the SmPC in order to add pharmacokinetic interaction information based non-clinical drug-drug interaction (DDI) studies. In addition, the MAH took the opportunity to update section 5.3 of the SmPC in line with the SmPC guideline."	
WS1790 **OPDIVO-EMEA/H/C/003985/WS1790/0082** **Yervoy-EMEA/H/C/002213/WS1790/0078** Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.8 and 5.1 of the SmPC in order to include at least 5 years (60 months) of follow-up for all subjects from study CA209067. Updated efficacy data provided in this submission include overall survival (OS), progression-free survival (PFS) and objective response rate (ORR)."	
WS1807 **Glyxambi-EMEA/H/C/003833/WS1807/0028** **Jardiance-EMEA/H/C/002677/WS1807/0051** **Synjardy-EMEA/H/C/003770/WS1807/**	

0048
Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "Update of section 4.5 of the SmPC, in order to add interaction information on interference with the 1,5-anhydroglucitol assay in line with the Company Core Data Sheet"

WS1814
Elebrato Ellipta-EMEA/H/C/004781/ WS1814/0017
Temybric Ellipta-EMEA/H/C/005254/ WS1814/0005
Trelegy Ellipta-EMEA/H/C/004363/ WS1814/0014
GlaxoSmithKline Trading Services Limited, Lead Rapporteur: Peter Kiely, Lead Co-Rapporteur: Janet Koenig, "Update of section 4.8 to add hypersensitivity reactions including anaphylaxis, angiooedema, urticaria and rash."

B.6.10. CHMP-PRAC assessed procedures

Alprolix - eftrenonacog alfa - EMEA/H/C/004142/II/0029, Orphan
Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Submission of a variation to update sections 4.2, 4.8 and 5.1 of the SmPC to add information on Previously Untreated Patients (PUPs) following the completion of the clinical study 998HB303 which was already assessed in EMEA/H/C/004142/P46 006. The PL and RMP have been updated accordingly."

Caprelsa - vandetanib - EMEA/H/C/002315/II/0043
Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "C.I.4 Update of section 5.1 of the SmPC in order to update pharmacodynamic information based on interim results from study D4200C00104, listed as a specific obligation in the Annex II. This is an observational study (including a retrospective arm to evaluate the Benefit/Risk of vandetanib (Caprelsa) 300 mg in RET mutation negative and RET mutation positive patients with symptomatic, aggressive, sporadic, unresectable, locally advanced/metastatic thyroid cancer (MTC)), to

confirm the efficacy and safety of Caprelsa in RET-negative patients with the aim to fulfil SOB001 and convert Caprelsa from conditional to normal Marketing Authorization. In addition the MAH takes to opportunity to rectify the Dutch translation of the Caprelsa Product Information."	
Darzalex - daratumumab - EMEA/H/C/004077/II/0039, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "C.I.4 Update of section 5.1 of the SmPC in order to update information regarding immunogenicity following completion of post-authorization commitments in procedures EMEA/H/C/004077/II/0030 and EMEA/H/C/004077/II/0032 as well as PAM-MEA-009.1 regarding re-analysis of all ADA samples taken from previously submitted clinical studies (MMY1001, MMY3003, MMY3004, SMM2001, MMY1004, MMY1008, MMY2040, MMY3012) using the Enhanced DT Method (previously developed as a result of PAM-MEA-005). As a result of the re-analyses of these data and considering the totality of data from the daratumumab program, the MAH proposes to remove immunogenicity as an Important Potential Risk from the DARZALEX RMP considering the additional pharmacovigilance activity of "Investigation of a new method for detecting antidrug antibodies has been completed. The RMP version 6.5 has been submitted."	
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0061, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "update of the RMP introducing changes to safety concerns following the assessment of the renewal R/0049. The MAH is taking this opportunity to include additional changes related to two post-authorisation measures; postponement of the completion date of study cat3 study PCI-32765MCL3002 of ibrutinib in combination with BR versus BR alone and removal of Study 54179060CLL1017 on DDI as assessed in II/0058."	

WS1792/G **Hexacima-EMEA/H/C/002702/WS1792/0099/G** **Hexaxim-EMEA/H/W/002495/WS1792/0104/G** **Hexyon-EMEA/H/C/002796/WS1792/0103/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus, Lead PRAC Rapporteur: Brigitte Keller-Stanislawski, "C.I.4 (type II) - Update of sections 4.4 and 5.1 of the SmPC in order to revise the warning regarding preterm infants and to add new information on immunogenicity in preterm infants and in infants born from women vaccinated during pregnancy, based on the final results from study A3L00053-EXT; this is an observational cohort study with DTaP-IPV-HB-PRP~T vaccine, aimed to describe the concentrations of IgG against the different antigens. The RMP version 12.0 has been submitted an updated accordingly, following revision 2 with consequential update to the safety concerns. C.I.z (type IB) - Update of sections 2 and 4.4 of the SmPC in order to add warning for excipients with known effect: phenylalanine, potassium and sodium, according to the European guideline "Excipients in the labeling and package leaflet of medicinal products for human use SANTE-2017-11668". The package leaflet is updated accordingly. In addition, the MAH/SOH took the opportunity to introduce editorial changes in sections 4.2, 4.4 and 4.5 of the SmPC and to update the list of local representatives in the Package Leaflet"	
WS1820 **Iscover-EMEA/H/C/000175/WS1820/0142** **Plavix-EMEA/H/C/000174/WS1820/0140** sanofi-aventis groupe, Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of section 4.2 of the SmPC in order to add 600 mg as an alternative loading dose to the existing 300 mg to be used at initiation of treatment in the indication "Secondary prevention of atherothrombotic events in adult patients suffering from acute coronary syndrome ". This update is based on a bibliographic review of published studies. The Package Leaflet is	

updated accordingly. The RMP version 2.0 has also been submitted."

WS1830
Entresto-EMEA/H/C/004062/WS1830/0032
Neparvis-EMEA/H/C/004343/WS1830/0029
Novartis Europharm Limited, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Anette Kirstine Stark, "C.I.13: Submission of the final report from study CLCZ696D2301 (PARAGON HF) listed as a category 3 study in the RMP. The intention of this submission is to fulfill postauthorisation measure (MEA 003) to evaluate cognitive function in this interventional multicenter, randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of LCZ696
compared to valsartan, on morbidity and mortality in heart failure patients (NYHA Class II-IV) with preserved ejection fraction. The RMP version 2.0 has also been submitted."

B.6.11. PRAC assessed procedures

PRAC Led
Erivedge - vismodegib - EMEA/H/C/002602/II/0046
Roche Registration GmbH, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, "Update of the Educational Materials provided as part of the Erivedge Pregnancy Prevention Program, following conclusion of PSUSA/00010140/201901. Annex IID is updated accordingly. Additionally, RMP v14.0 is submitted. Furthermore, section 4.4 of the SmPC is updated to remove the warning on cutaneous squamous cell carcinoma. The MAH also took the opportunity to update the Package Leaflet with the recommended wording on sodium content."

PRAC Led
Esbriet - pirfenidone - EMEA/H/C/002154/II/0066/G, Orphan
Roche Registration GmbH, Rapporteur: Peter Kiely, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Update of sections

4.4 and 4.8 of the SmPC in order to amend an existing warning on DILI subsequent to EMEA/H/C/PSUSA/00002435/ 201902 and EMEA/H/C/2154/LEG/015. The Package Leaflet is updated accordingly. The RMP version 10.0 has also been submitted. In addition, the MAH took the opportunity to add in the PL information about sodium content in line with excipients guideline (EMA/CHMP/302620/2017) and to correct formatting, punctuation and spelling mistakes in the PI. Update of sections 4.4 and 4.8 of the SmPC in order to add a warning on Hyponatraemia and to add Hyponatraemia to the list undesirable effects subsequent to EMEA/H/C/PSUSA/ 00002435/201902 and EMEA/H/C/2154/LEG/ 015. The requested group of variations proposed amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP)."	
PRAC Led **Grastofil - filgrastim - EMEA/H/C/002150/II/0030** Accord Healthcare S.L.U., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, PRAC-CHMP liaison: Tuomo Lapveteläinen, "Submission of an updated RMP version 6.0 in order to update the safety concerns and section of additional pharmacovigilance activities (removal of SCNIR and EBMT registry) in-line with latest approved Accofil (Filgrastim) RMP v4.0, dated 25-Jun-2019 approved on 03-Oct-2019 with procedure EMEA/H/C/003956/II/0037 as per the transfer of Marketing Authorisation of Grastofil from Apotex Netherland B.V to Accord healthcare S.L.U. Spain, for Grastofil 30 MU/0.5 ml & 48 MU/0.5 ml solution for injection or infusion in pre-filled syringe"	
PRAC Led **Jinarc - tolvaptan - EMEA/H/C/002788/II/0029** Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, "To update the RMP for Jinarc to version 14.4 to include dehydration and pregnancy prevention programme as requiring additional risk minimisation measures	

in accordance with Annex II.”

PRAC Led

Tasigna - nilotinib -

EMEA/H/C/000798/II/0103

Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, “Update of the RMP version 22 following the PRAC request to add 'growth retardation' to the list of important identified risks, and study AMN107A2203 as an additional pharmacovigilance activity for the important identified risk of ‘growth retardation’ to the pharmacovigilance plan. The MAH took the opportunity to revise the list of safety concerns in the EU RMP, in line with the GVP Module V (rev 2) recommendations and implemented the requested changes from PRAC.
In addition, the additional pharmacovigilance activity of collection of gene signature data in patients who relapse on TFR compared to patients who relapse on treatment' has been deleted from the EU RMP as previously agreed during the procedure EMEA/H/C/000798/PAM/MEA/051.1. Other updates to reflect current study status are proposed through the RMP.”

PRAC Led

Xeljanz - tofacitinib -

EMEA/H/C/004214/II/0023

Pfizer Europe MA EEIG, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of the final report from study A3921205 listed as a category 3 study in the RMP. This is an Observational, Post-Authorization Safety Study (PASS) within the Consortium of Rheumatology Researchers of North America (CORRONA) Registry Comparing Rates of Malignancy, Cardiovascular and Serious Infection Outcomes among Patients Treated for Moderately to Severely Active Rheumatoid Arthritis. The RMP version 10.1 has also been submitted.”

PRAC Led

XGEVA - denosumab -

EMEA/H/C/002173/II/0072/G

Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga,

PRAC-CHMP liaison: Kristina Dunder, "Submission of the final reports for the following Category 3 studies within the XGEVA Risk Management Plan (RMP) v35:

· Study 20101363 - A non-interventional pharmacovigilance study of osteonecrosis of the jaw and infection leading to hospitalization among patients with cancer treated with XGEVA or zoledronic acid in Sweden, Denmark, and Norway Ongoing.

· Study 20170728 - Incidence of new primary malignancies among patients with bone metastases from breast, prostate, or lung cancer treated with XGEVA or intravenous zoledronic acid: a retrospective cohort study.

The RMP (v35) has been updated to reflect submission of the study reports. In addition, the format of this RMP has been updated to align with the EMA EU RMP template Rev 2.0.1, which accompanies the EMA Guideline on Good Pharmacovigilance Practices Module V Rev 2."

PRAC Led

Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0061

Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "to update the Summary of Product Characteristics section 4.4 and 4.5 and package leaflet as per the PRAC recommendations published on 10th Feb 2020 to add a new warning on Hypoglycemia, the Package Leaflet are updated accordingly. In addition, the MAH took the opportunity to introduce some minor updates have also been made to Annex II of the product information"

PRAC Led

WS1791

Glidipion-EMEA/H/C/002558/WS1791/0013

Pioglitazone Actavis-EMEA/H/C/002324/WS1791/0014

Pioglitazone Teva-EMEA/H/C/002297/WS1791/0023

Pioglitazone Teva Pharma-EMEA/H/C/002410/WS1791/0023

Teva B.V., Generic, Generic of Actos, Glustin, Lead Rapporteur: Peter Kiely, Lead PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Update of all safety

concerns of the RMP (i.e. deleting them all from the RMP) in line with the principles of GVP V rev 2 (and in line with the originator RMP). Removal of the aRMMs as per outcome of the last PSUSA of pioglitazone PSUSA/00002417/201807."	

B.6.12. CHMP-CAT assessed procedures

Alofisel - darvadstrocel - EMEA/H/C/004258/II/0016/G, Orphan, ATMP Takeda Pharma A/S, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder	
Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0021/G, Orphan, ATMP Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang	
Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0022/G, Orphan, ATMP Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang	

B.6.13. CHMP-PRAC-CAT assessed procedures

Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - EMEA/H/C/003854/II/0026, Orphan, ATMP Orchard Therapeutics (Netherlands) BV, Rapporteur: Sol Ruiz, CHMP Coordinator: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst, "Submission of an updated RMP version 2.0 in order to introduce changes to the design of the post-authorisation study STRIM-002 to reflect a change in the proposed RIS analysis methodology from SLiM-PCR to S-EPTS/LM-PCR and shifting the timelines."	
Yescarta - axicabtagene ciloleucel - EMEA/H/C/004480/II/0021, Orphan, ATMP Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus, PRAC Rapporteur: Anette Kirstine Stark, "Submission of a variation to allow clinicians to administer Yescarta to seriously ill	

patients with relapsed/refractory Non-Hodgkin lymphoma while having on site an adequate supply of tocilizumab (i.e. to ensure that 1 dose of tocilizumab per patient is available at the treating centres to manage CRS, in addition, treatment centres should have access to an additional dose within 8 hours of each previous dose). The PL and RMP have been updated accordingly."

B.6.14. PRAC assessed ATMP procedures

PRAC Led
Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0016, ATMP
CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of the RMP to bring it in line with GVP Module V Rev. 2 template.
The educational materials described in Annex II have been updated accordingly."

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

WS1774
Emtriva-EMEA/H/C/000533/WS1774/0132
Truvada-EMEA/H/C/000594/WS1774/0163
Viread-EMEA/H/C/000419/WS1774/0198
Gilead Sciences Ireland UC, Lead Rapporteur: Bruno Sepodes, "To align the pregnancy language in the package leaflet with the wording in the SmPC.
In addition the PI for Truvada and Viread has been updated to comply with the excipients guidance on sodium as well as aligning with the curent QRD template. Furthermore, the MAH has made minor administrative updates to the annexes."

WS1785/G
Infanrix hexa-EMEA/H/C/000296/WS1785/0274/G
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke

WS1787/G

M-M-RVAXPRO-EMEA/H/C/000604/ WS1787/0099/G
ProQuad-EMEA/H/C/000622/ WS1787/0140/G
MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus

WS1803
Efficib-EMEA/H/C/000896/WS1803/0093
Janumet-EMEA/H/C/000861/WS1803/ 0093
Januvia-EMEA/H/C/000722/WS1803/ 0070
Ristaben-EMEA/H/C/001234/WS1803/ 0062
Ristfor-EMEA/H/C/001235/WS1803/0080
TESAVEL-EMEA/H/C/000910/WS1803/ 0070
Velmetia-EMEA/H/C/000862/WS1803 /0096
Xelevia-EMEA/H/C/000762/WS1803/0074
Merck Sharp & Dohme B.V., Lead Rapporteur: Johann Lodewijk Hillege, "To update section 4.4 of the SmPC and section 2 of the Package Leaflet to comply with the revised Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal products for human use'."

WS1816
Nuwiq-EMEA/H/C/002813/WS1816/0035
Vihuma-EMEA/H/C/004459/WS1816/ 0017
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus

WS1818
Rasilez-EMEA/H/C/000780/WS1818/0124
Rasilez HCT-EMEA/H/C/000964/WS1818/ 0094
Noden Pharma DAC, Lead Rapporteur: Daniela Melchiorri

WS1824
Fluenz Tetra-EMEA/H/C/002617/WS1824/ 0100
Pandemic influenza vaccine H5N1 AstraZeneca-EMEA/H/C/003963/ WS1824/0034
AstraZeneca AB, Lead Rapporteur: Christophe Focke

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 27-30 April 2020 CHMP plenary:

G.3.2. List of procedures starting in April 2020 for May 2020 CHMP adoption of outcomes

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