14 October 2019
EMA/CHMP/556731/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Agenda for the meeting on 14-17 October 2019

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

14 October 2019, 13:00 – 19:30, room 1C

15 October 2019, 08:30 – 19:30, room 1C

16 October 2019, 08:30 – 19:30, room 1C

17 October 2019, 08:30 – 16:00, room 1C

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

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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 14-17 October 2019. See October 2019 CHMP minutes (to be published post November 2019 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 14-17 October 2019

1.3. Adoption of the minutes

CHMP minutes for 16-19 September 2019.

CHMP ORGAM minutes for 7 October 2019.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. fostamatinib - EMEA/H/C/005012

indicated for the treatment of thrombocytopenia

Scope: Possible oral explanation

Action: Possible oral explanation to be held on Thursday, 17 October 2019 at 09:00

List of Outstanding Issues adopted on 19.09.2019, 27.06.2019. List of Questions adopted on 31.01.2019.

2.1.2. ciprofloxacin - EMEA/H/C/004394

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

Scope: Oral explanation

Action: Oral explanation to be held on Tuesday, 15 October at 09:00

List of Outstanding Issues adopted on 28.03.2019. List of Questions adopted on 26.07.2018.

2.1.3. solriamfetol - EMEA/H/C/004893

indicated to improve wakefulness in patients with narcolepsy or obstructive sleep apnoea.

Scope: Possible oral explanation

Action: Possible oral explanation to be held on 16 October 2019 at 09:00

List of Outstanding Issues adopted on 25.07.2019. List of Questions adopted on 28.03.2019.

2.2. Re-examination procedure oral explanations

2.2.1. Evenity - romosozumab - EMEA/H/C/004465

UCB Pharma S.A.; Treatment of osteoporosis

Scope: Oral explanation/Opinion, Report of ad-hoc expert group meeting scheduled on 3 October 2019

Letters from third parties

Action: Oral explanation to be held on Tuesday, 15 October 2019 at 14:00

Participation of patient representatives

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

Opinion adopted on 27.06.2019, List of Outstanding Issues adopted on 29.05.2019, 28.02.2019, 15.11.2018, 20.09.2018. List of Questions adopted on 26.04.2018.

See 3.5

2.3. Post-authorisation procedure oral explanations

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

Pfizer Europe MA EEIG

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

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

Possible oral explanation/Opinion

Action: Possible oral explanation to be held on Wednesday, 16 October 2019 at 15:30

List of Outstanding Issues adopted on 27.06.2019, 31.01.2019. List of Questions adopted on 26.07.2018.

See 4.1

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

Novartis Europharm Limited

Re-examination Rapporteur: Milena Stain and re-examination Co-Rapporteur: Sinan B Sarac

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

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

Oral explanation/Opinion

Report from ad hoc expert group meeting scheduled on 7 October 2019

Action: Oral explanation to be held on Tuesday, 15 October 2019 at 16:00

Opinion adopted on 27.06.2019. Oral explanation held on 24.06.2019. Request for Supplementary Information adopted on 28.02.2019, 15.11.2018, 26.07.2018.

See 5.3

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

PTC Therapeutics International Limited

Re-examination rapporteur: Kristina Dunder, Re-examination co-rapporteur: Alexander Moreau

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

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

Opinion, SAG Report

The final list of experts for the SAG Neurology was adopted via written procedure on 10 October 2019.

Action: Oral explanation to be held on Tuesday, 15 October 2019 at 11:00

Opinion adopted on 27.06.2019. Oral explanation held on 25.06.2019. Request for Supplementary Information adopted on 28.02.2019, 13.12.2018.

See 5.3

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. glucagon - EMEA/H/C/003848

treatment of severe hypoglycaemia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 25.07.2019, 26.04.2019. List of Questions adopted on

13.12.2018.

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

Ebola Vaccine

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 17.09.2019. List of Questions adopted on 25.06.2019.

3.1.3. budesonide / formoterol fumarate dihydrate - EMEA/H/C/004882

treatment of asthma and COPD

Scope: Opinion

Action: For adoption

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

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

Scope: Opinion

Action: For adoption

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

3.1.5. pegfilgrastim - EMEA/H/C/005312

treatment of neutropenia

Scope: Opinion

Action: For adoption

3.1.6. delafloxacin - EMEA/H/C/004860

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 19.09.2019, 29.05.2019. List of Questions adopted on 20.09.2018.

3.1.7. upadacitinib - EMEA/H/C/004760

treatment of moderate to severe active rheumatoid arthritis

Scope: Opinion

Action: For adoption

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

3.1.8. esketamine - EMEA/H/C/004535

treatment-resistant depression

Scope: Opinion

Action: For adoption

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

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

Daiichi Sankyo Europe GmbH; treatment of acute myeloid leukaemia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 29.01.2019.

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

3.2.1. adalimumab - EMEA/H/C/004879

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.03.2019.

3.2.2. azacitidine - EMEA/H/C/005147

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 29.05.2019.

3.2.3. azacitidine - EMEA/H/C/005075

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 29.05.2019.

3.2.4. brolucizumab - EMEA/H/C/004913

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 27.06.2019.

3.2.5. cinacalcet - EMEA/H/C/005236

treatment of secondary hyperparathyroidism and hypercalcaemia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 29.05.2019.

3.2.6. osilodrostat - Orphan - EMEA/H/C/004821

Novartis Europharm Limited; treatment of Cushing's syndrome

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 25.07.2019. List of Questions adopted on 28.03.2019.

3.2.7. entrectinib - EMEA/H/C/004936

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 29.05.2019.

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

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.03.2019.

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

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 29.05.2019.

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

3.3.1. apixaban - EMEA/H/C/005358

prevention of venous thromboembolic events (VTE)

Scope: List of questions

Action: For adoption

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

Novartis Europharm Limited; Treatment of sickle cell disease

Scope: List of questions

Action: For adoption

3.3.3. dasatinib - EMEA/H/C/005446

treatment of leukaemia

Scope: List of questions

Action: For adoption

3.3.4. dasatinib - EMEA/H/C/005317

treatment of leukaemia

Scope: List of questions

Action: For adoption

3.3.5. bupivacaine - EMEA/H/C/004586

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

Scope: List of questions

Action: For adoption

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

Accelerated assessment

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

Scope: List of questions

Action: For adoption

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

treatment of diabetes mellitus

Scope: List of questions

Action: For adoption

3.3.8. obiltoxaximab - Orphan - EMEA/H/C/005169

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

Scope: List of questions

Action: For adoption

3.3.9. doxorubicin - EMEA/H/C/005320

treatment of breast cancer, ovarian cancer, progressive multiple myeloma and AIDS-related Kaposi's sarcoma

Scope: List of questions

Action: For adoption

3.3.10. 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 questions

Action: For adoption

3.3.11. lefamulin - EMEA/H/C/005048

treatment of community-acquired pneumonia (CAP)

Scope: List of questions

Action: For adoption

3.3.12. trastuzumab - EMEA/H/C/005209

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

Scope: List of questions

Action: For adoption

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

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

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

Scope: Request by the applicant dated 01 October 2019 for an extension to the clock stop to

respond to the List of Outstanding Issues adopted on 19.09.2019

Action: For adoption

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

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

for application into the surgical site to reduce postoperative pain

Scope: Request by the applicant dated 30 September 2019 for an extension to the clock stop to respond to the List of Questions adopted on 25.07.2019

Action: For adoption

List of Questions adopted on 25.07.2019.

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

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

Scope: Update on the CAT discussions at their October meeting

Action: For discussion

List of Outstanding Issues adopted on 21.06.2019, 14.09.2018, 25.05.2018. List of Questions adopted on 08.09.2017.

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

3.5.1. Evenity - romosozumab - EMEA/H/C/004465

UCB Pharma S.A.; Treatment of osteoporosis

Scope: Oral explanation/Opinion, Report of ad-hoc expert group meeting held on 3 October 2019

Letters from third parties

Action: For adoption

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

Opinion adopted on 27.06.2019, List of Outstanding Issues adopted on 29.05.2019, 28.02.2019, 15.11.2018, 20.09.2018. List of Questions adopted on 26.04.2018.

See 2.2

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

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

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

Scope: Letter from the applicant dated 02 October 2019 informing about the withdrawal of marketing authorisation application

Action: For information

List of Questions adopted on 29.05.2019.

3.7.2. omadacycline - EMEA/H/C/004715

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

Scope: Letter from the applicant dated 09 October 2019 informing about the withdrawal of marketing authorisation application

Action: For information

List of Outstanding Issues adopted on 19.09.2019, 27.06.2019. List of Questions adopted on 31.01.2019.

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

Eli Lilly Nederland B.V.

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

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

Action: For adoption

List of Questions adopted on 27.06.2019.

4.1.2. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/X/0075/G

Vertex Pharmaceuticals (Ireland) Limited

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

Scope: “Extension application to add a new strength of 25 mg granules in sachet in the treatment of cystic fibrosis in children aged 6 to less than 12 months old.
C.I.4 - To update sections 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC, and sections 2 and 3 of the PL for the 150 mg film-coated tablet presentations to bring it in line with the new dosage form

(25 mg granules), which supports the extension of indication for children aged 6 to 12 months old. The RMP (version 8.3) is updated in accordance.
In addition, the MAH took the opportunity to implement minor updates in the Product Information."

Action: For adoption

List of Outstanding Issues adopted on 25.07.2019. List of Questions adopted on 26.04.2019.

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

Pfizer Europe MA EEIG

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

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

Action: For adoption

List of Questions adopted on 29.05.2019.

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

Pfizer Europe MA EEIG

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

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

Possible oral explanation/Opinion

Action: For adoption

List of Outstanding Issues adopted on 27.06.2019, 31.01.2019. List of Questions adopted on 26.07.2018.

See 2.3

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

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

Astellas Pharma Europe B.V.

Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to introduce a new pharmaceutical form associated with new strength (40 mg/ml granules for oral suspension) grouped with a type II variation (C.I.6.a) to include paediatric use of Dificlir in children from birth to less than 18 years of age.
The RMP (version 11.0) is updated in accordance.
Consequential updates have been made to the SmPC of Dificlir 200 mg Film-coated tablet.
The labelling and package leaflet (PL) are updated accordingly.
The PL is also being amended to include a statement that Dificlir is essentially 'sodium-free' (in accordance with the Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. The details of the local representative of the MAH in the Czech Republic are also updated."

Action: For adoption

List of Questions adopted on 29.05.2019.

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. 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

4.3.2. 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

4.4. Update on on-going extension application according to Annex I of Commission Regulation (EC) No 1234/2008

No items

4.5. Re-examination procedure of extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008

No items

5. Type II variations - variation of therapeutic indication procedure according to Annex I of Commission Regulation (EC) No 1234/2008

5.1. Type II variations - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008; Opinions or Requests for supplementary information

5.1.1. Adcetris - brentuximab vedotin - Orphan - EMEA/H/C/002455/II/0070

Takeda Pharma A/S

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

Scope: "treatment of adults with previously untreated CD30+ PTCL"

Action: For adoption

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

Obvius Investment B.V

Rapporteur: Natalja Karpova, 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

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

Eli Lilly Nederland B.V.

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

Scope: "Extension of indication for Cyramza, to include in combination with erlotinib, the first-line treatment of adult patients with metastatic non-small cell lung cancer with activating epidermal growth factor receptor (EGFR) mutations. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated accordingly. The RMP version 9 has also been submitted."

Action: For adoption

5.1.4. Darzalex - daratumumab - Orphan - EMEA/H/C/004077/II/0029

Janssen-Cilag International NV

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

Scope: "Extension of indication to extend the existing therapeutic indication for Darzalex (daratumumab) in combination with lenalidomide and dexamethasone (Rd) for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant (ASCT); as a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP (Version 6, Succession 1) has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 25.07.2019.

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

Janssen-Cilag International NV

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

Scope: "Extension of indication to extend the existing therapeutic indication for Darzalex (daratumumab) in combination with bortezomib, thalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant (ASCT); as a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP (Version 6, Succession 1) has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 25.07.2019.

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

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication to include, as monotherapy or in combination with platinum and 5-fluorouracil (5-FU) Chemotherapy, first-line treatment of recurrent or metastatic head

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

Action: For adoption

Request for Supplementary Information adopted on 19.09.2019, 27.06.2019, 28.03.2019.

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

AstraZeneca AB

Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, 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."

Action: For adoption

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

Roche Registration GmbH

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

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

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019.

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

Celgene Europe BV

Rapporteur: Peter Kiely, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Eva A. Segovia

Scope: "Extension of indication to include treatment of adult patients with oral ulcers associated with Behçet's disease (BD) who are candidates for systemic therapy. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC and sections 1, 2 and 4 of the PL are updated accordingly. The updated RMP version 12.0 has also been submitted.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

5.1.10. Rezolsta - darunavir / cobicistat - EMEA/H/C/002819/II/0033

Janssen-Cilag International NV

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ilaria Baldelli

Scope: "To extend the approved therapeutic indication of Rezolsta to include the adolescent population (aged 12 years old and older with body weight at least 40 kg). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and sections 1, 2 and 3 of the PL are updated accordingly. The updated RMP version 6.0 has also been submitted.
The RMP of the product has been updated to meet the requirements and updated definitions in the European Medicines Agency (EMA) Guideline on good pharmacovigilance practices (GVP) Module V Revision 2 (EMA/838713/2011; Rev 2) and Guidance on the format of the RMP in the European Union (EMA/164014/2018 Rev 2.0.1) including proposed removal of safety concerns. In addition, in order to align the PI with recommendations for other HIV products, the MAH has also taken the opportunity to update section 4.2 of the SmPC with regards to administration of Rezolsta in case of vomiting."

Action: For adoption

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

Janssen-Cilag International NV

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

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

Action: For adoption

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

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

Janssen-Cilag International NV

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

Scope: "Extension of indication to include a new population for Stelara solution for injection in children aged 6 to 12 years with moderate to severe psoriasis based on the results of study CNTO1275PSO3013; as a consequence sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated accordingly. The Package Leaflet is updated in accordance. Section 4.8 for Stelara concentrate for solution for infusion is updated accordingly.
Minor editorial changes are made to section 4.5 for both formulations.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 15.0 has also been submitted. The MAH took the opportunity to add "follow-up of pregnancy registry" in Part III.1 of the RMP in line with the existing information in Part V.3 of the RMP."

Action: For adoption

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

sanofi-aventis groupe

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

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

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019.

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

Sanofi-Aventis Deutschland GmbH

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

Scope: "Extension of indication to include new population for Toujeo (i.e. adolescents and children from the age of 6 years). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019.

5.1.15. Tybost - cobicistat - EMEA/H/C/002572/II/0051

Gilead Sciences Ireland UC

Rapporteur: Bruno Sepodes, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "To modify the approved therapeutic indication to include new population (adolescents aged 12 years and older weighing at least 35 kg) for the treatment of HIV-1 . As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 of the SmPC and sections 1, 2, 3 of the PL are updated accordingly. The updated RMP version 4.1 is also been submitted"

Action: For adoption

5.1.16. Venclyxto - venetoclax - EMEA/H/C/004106/II/0023/G

AbbVie Deutschland GmbH & Co. KG

Rapporteur: Filip Josephson, PRAC Rapporteur: Eva Jirsová

Scope: "Extension of the indication to include treatment with Venclyxto in combination with an anti-CD20 antibody (obinutuzumab) for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL) based on the results of the pivotal CLL14/BO25323 phase 3 study. Consequently, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the SmPC and corresponding sections of the PL have been revised. The updated RMP version 5.1 has been submitted.
Additionally, the SmPC section 5.3 has been updated based on the 6 month carcinogenicity mouse study report, supported by the 4 week dose ranging study in mice and the embryo-foetal development (EFD) data. Minor editorial changes have been introduced throughout the PI."

Action: For adoption

5.1.17. Xtandi - enzalutamide - EMEA/H/C/002639/II/0047/G

Astellas Pharma Europe B.V.

Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia

Scope: "C.1.6: Extension of indication to include the treatment of adult men with metastatic hormone-sensitive prostate cancer (mHSPC) for Xtandi in combination with androgen deprivation therapy; As a consequence, sections 4.1, 4.7, 4.8, 5.1, 5.3 and 6.6 of the SmPC are updated. Furthermore the MAH took the opportunity to make corrections to section 4.7. The Package Leaflet is updated in accordance. The RMP version 13.0 has also been submitted. C.1.4: Update of section 5.1 of the SmPC based the 5-year Overall Survival (OS) results obtained from the PREVAIL study (MDV310003), a phase 3 study of enzalutamide in chemotherapy naïve patients with metastatic prostate cancer that progressed on ADT."

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

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

Novartis Europharm Limited

Re-examination Rapporteur: Milena Stain and re-examination Co-Rapporteur: Sinan B Sarac

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

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

Possible oral explanation/opinion

Report from the ad hoc expert group meeting held on 7 October 2019

Action: For adoption

Opinion adopted on 27.06.2019. Oral explanation held on 24.06.2019. Request for Supplementary Information adopted on 28.02.2019, 15.11.2018, 26.07.2018.

See 2.3

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

PTC Therapeutics International Limited

Re-examination rapporteur: Kristina Dunder, Re-examination co-rapporteur: Alexander Moreau

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

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

Opinion, SAG Report

Action: For adoption

Opinion adopted on 27.06.2019. Oral explanation held on 25.06.2019. Request for Supplementary Information adopted on 28.02.2019, 13.12.2018.

See 2.3

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. autologous CD34+ enriched cell fraction that contains CD34+ cells genetically modified ex vivo using a lentiviral vector encoding for the human arylsulfatase A(ARSA) cDNA sequence - Orphan - ATMP - H0005321

Orchard Therapeutics (Netherlands) BV; Treatment of patients with Metachromatic Leukodystrophy (MLD)

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

Action: For adoption

8.1.2. valoctocogene roxaparvovec - ATMP - H0004749

Treatment of Haemophilia A

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

Action: For adoption

8.1.3. ICOSAPENT ETHYL - H0005398

intended to reduce cardiovascular risk as an adjunct to statin therapy in adult patients with elevated triglyceride levels and other risk factors for cardiovascular disease.

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

Action: For adoption

8.1.4. BALOXAVIR MARBOXIL - H0004974

indicated for the treatment of influenza in patients aged 12 and above who have been symptomatic for no more than 48 hours.
indicated for treatment of influenza in patients aged 12 and above who have been symptomatic for no more than 48 hours, and are at high risk of developing influenza complications.
indicated for the post-exposure prophylaxis of influenza in patients aged 12 and above.

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. OCALIVA - obeticholic acid – Orphan - EMEA/H/C/004093/R/0018

Intercept Pharma International Limited

Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst

Scope: Renewal

Request for Supplementary Information adopted on 19.09.2019.

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

MolMed S.p.A

Rapporteur: Carla Herberts, Co-Rapporteur: Sol Ruiz, CHMP Coordinators: Paula Boudewina van Hennik and Maria Concepcion Prieto Yerro, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Withdrawal of marketing authorisation

Action: For information

9.1.3. WS1636/G
Mekinist-EMEA/H/C/002643/WS1636/0035/G
Tafinlar-EMEA/H/C/002604/WS1636/0040/G

Novartis Europharm Limited

Lead Rapporteur: Filip Josephson

Scope: "Update of section 5.1 of the Mekinist (trametinib) and Tafinlar (dabrafenib) SmPC to include the 5-years overall survival (OS) results from study MEK115306 (COMBI-d), a phase III, randomised, double-blinded study comparing the combination of dabrafenib and trametinib to dabrafenib and placebo in first-line therapy for subjects with unresectable or metastatic BRAF V600/K mutation-positive cutaneous melanoma and the 5-years overall survival (OS) results from study MEK116513 (COMBI-v), a phase III, open-label, 2 arm, randomised study comparing dabrafenib and trametinib combination therapy with vemurafenib monotherapy in BRAF V600 mutation-positive metastatic melanoma."

Action: For adoption

9.1.4. WS1683
Elebrato Ellipta-EMEA/H/C/004781/ WS1683/0012
Temybric Ellipta-EMEA/H/C/005254/ WS1683/0001
Trelegy Ellipta-EMEA/H/C/004363/ WS1683/0010

GlaxoSmithKline Trading Services Limited

Lead Rapporteur: Peter Kiely

Scope: "Update of SmPC in order to add information in section 5.1 on survival data from the IMPACT study"

Action: For adoption

9.1.5. Zynteglo - autologous cd34+ cell enriched population that contains hematopoietic stem cells transduced with lentiglobin bb305 lentiviral vector encoding the beta-a-t87q-globin gene - EMEA/H/C/003691/II/0001/G, Orphan, ATMP

bluebird bio (Netherlands) B.V

Rapporteur: Carla Herberts, CHMP Coordinator: Paula Boudewina van Hennik

Scope: quality variation

Request for Supplementary Information adopted on 13.09.2019.

10. Referral procedures

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

No items

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

No items

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

No items

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

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

Geiser Pharma S.L.

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Johann Lodewijk Hillege

Scope: Opinion

Action: For adoption

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

10.4.2. Budesonide SUN – budesonide – EMEA/H/A-29(4)/1492

Sun Pharmaceutical Industries Europe B.V.

Rapporteur: TBC, Co-Rapporteur: TBC

Scope: Start of procedure, appointment of Rapporteurs, list of questions, timetable

Action: For adoption

The applicant has submitted an Art. 10(3) application for Budesonide SUN nebuliser suspension and associated names. Concerns regarding the demonstration of bioequivalence have been raised by IT and UK who were of the view that the data presented (comparative in vitro data of the product before nebulisation, including Particle Size Distribution (PSD) of the active substance) are not sufficient to demonstrate bioequivalence. The procedure was initiated because of disagreements regarding which in-vitro data are considered pivotal.

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. Gadolinium-containing contrast agents (GdCA): Gadobutrol (NAP); gadodiamide (NAP); gadopentetic acid (NAP); gadoteric acid (NAP); gadoteridol (NAP); gadoxetic acid (NAP) - EMEA/H/A-31/1097

Applicant: various

Lead Rapporteur: Johann Lodewijk Hillege

Scope: Annual cumulative reviews on NSF cases submission as a post-authorisation measure resulting from the 2010 Article 20 and Article 31 referral procedures for gadolinium-containing contrast agents

Opinion

Action: For adoption

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

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

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

Scope: List of Outstanding Issues

Action: For adoption

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

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

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

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

Action: For information

13.2. Innovation Task Force briefing meetings

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

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

CHMP-PRAC Strategic Review and Learning Meeting (SRLM) under the Finnish presidency of

the European Union (EU) Council – Helsinki, Finland, 21-23 October 2019

Final agenda

Action: For information

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 30 September - 03 October 2019

Action: For information

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

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 09-11 October 2019

Action: For information

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 23-24 September 2019

Action: For information

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at October 2019 PDCO

Action: For information

Report from the PDCO meeting held on 15-18 October 2019

Action: For information

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 08-10 October 2019

Action: For information

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

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 15-17 October 2019

Action: For information

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

14.3.1. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 30 September - 03 October 2019. Table of conclusions

Action: For information

Scientific advice letters

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

14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 17-18 September 2019

Action: For adoption

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP October 2019 meeting to CHMP for adoption:

- 14 reports on products in scientific advice and protocol assistance
- 8 reports on products in pre-authorisation procedures
- 2 reports on products in plasma master file

Action: For adoption

14.3.4. Safety Working Party (SWP)

Chair: Jan Willem Van der Laan

Election of SWP vice-chair

Mikael Andersson's first 3-year term will expire in October 2019.

14.3.5. Biosimilar Medicinal Product Working Party (BMWP)

Chair(s): TBC/Niklas Ekman

Election of BMWP chair

Elena Wolff-Holz's first 3-year term will expire in October 2019.

14.3.6. Pharmacokinetics Working Party (PKWP)

Chair(s): TBC/Henrike Potthast

Election of PKWP chair

Jan Welink's second 3-year term is expiring in September 2019.

14.3.7. Oncology Working Party (ONCWP)

Chair(s): Sinan B. Sarac/TBC

Election of ONCWP vice-chair

Paolo Foggi's first 3-year term will expire in October 2019.

14.3.8. Vaccines Working Party (VWP)

Chair(s): TBC

Election of VWP chair

Mair Powell's first 3-year term will expire in October 2019.

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. Preparedness of the system and capacity increase

Action: For information

15.1.2. Oncology Training

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)*

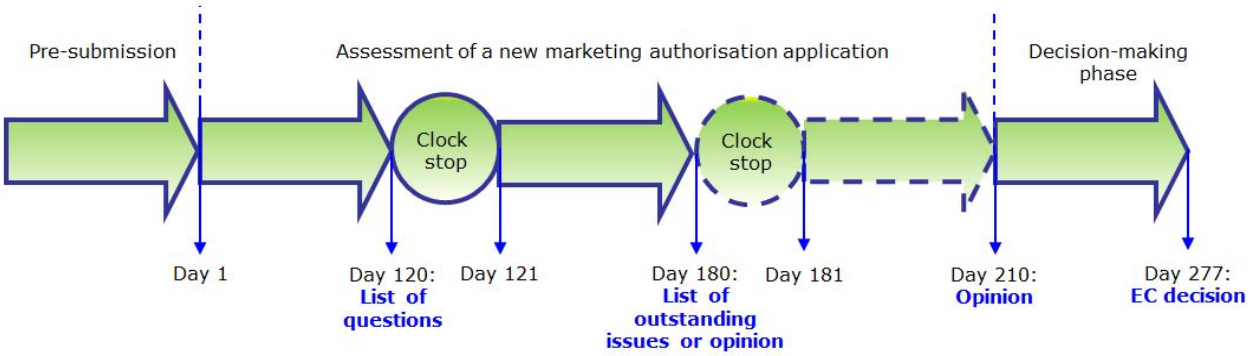
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

10 October 2019
EMA/CHMP/557381/2019 Rev. 1

Annex to 14-17 October 2019 CHMP Agenda

Pre submission and post authorisations issues

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A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

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

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

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

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

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

Atriance - nelarabine -
EMEA/H/C/000752/S/0048
Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted

Chenodeoxycholic acid Leadiant -
chenodeoxycholic acid -
EMEA/H/C/004061/S/0010, Orphan
Leadiant GmbH, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Adam Przybylkowski
Request for Supplementary Information adopted on 25.07.2019.

Qarziba - dinutuximab beta -
EMEA/H/C/003918/S/0016, Orphan
EUSA Pharma (Netherlands) B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Sivextro - tedizolid phosphate - EMEA/H/C/002846/R/0031

Merck Sharp & Dohme B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Maria del Pilar Rayon

Request for Supplementary Information adopted on 19.09.2019.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Akynzeo - fosnetupitant / netupitant / palonosetron - EMEA/H/C/003728/R/0024

Helsinn Birex Pharmaceuticals Limited, Rapporteur: Peter Kiely, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ilaria Baldelli

Cerdelga - eliglustat - EMEA/H/C/003724/R/0022, Orphan

Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Eva A. Segovia

Request for Supplementary Information adopted on 25.07.2019.

Kengrexal - cangrelor - EMEA/H/C/003773/R/0020

Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Ilaria Baldelli

Quinsair - levofloxacin - EMEA/H/C/002789/R/0022

Chiesi Farmaceutici S.p.A., Rapporteur: Ondřej Slanař, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maria del Pilar Rayon

Saxenda - liraglutide - EMEA/H/C/003780/R/0024

Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Menno van der Elst

B.2.3. Renewals of Conditional Marketing Authorisations

Caprelsa - vandetanib - EMEA/H/C/002315/R/0041

Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni	
CRYSVITA - burosumab - EMEA/H/C/004275/R/0009, Orphan Kyowa Kirin Holdings B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Brigitte Keller-Stanislawski	
Holoclar - ex vivo expanded autologous human corneal epithelial cells containing stem cells - EMEA/H/C/002450/R/0026, Orphan, ATMP Chiesi Farmaceutici S.p.A., Rapporteur: Egbert Flory, Co-Rapporteur: Paolo Gasparini, CHMP Coordinators: Jan Mueller-Berghaus and Daniela Melchiorri, PRAC Rapporteur: Rhea Fitzgerald	
OCALIVA - obeticholic acid - EMEA/H/C/004093/R/0018, Orphan Intercept Pharma International Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 19.09.2019.	See 9.1

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 30. September – 3 October 2019 PRAC:

Signal of myasthenia gravis:

Imfinzi - Durvalumab – EMEA/H/C/004771

Rapporteur: Sinan B Sarac, Co-Rapporteur: Jorge Camarero Jimenez

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 October 2019 meeting:

EMEA/H/C/PSUSA/00000944/201902
(degarelix)
CAPS:
Firmagon (EMEA/H/C/000986) (degarelix), Ferring Pharmaceuticals A/S, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, “From: 17/02/2016 To: 17/02/2019”

EMEA/H/C/PSUSA/00001393/201902
(fingolimod)
CAPS:
Gilenya (EMEA/H/C/002202) (fingolimod), Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, “01/03/2018 To: 28/02/2019”

EMEA/H/C/PSUSA/00002059/201903
(mifamurtide)
CAPS:
Mepact (EMEA/H/C/000802) (mifamurtide), Takeda France SAS, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, “Period Covered From: 04/03/2016 To: 04/03/2019”

EMEA/H/C/PSUSA/00009200/201903
(ipilimumab)
CAPS:
Yervoy (EMEA/H/C/002213) (ipilimumab), Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, “From: 23/03/2018 To: 23/03/2019”

EMEA/H/C/PSUSA/00010182/201903
(cholic acid (CTX, AMACR or cholesterol 7α-hydroxylase deficiency indication))
CAPS:
Kolbam (EMEA/H/C/002081) (cholic acid), Retrophin Europe Ltd, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Agni Kapou, “From: 17/03/2018 To: 17/03/2019”

EMEA/H/C/PSUSA/00010368/201903
(oritavancin)
CAPS:
Orbactiv (EMEA/H/C/003785) (oritavancin), Menarini International Operations Luxembourg S.A., Rapporteur: Janet Koenig, PRAC Rapporteur: Adam Przybylkowski, “From: 20/09/2018 To: 19/03/2019”

EMEA/H/C/PSUSA/00010662/201903 (ocrelizumab) CAPS: **Ocrevus** (EMEA/H/C/004043) (ocrelizumab), Roche Registration GmbH, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Brigitte Keller-Stanislawski, “From: 27/09/2018 To: 27/03/2019”	
EMEA/H/C/PSUSA/00010733/201903 (galcanezumab) CAPS: **Emgality** (EMEA/H/C/004648) (galcanezumab), Eli Lilly Nederland B.V., Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Kirsti Villikka, “Period Covered From: 26/09/2018 To: 26/03/2019”	
EMEA/H/C/PSUSA/00010753/201903 (naldemedine) CAPS: **Rizmoic** (EMEA/H/C/004256) (naldemedine), Shionogi B.V., Rapporteur: Mark Ainsworth, PRAC Rapporteur: Rhea Fitzgerald, “21/09/2018 To: 21/03/2019”	

B.4. EPARs / WPARs

Arsenic trioxide Accord - arsenic trioxide - EMEA/H/C/005175 Accord Healthcare S.L.U., treatment of relapsed acute promyelocytic leukaemia (APL), Generic, Generic of Trisenox, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Bortezomib Fresenius Kabi - bortezomib - EMEA/H/C/005074 Fresenius Kabi Deutschland GmbH, treatment of multiple myeloma, Generic, Generic of VELCADE, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Ivozall - clofarabine - EMEA/H/C/005039 ORPHELIA Pharma SAS, treatment of acute lymphoblastic leukaemia, Generic, Generic of Evoltra, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Qtrilmet - metformin hydrochloride / saxagliptin / dapagliflozin - EMEA/H/C/004910 AstraZeneca AB, - to improve glycaemic control when metformin with or without sulphonylurea	For information only. Comments can be sent to the PL in case necessary.

(SU) does not provide adequate glycaemic control and where simultaneous addition of dapagliflozin and saxagliptin is considered necessary - to improve glycaemic control when metformin with or without sulphonylurea (SU) and either dapagliflozin or saxagliptin does not provide adequate glycaemic control - when already being treated with dapagliflozin and saxagliptin and metformin., Fixed combination application (Article 10b of Directive No 2001/83/EC)	
Rhokiinsa - netarsudil - EMEA/H/C/004583 Aerie Pharmaceuticals Ireland Ltd, indicated for the reduction of elevated intraocular pressure (IOP) in adults with open-angle glaucoma or ocular hypertension, 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.
Senstend - lidocaine / prilocaine - EMEA/H/C/005298 Plethora Pharma Solutions Limited, treatment of primary premature ejaculation, Informed Consent of Fortacin, Informed consent application (Article 10c of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
XOSPATA - gilteritinib - EMEA/H/C/004752, Orphan Astellas Pharma Europe B.V., treatment of patients who have relapsed or refractory acute myeloid leukemia (AML) with a FLT3 mutation, 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

Accofil - filgrastim - EMEA/H/C/003956/II/0034/G Accord Healthcare S.L.U., Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 12.09.2019.	
AMGEVITA - adalimumab - EMEA/H/C/004212/II/0019/G Amgen Europe B.V., Rapporteur: Kristina Dunder	Positive Opinion adopted by consensus on 26.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Opinion adopted on 26.09.2019.	recommendation.
Bexsero - meningococcal group B vaccine (recombinant, component, adsorbed) - EMEA/H/C/002333/II/0079/G GSK Vaccines S.r.l, Rapporteur: Kristina Dunder Opinion adopted on 10.10.2019.	Positive Opinion adopted by consensus on 10.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0079/G UCB Pharma S.A., Rapporteur: Kristina Dunder Opinion adopted on 26.09.2019. Request for Supplementary Information adopted on 11.07.2019.	Positive Opinion adopted by consensus on 26.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cresemba - isavuconazole - EMEA/H/C/002734/II/0024/G, Orphan Basilea Pharmaceutica Deutschland GmbH, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 26.09.2019.	Positive Opinion adopted by consensus on 26.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Dupixent - dupilumab - EMEA/H/C/004390/II/0018/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 12.09.2019, 25.07.2019.	
Empliciti - elotuzumab - EMEA/H/C/003967/II/0019/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 03.10.2019.	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Empliciti - elotuzumab - EMEA/H/C/003967/II/0020/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 10.10.2019.	Positive Opinion adopted by consensus on 10.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Erelzi - etanercept - EMEA/H/C/004192/II/0018 Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 26.09.2019. Request for Supplementary Information adopted on 11.07.2019.	Positive Opinion adopted by consensus on 26.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
GONAL-f - follitropin alfa - EMEA/H/C/000071/II/0145/G Merck Europe B.V., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 10.10.2019.	Request for supplementary information adopted with a specific timetable.

Kevzara - sarilumab - EMEA/H/C/004254/II/0015/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus	
LIBTAYO - cemiplimab - EMEA/H/C/004844/II/0002/G Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Sinan B. Sarac	
Mozobil - plerixafor - EMEA/H/C/001030/II/0040/G, Orphan Genzyme Europe BV, Rapporteur: Paula Boudewina van Hennik	
NeuroBloc - botulinum toxin type B - EMEA/H/C/000301/II/0104/G Sloan Pharma S.a.r.l, Rapporteur: Bruno Sepodes Request for Supplementary Information adopted on 26.09.2019.	Request for supplementary information adopted with a specific timetable.
NovoSeven - eptacog alfa (activated) - EMEA/H/C/000074/II/0106 Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 06.06.2019, 07.03.2019, 20.09.2018.	
Pelgraz - pegfilgrastim - EMEA/H/C/003961/II/0011/G Accord Healthcare S.L.U., Rapporteur: Sol Ruiz Request for Supplementary Information adopted on 12.09.2019.	
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0154/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 26.09.2019.	Request for supplementary information adopted with a specific timetable.
Repaglinide Accord - repaglinide - EMEA/H/C/002318/II/0009/G Accord Healthcare S.L.U., Generic, Generic of NovoNorm, Rapporteur: Melinda Sobor Request for Supplementary Information adopted on 10.10.2019, 26.04.2019.	Request for supplementary information adopted with a specific timetable.
Semglee - insulin glargine - EMEA/H/C/004280/II/0009 Mylan S.A.S, Rapporteur: Martina Weise Opinion adopted on 26.09.2019. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 26.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 17.01.2019.	
Simulect - basiliximab - EMEA/H/C/000207/II/0101/G Novartis Europharm Limited, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 10.10.2019.	Request for supplementary information adopted with a specific timetable.
Viramune - nevirapine - EMEA/H/C/000183/II/0141/G Boehringer Ingelheim International GmbH, Rapporteur: Bruno Sepodes Request for Supplementary Information adopted on 10.10.2019.	Request for supplementary information adopted with a specific timetable.

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

Afstyla - lonoctocog alfa - EMEA/H/C/004075/II/0024 CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, “Update of sections 4.4 and 4.8 of the SmPC with safety information regarding the development of factor VIII inhibitors in patients treated with Afstyla based on clinical trial and post-marketing data reviewed recently with data lock point 03 January 2019. The PL is updated accordingly. Additionally, local representatives' details for Bulgaria and Croatia have been updated.”	
Atriance - nelarabine - EMEA/H/C/000752/II/0046/G Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, “Update to the Annex II to remove the SOB based on final results from the Study NLR506AUS02T (COG AALL0434) 'Intensified methotrexate, nelarabine and augmented BFM therapy for children and young adults with newly diagnosed T-ALL and T-LBL'. As a result sections 4.8 and 5.1 of the SmPC are updated. Additionally the MAH took the opportunity to update section 4.6 of the SmPC to revise information on the male and female contraception taking into consideration available non-clinical and clinical safety data as well as internal MAH's guidelines based on information from literature, health authority and working group guidelines. Moreover, the MAH took the opportunity to	

update details of the local representatives in the PL and introduce minor editorial changes in the PI. The revised RMP version 10 is included in this submission." Request for Supplementary Information adopted on 25.07.2019, 28.02.2019.	
Baraclude - entecavir - EMEA/H/C/000623/II/0063 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, "Submission of responses to the final clinical study report (CSR) from a Paediatric Safety and Efficacy Study (AI463189), a comparative study of the antiviral efficacy and safety of Entecavir (ETV) versus placebo in paediatric subjects with chronic Hepatitis B Virus (HBV) infection who are HBeAg positive, in order to provide additional clarification regarding the on-treatment and long-term follow-up haematology findings. The final CSR for AI463189 was already submitted and assessed within the context of procedure EMEA/H/C/000623/P46/010." Request for Supplementary Information adopted on 10.10.2019.	Request for supplementary information adopted with a specific timetable.
CRYSVITA - burosumab - EMEA/H/C/004275/II/0004, Orphan Kyowa Kirin Holdings B.V., Rapporteur: Kristina Dunder, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC, to reflect the results of study UX023-CL301, a phase III study undertaken to further assess the efficacy, safety and pharmacodynamics in paediatric patients aged 1-12 years with X-linked Hypophosphataemia (XLH). The provision of the final CSR addresses Specific Obligation 2 (ANX 002) and the requirements of article 46 of the paediatric regulation. The Package Leaflet and Annex IIE have been updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the SmPC to increase readability." Request for Supplementary Information adopted on 27.06.2019.	
Empliciti - elotuzumab - EMEA/H/C/003967/II/0018 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, "Update of section 5.1 of the SmPC with final overall survival data from study CA204004 (A Phase 3, Randomized, Open Label Trial of lenalidomide/dexamethasone	Positive Opinion adopted by consensus on 26.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

With or Without Elotuzumab in Relapsed or Refractory Multiple Myeloma).” Opinion adopted on 26.09.2019.	
EVOTAZ - atazanavir / cobicistat - EMEA/H/C/003904/II/0030 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, “Update of sections 4.3 and 4.5 of the SmPC in order to add as contraindications the concomitant administration of dabigatran or lomitapide with Evotaz, and to add drug-drug interaction recommendations between Evotaz with direct oral anticoagulants and lomitapide (lipid modifying agent), based on already updated information in other marketing authorisations. Section 4.6 of the SmPC is also updated to reflect the accumulated information on the use of cobicistat during pregnancy, based on published literature. The package leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.”	
Glivec - imatinib - EMEA/H/C/000406/II/0117 Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, “Update of section 4.6 of the SmPC to include that women of childbearing potential must be advised to use effective contraception for at least 15 days after stopping treatment with imatinib, based on a company review of the company Core Data Sheet. The PL has been updated accordingly.” Request for Supplementary Information adopted on 10.10.2019.	Request for supplementary information adopted with a specific timetable.
Herzuma - trastuzumab - EMEA/H/C/002575/II/0023 Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus, “C.I.13: Submission of the final report of study CT-P6 3.2; this is a phase 3, double blind, randomized, parallel-group, active-controlled study to compare the efficacy and safety of CT-P6 and Herceptin as Neoadjuvant and Adjuvant treatment in patients with HER2 positive early breast cancer.” Opinion adopted on 10.10.2019.	Positive Opinion adopted by consensus on 10.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0110/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, “Update of sections 4.2, 4.8	

and 5.1 of the SmPC in order to include the number of PID patients, to include prescriber information and tolerability information for manual push infusion, to update prescriber information on device-assisted infusion and to include safety information, based on final results from study IgPro20_4004, an open-label study to evaluate the safety and tolerability of higher infusion parameters of Hizentra infused manually or with pump assistance in PID patients. Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update the number of PID patients and to include safety information based on final results from study IgPro_4005, a phase 4, open-label, single-sequence, crossover study to investigate the tolerability, safety and efficacy of biweekly Hizentra dosing in PID patients. The Package Leaflet is updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the list of local representative in the Package Leaflet, to make some editorial updates in sections 4.2, 5.1 and 5.2 of the SmPC and to bring the PI in line with the latest QRD template version 10.1."	
IBRANCE - palbociclib - EMEA/H/C/003853/II/0016 Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to update with information following submission of the final results from the pivotal Study A5481023 "A double blind, Phase 3 trial of fulvestrant with or without palbociclib in pre- and postmenopausal women with hormone receptor positive, HER2-negative metastatic breast cancer that progressed on prior endocrine therapy" listed as a recommendation at the time of initial MA." Request for Supplementary Information adopted on 26.09.2019, 25.07.2019, 02.05.2019, 31.01.2019.	Request for supplementary information adopted with a specific timetable.
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0053, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, "the submission of final report on PFS by investigator assessment in Study PCYC-1112-CA, including PFS2 and overall survival data until study closure per protocol (ANX_003)" Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 03.10.2019.	
Increlex - mecasermin - EMEA/H/C/000704/II/0059 Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, "Submission of the final analysis for the Category 3, Additional Pharmacovigilance Activity MEA 020.3, on Lowest Effective Dose for mecasermin. No changes to the SmPC or Patient Leaflet are proposed as part of this final analysis on Lowest Effective Dose of mecasermin." Opinion adopted on 10.10.2019. Request for Supplementary Information adopted on 16.05.2019.	Positive Opinion adopted by consensus on 10.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Instanyl - fentanyl - EMEA/H/C/000959/II/0051 Takeda Pharma A/S, Rapporteur: Alexandre Moreau, "Update of section 4.8 to include dyspnoea. The MAH has also taken the opportunity to include editorial changes in Patient Leaflet." Opinion adopted on 10.10.2019.	Positive Opinion adopted by consensus on 10.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Invanz - ertapenem - EMEA/H/C/000389/II/0060 Merck Sharp & Dohme B.V., Rapporteur: Bruno Sepodes, "To update sections 4.8 and 5.1 of the SmPC to update the safety information with the addition of a new post-marketing adverse reaction term: acute generalized exanthematous pustulosis (AGEP) and to update the breakpoints table with the most recent EUCAST recommendation (v 9.0, Jan 2019) on clinical breakpoints for ertapenem. Section 4 of the Package Leaflet is updated accordingly. The MAH is also updating the labelling section and the rest of the Product Information according to the latest QRD requirements and is updating List of Local Representatives." Opinion adopted on 10.10.2019.	Positive Opinion adopted by consensus on 10.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kyntheum - brodalumab - EMEA/H/C/003959/II/0011 LEO Pharma A/S, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC "Mechanism of action" subsection with information about the cytokine IL-17C." Opinion adopted on 26.09.2019. Request for Supplementary Information adopted on 25.07.2019.	Positive Opinion adopted by consensus on 26.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

MabThera - rituximab - **EMEA/H/C/000165/II/0165** Roche Registration GmbH, Rapporteur: Sinan B. Sarac, “Change in the posology section as 8 cycles of MabThera should be used in combination with 6-8 (previously 8) cycles of CHOP chemotherapy.” Request for Supplementary Information adopted on 25.07.2019.	
Mepsevii - vestronidase alfa - **EMEA/H/C/004438/II/0008, Orphan** Ultragenyx Germany GmbH, Rapporteur: Johann Lodewijk Hillege, “Update of section 5.3 of the SmPC based on the final results from study UX003-PC010 a Developmental and Perinatal/Postnatal reproduction non-clinical study in rats including a Post-natal Behavioural/Functional Evaluation. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1.”	
Mylotarg - gemtuzumab ozogamicin - **EMEA/H/C/004204/II/0010/G, Orphan** Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, “A group of two type II variations, to submit the non-clinical in vitro study reports PFZ-07 and 6000572 relating to the effects of gemtuzumab ozogamicin on platelet development as well as on human platelet function.” Request for Supplementary Information adopted on 10.10.2019.	Request for supplementary information adopted with a specific timetable.
PREVYMIS - letermovir - **EMEA/H/C/004536/II/0013, Orphan** Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, “Update of section 5.1 of the SmPC in order to update the viral resistance profile that may be associated with a change in susceptibility to letermovir considering new intro pharmacology data based on the analysis of the patients’ samples included in the study MK-8228. This study is a Phase III Randomized, Placebo-Controlled Clinical Trial to Evaluate the Safety and Efficacy of MK-8228 (Letermovir) for the Prevention of Clinically Significant Human Cytomegalovirus (CMV) Infection in Adult, CMV Seropositive Allogeneic Hematopoietic Stem Cell. This variation follows the recommendation dated 9th November 2017 that asked for the	

submission when available of the results to update the CMV phenotypic resistance analyses of all clinical isolates for subjects failing letermovir treatment and to explore the possibility to obtain additional pre-failure CMV genotypic data from available samples."	
Xarelto - rivaroxaban - EMEA/H/C/000944/II/0068 Bayer AG, Rapporteur: Kristina Dunder, "Update of section 5.1, of the SmPC based on results from the pantoprazole/placebo randomization part of the COMPASS study; this is part of a double-blind, double-dummy randomized trial in which pantoprazole is being compared with placebo in patients participating in the trial who are not receiving a proton-pump inhibitor. In addition, an amendment to the COMPASS Clinical Study Report is submitted to correct values caused by a programming error in the statistical outputs in this study. No changes on the approved label are proposed due to this correction." Request for Supplementary Information adopted on 03.10.2019.	Request for supplementary information adopted with a specific timetable.
XGEVA - denosumab - EMEA/H/C/002173/II/0069 Amgen Europe B.V., Rapporteur: Kristina Dunder, "Update of SmPC sections 4.2, 4.8, 5.1 and 5.2 based on the final analysis from study 20062004; a phase 2, open-label, single-group study to evaluate the safety and pharmacokinetics of denosumab in adult and adolescent subjects with giant cell tumour of bone (GCTB). The final CSR for study 20062004 was previously assessed by CHMP as part of procedure P46 027 and the finalisation of the study addresses the final PIP measure. Further, section 4.8 of the SmPC is being updated to include the new ADR 'alopecia' with a frequency of 'common', upon request by PRAC following the assessment of PSUSA/00009119/201809. In addition, the MAH took the opportunity to update the description of ONJ incidence in section 4.8 of the SmPC in order to express events per 100 patient years without a percentage sign. The Package Leaflet has been updated accordingly." Request for Supplementary Information adopted on 14.06.2019.	
Zytiga - abiraterone acetate -	Request for supplementary information adopted

EMEA/H/C/002321/II/0058 Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez, "To update section 5.1 of the SmPC based on final results from study PCR3011 (Lattitude); this is a randomized, double-blind, placebo-controlled study designed to determine the efficacy of abiraterone acetate and low-dose prednisone in men with metastatic hormone-naive prostate cancer." Request for Supplementary Information adopted on 10.10.2019.	with a specific timetable.
Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0059 Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez, "To update sections 4.4 and 4.8 of the SmPC with safety information on QT prolongation and Torsades de Pointes following a cumulative review of QT Prolongation/Torsades de pointes occurrence." Request for Supplementary Information adopted on 10.10.2019.	Request for supplementary information adopted with a specific timetable.
WS1636/G **Mekinist-EMEA/H/C/002643/WS1636/0035/G** **Tafinlar-EMEA/H/C/002604/WS1636/0040/G** Novartis Europharm Limited, Lead Rapporteur: Filip Josephson, "Update of section 5.1 of the Mekinist (trametinib) and Tafinlar (dabrafenib) SmPC to include the 5-years overall survival (OS) results from study MEK115306 (COMBI-d), a phase III, randomised, double-blinded study comparing the combination of dabrafenib and trametinib to dabrafenib and placebo in first-line therapy for subjects with unresectable or metastatic BRAF V600/K mutation-positive cutaneous melanoma and the 5-years overall survival (OS) results from study MEK116513 (COMBI-v), a phase III, open-label, 2 arm, randomised study comparing dabrafenib and trametinib combination therapy with vemurafenib monotherapy in BRAF V600 mutation-positive metastatic melanoma."	See 9.1
WS1637 **Ebymect-EMEA/H/C/004162/WS1637/0039** **Edistride-EMEA/H/C/004161/WS1637/0032** **Forxiga-EMEA/H/C/002322/WS1637/**	

0051 **Xigduo-EMEA/H/C/002672/WS1637/0050** AstraZeneca AB, Lead Rapporteur: Kristina Dunder, “Update of sections 4.4 (Special warnings and precautions for use) and 4.8 (Undesirable effects) of the SmPC of dapagliflozin-containing products with respect to the Fournier’s gangrene class labelling language, following results from the DECLARE study (a Multicentre, Randomized, Double-Blind, Placebo-Controlled cardiovascular outcome trial in Patients with Type 2 Diabetes). The Package Leaflet is updated accordingly.” Request for Supplementary Information adopted on 27.06.2019.	
WS1683 **Elebrato Ellipta-EMEA/H/C/004781/WS1683/0012** **Temybric Ellipta-EMEA/H/C/005254/WS1683/0001** **Trelegy Ellipta-EMEA/H/C/004363/WS1683/0010** GlaxoSmithKline Trading Services Limited, Lead Rapporteur: Peter Kiely, “Update of SmPC in order to add information in section 5.1 on survival data from the IMPACT study”	See 9.1

B.5.3. CHMP-PRAC assessed procedures

Bydureon - exenatide - EMEA/H/C/002020/II/0064 AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, “Update of sections 4.2 and 4.4 of the SmPC in order to remove the limitation of use in patients with moderate renal impairment (creatinine clearance [CrCl] 30 to 50 mL/min) based on pooled data from 8 EQW/EQWS studies undertaken in patients with mild renal impairment/chronic kidney disease stage 2 or moderate renal impairment/chronic kidney disease stage 3, and on supportive data from EXSCEL (Study D5551C00003/BCB109) including a subset of patients with moderate renal impairment. In addition, the MAH took the opportunity to introduce GFR as the main indicator of renal function rather than CrCl. The Package Leaflet has been updated accordingly and the MAH has taken the opportunity to implement some minor	

changes in the labelling. An updated RMP version 34 was provided with the application, which includes consequential changes as well as a proposal for the removal of Acute Renal Failure (ARF) as an Important Identified Risk based on the GVP V Rev2 guidance. In addition, upon request following the assessment of II/54, a Pan EU epidemiological study to monitor events of pancreatic cancer has been included as an additional planned pharmacovigilance activity."	
Eliquis - apixaban - EMEA/H/C/002148/II/0063 Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4 and 4.9 of the SmPC in order to reflect the availability of a reversal agent for apixaban following the recent approval of andexanet alfa in the EU; the Package Leaflet and Labelling are updated accordingly. The RMP version 20.1 has also been submitted, with updates due to the availability of a reversal agent and implement the revised GVP template Rev.2. As a result, the list of safety concerns has been updated and a number of safety concerns listed as missing information have been reclassified and have been removed from the RMP. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to update the information in the SmPC and Package Leaflet in accordance with the most recent guidance on labelling of excipients of medicinal products for human use." Opinion adopted on 03.10.2019.	Positive Opinion adopted by consensus on 03.10.2019. 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/0033 MSD Vaccins, Rapporteur: Kristina Dunder, PRAC Rapporteur: Jean-Michel Dogné, "Update of sections 4.2, 4.6, 4.8 and 5.1 of the SmPC in order to update the safety and immunogenicity information based on final results from study V503-P004 listed as a category 3 study in the RMP (MEA007); this is an open-label phase III clinical trial to study the immunogenicity and tolerability of Gardasil 9 in adult women (27 to 45 year-olds) compared to young adult women (16	Request for supplementary information adopted with a specific timetable.

to 26 year-olds); the Package Leaflet is updated accordingly. The RMP version 4.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.4 of the SmPC according to the Guideline on quality aspects included in the product information for vaccines for human use (EMA/CHMP/BWP/133540/2017), and to include editorial changes in section 5.1 of the SmPC" Request for Supplementary Information adopted on 03.10.2019.	
Giotrif - afatinib - EMEA/H/C/002280/II/0031 Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "Update of sections 4.4 and 4.8 of the SmPC in order to add gastrointestinal (GI) perforation as an additional side effect based on summarises of clinical trial and post-marketing safety data. The Package Leaflet and the RMP are updated accordingly. The RMP version 8.0 has been submitted including also the update of the RMP due to transition to the revision 2 template as per pharmacovigilance guidance and taking in consideration the recommendation received during renewal procedure EMEA/H/C/002280/R/0026. In addition the MAH took the opportunity to correct some typographical errors in the German, Austrian and Spanish PIs, to include a linguistic review comments received from Czech Authority during linguistic review of procedure EMEA/H/C/002280/R/0026 in the SmPC and to update the list of the local representatives for Austria in the package leaflet." Request for Supplementary Information adopted on 03.10.2019, 11.07.2019.	Request for supplementary information adopted with a specific timetable.
IBRANCE - palbociclib - EMEA/H/C/003853/II/0019/G Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Hans Christian Siersted, "Update of section 4.8 of the SmPC in order to include ILD/pneumonitis as ADRs based on a safety cumulative review together with reclassification of the risk from potential to identified in the RMP (version 1.6). The Package Leaflet is updated accordingly. The MAH has also submitted the updated RMP version 1.6 in order to remove long term use from missing information in the list of safety concerns. In	

addition, the MAH is proposing to change the due date for submission of the final CSR of study A5481027 listed as a Category 3 study in the RMP." Request for Supplementary Information adopted on 14.06.2019.	
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0052, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "Submission of the final report on the long term safety study PAM 3038-1, which assessed long term safety data collected from predefined cohorts of subjects treated with ibrutinib for up to 5 years or until disease progression or unacceptable toxicity at the recommended daily doses of 420 mg/day for CLL/SLL and 560 mg/day for MCL. This final report fulfils the milestone for the Post Approval Measure MEA025" Request for Supplementary Information adopted on 03.10.2019.	Request for supplementary information adopted with a specific timetable.
Insuman - insulin human - EMEA/H/C/000201/II/0130 Sanofi-Aventis Deutschland GmbH, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Jean-Michel Dogné, "Submission of the final report from a completed Phase 3 study, HUBIN-L-05335, listed as a category 3 post-authorisation efficacy / safety study in the RMP. This study covers the evaluation of Insuman Implantable 400 IU/mL in patients with Type 1 diabetes treated with the Medtronic MiniMed Implantable Pump System using Insuplant 400 IU/mL, addressing the Post-Authorisation Measure MEA040. In this application, the RMP v4.0 combines the updates related to HUBIN-L-05335 study final results and the approval of amended protocol V2 of the ongoing Post Authorization Safety Study HUBIN-C-06380 (MEA/047.4 & MEA/047.5, concerning PRAC decision: EMA/PRAC/256519/2018 dated 17-May-2018; updates are limited to Annex 3 of Part VII)." Opinion adopted on 03.10.2019. Request for Supplementary Information adopted on 11.07.2019.	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Jakavi - ruxolitinib - EMEA/H/C/002464/II/0044	Request for supplementary information adopted with a specific timetable.

Novartis Europharm Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Annika Folin, “Update of the SmPC sections 5.1 and 4.8 with the efficacy and safety information to reflect the 5-year follow-up data from the B2301 Week 256 final clinical study report (CSR). The final analyses presented in the CSR are submitted to fulfil the Post-Authorisation Measure, therefore the Annex II.D of the Product Information is updated accordingly. The changes have been reflected in the RMP version 11 submitted with the procedure II/43.”
Request for Supplementary Information adopted on 03.10.2019.

Keytruda - pembrolizumab - EMEA/H/C/003820/II/0080

Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Menno van der Elst, “To update sections 4.2, 4.4 and 4.8 of the SmPC on the safety information for immune-related endocrinopathies following a safety review for Addison’s disease/Primary adrenal insufficiency. The updated RMP version 26.1 has also been submitted. The MAH also took the opportunity to include the changes in Annex II related to the new EMA QRD template version 10.1 and to update the List of Local Representatives of Portugal in the Package Leaflet.”

Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0075

Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, “Update of sections 4.4 and 5.1 of the Summary of Product Characteristics in order to reflect change in the existing warning on immunogenicity and immunomodulation and add new clinical information on infantile onset patients (IOPD) immune tolerance induction based on data on use of immune tolerance induction in infantile onset Pompe disease patients from two exploratory Phase 4 studies (AGLU03707 / MSC12817 and companion study AGLU03807/ MSC12892) and the Duke Center of Excellence Observational Study (01562).
The updated RMP version 9.0 has also been submitted.”

Raxone - idebenone - EMEA/H/C/003834/II/0016, Orphan

Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli, “C.I.11 for SOB studies: Submission of the final report from study SNT-CRS-002 listed as a Specific Obligation (SOB10, former SOB2) in the Annex II of the Product Information. This is a Historical case record survey (CRS) of visual acuity data from patients with Leber’s hereditary optic neuropathy (LHON). The goal is to generate a natural history group to serve as a comparator group of idebenone-naïve patients for the open-label study SNT-IV-005 which will assess long-term efficacy and safety in patients with LHON treated with Raxone. Annex II is modified accordingly. Submission of an updated RMP version 1.8 accordingly.”	
Reagila - cariprazine - EMEA/H/C/002770/II/0010 Gedeon Richter Plc., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ana Sofia Diniz Martins, “Submission of in vitro metabolism study report (R188-A15) and consequential update of the Risk Management Plan (version 1.7).” Opinion adopted on 03.10.2019. Request for Supplementary Information adopted on 11.07.2019.	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
RoActemra - tocilizumab - EMEA/H/C/000955/II/0086/G Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Grouping of 3 variations: 2 variations C.I.11.z supporting RMP updates: Submission of an updated RMP version 25.2 in order to remove the reference to the Neutropenia Guided Questionnaire as per the Guidance on the format of the RMP in EU EMA/164014/2018 Rev.2.0.1 accompanying GVP Module V Rev.2 and to remove all references to the US Claims Database from the RMP resulting from the conversion of the RMP to the new template. The MAH also took the opportunity to make the following minor changes to the RMP: - Removal of study WA22479 (British Society of Rheumatology Biologics Register (BSRBR)) in response to the fulfilment of PAM MEA-045. - Removal of OTIS registry from additional pharmacovigilance activities which was erroneously retained in EU- RMP version 24.1 approved with the variation procedure	

EMEA/H/C/00955/II/76. - Inclusion of the ZUMA-8 (KTE-X19-108) study in routine pharmacovigilance activities in line with previous PRAC/CHMP request as part of variation procedure EMEA/H/C/000955/II/0076. - Removal of study WA29358 which was erroneously introduced into RMP v24.1 as an additional PV activity 1 variation C.I.4 affecting the PI Update of sections 4.8 of the SmPC the change the frequency for anaphylaxis (fatal) and Stevens-Johnson Syndrome to “rare” in the SmPC; the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to sections 4.2, 4.8 and 5.1 of the SmPC, the Annex IID and Section 4 of the Package Leaflet.”	
Signifor - pasireotide - EMEA/H/C/002052/II/0041/G, Orphan Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, “Submission of the final CSR from Study CSOM230B2219; a multi-centre, randomized, open-label, Phase IV study to investigate the management of pasireotide-induced hyperglycemia with incretin based therapy or insulin in adult patients with Cushing’s disease or acromegaly (listed as a category 3 study in the RMP). A revised RMP version 7.1, updated in line with the revised GVP Module V, including changes to the safety concerns, was agreed during the procedure.” Opinion adopted on 03.10.2019. Request for Supplementary Information adopted on 14.06.2019.	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tamiflu - oseltamivir - EMEA/H/C/000402/II/0142 Roche Registration GmbH, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, “Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC following completion of the paediatric studies NV25719 and NV20234 and downstream population PK and PK/PD analysis, listed in the approved Tamiflu Paediatric Investigation Plan (PIP) (EMEA-000365-PIP01-08-M10); the study NV25719 was a prospective, open-label, randomized study which investigated PK and PD	

of two weight adjusted oseltamivir doses for the treatment of influenza-infected immunocompromised (IC) children less than 13 years of age. The study NV20234 was a prospective, double-blind, randomized trial which investigated safety and viral resistance to oseltamivir treatment in influenza-infected IC adults, adolescents and children. The purpose of this variation is to establish a dose recommendation for the treatment of paediatric IC patients. The Package Leaflet and Labelling are updated accordingly. The updated RMP version 19 has also been submitted."	
Vemlidy - tenofovir alafenamide - EMEA/H/C/004169/II/0020 Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, PRAC Rapporteur: Ilaria Baldelli, "Update of sections 4.8 and 5.1 of the SmPC based on safety information from interim results at Week 48 of a phase 3, randomized, double blind study (GS-US-320-4018) conducted to evaluate the efficacy and safety of switching from tenofovir disoproxil fumarate (TDF) 300 mg QD to tenofovir alafenamide (TAF) 25 mg QD in subjects with CHB who are virologically suppressed, listed as a category 3 study in the RMP; the Package Leaflet is updated accordingly. The RMP version 4.1 has also been submitted." Request for Supplementary Information adopted on 25.07.2019.	
VeraSeal - human fibrinogen / human thrombin - EMEA/H/C/004446/II/0006/G Instituto Grifols, S.A., Rapporteur: Andrea Laslop, PRAC Rapporteur: Amelia Cupelli"B.IV.1.a.3 – Type II - To add a new CE marked applicator tip. The safety concern of air or gas embolism that is currently included in the Risk Management Plan (RMP) is no longer applicable, consequently the RMP has been updated accordingly (version 4.0) and is provided in Module 1.8.2. RMP version 4.0 has been restructured in order to adapt to the new format of GVP Module V. B.II.e.6.a – Type 1BB.II.e.6.a – Type 1B B.II.b.3.a – Type 1A B.II.b.3.a – Type 1A	
Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0015, Orphan	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP

Ipsen Pharma, Rapporteur: Martina Weise, PRAC Rapporteur: Adam Przybylkowski, "To update section 5.1 of the SmPC based on final results from study LX1606.1-302.CS (TELEPATH) listed as a category 3 study in the RMP; this is a multicentre, phase III, long-term extension study to further evaluate the safety and tolerability of telotristat etiprate in patients with carcinoid syndrome (CS). The updated RMP version 4.0 has also been submitted, also updating to GVP Module V (Rev 2)." Opinion adopted on 03.10.2019. Request for Supplementary Information adopted on 11.07.2019.	Members were in agreement with the CHMP recommendation.
Yervoy - ipilimumab - EMEA/H/C/002213/II/0064 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4 and 4.8 of the SmPC to add stomatitis to the list of ADRs with a frequency uncommon, to further explain the components of the existing ADR musculoskeletal pain in a footnote and to update safety information based on final results from study CA184143 (A Multi-National, Prospective, Observational Study in Patients with Unresectable or Metastatic Melanoma) listed as a category 3 study in the RMP (MEA017.11); the Package Leaflet and the RMP have been updated accordingly (version 26.2). In addition, minor changes to improve clarity were introduced in section 5.1 of the SmPC and to the Annex II of the Product Information and minor changes were also made in relation to the Dutch Melanoma Treatment Registry (DMTR) in the RMP, partly as recommended in conclusion to MEA 036.1." Opinion adopted on 03.10.2019. Request for Supplementary Information adopted on 14.06.2019, 14.03.2019.	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.4. PRAC assessed procedures

PRAC Led **Accofil - filgrastim - EMEA/H/C/003956/II/0037** Accord Healthcare S.L.U., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, PRAC-CHMP liaison: Tuomo Lapveteläinen, "Submission of an updated RMP version 4.0 in	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

order to update the section of additional pharmacovigilance activities (removal of SCNIR and EBMT registry) in follow-up to the assessment of the `Accofil Severe Chronic Neutropenia International Registry (SCNIR)' and 'European Group for Blood and Marrow Transplantation (EBMT)' Combined Analysis Report. The MAH has also taken the opportunity to implement the RMP template based on GVP module V rev.2." Opinion adopted on 03.10.2019.	
PRAC Led **Caprelsa - vandetanib - EMEA/H/C/002315/II/0040** Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 13 in order to remove the Health Care Professionals survey from the list of additional Pharmacovigilance Activities and to remove several safety concerns from the list of important identified and potential risks and missing information to follow revised guidance in the GVP Module V Rev.2 as requested during variation procedure EMEA/H/C/002315/II/0028." Opinion adopted on 03.10.2019.	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Edurant - rilpivirine - EMEA/H/C/002264/II/0037** Janssen-Cilag International NV, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "C.I.13: Submission of the final report from a Drug Utilization Study (DUS), with register number EUPAS5766, in the EuroSIDA cohort listed as a category 3 study in the RMP. This is a Observational Cohort Study to assess rilpivirine (RPV) utilization according to the European SmPC. The RMP version 9.0 has also been submitted." Request for Supplementary Information adopted on 03.10.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **EXJADE - deferasirox - EMEA/H/C/000670/II/0068** Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre	Request for supplementary information adopted with a specific timetable.

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 used 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 03.10.2019.	
PRAC Led **Glivec - imatinib -** **EMEA/H/C/000406/II/0115** Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, “Submission of an updated RMP version 12 in order to revise the lists of safety concerns in EU RMP and align with the current GVP Rev 2 based on the PRAC advice received on the latest PSUR (11-May-2015 to 10-May-2018).” Request for Supplementary Information adopted on 03.10.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Jakavi - ruxolitinib -** **EMEA/H/C/002464/II/0043** Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Filip Josephson, “Submission of the final report from a safety study (INC424AIC01T) of ruxolitinib in myelofibrosis (MF) listed as a category 3 study in the RMP. This is a non-interventional, observational post-authorisation safety study (PASS) intended to provide real-world safety data on patients with MF who were exposed and non-exposed to ruxolitinib and thereby provide insights into disease management and the safety profile of ruxolitinib. The RMP version 11 has also been submitted. The updated RMP v11 reflects the completion of additional pharmacovigilance studies including the above-mentioned PASS (INC424AIC01T, Category 3) as well as the RESPONSE study (INC424B2301, Category 1). This RMP is incorporated in this variation and will be cross-referred in the variation forthcoming submission for the RESPONSE study within a	Request for supplementary information adopted with a specific timetable.

month of this submission." Request for Supplementary Information adopted on 03.10.2019.	
PRAC Led **Noxafil - posaconazole - EMEA/H/C/000610/II/0057** Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP (version 15.1) in order to bring it in line with the guidance included in Good Phamacovigilance Practices (GVP) Module V (Rev. 2), with the consequent applicable re-evaluation of some safety concerns. In addition to the above updates, the MAH took the opportunity to include data from the completed clinical trial in paediatric subjects PN097 (the CSR for which was submitted to the Agency in February 2019: P46 029), and update the due date for submission of the final report for the ongoing post-marketing efficacy trial PN069 (changed from December 2019 to 4th quarter of 2020)." Opinion adopted on 03.10.2019. Request for Supplementary Information adopted on 11.07.2019.	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Onivyde - irinotecan hydrochloride trihydrate - EMEA/H/C/004125/II/0015, Orphan** Les Laboratoires Servier, PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Ingrid Wang, "Submission of an updated RMP version 2.7 in order to update the RMP further to the last PSUSA procedures (PSUSA/00010534/201804 and (PSUSA/00010534/201810) and in accordance with GVP Module V Rev.2." Request for Supplementary Information adopted on 03.10.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **ProQuad - measles, mumps, rubella and varicella vaccine (live) - EMEA/H/C/000622/II/0134** MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP (version 6.1) in order to adhere to Version 2 of the RMP template. As a consequence, the following changes are	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

carried out: - Removal of the important identified risks febrile seizure, fever, measles-like rash, and thrombocytopenia and the addition of disseminated disease caused by Oka/Merck vaccine virus strain. - The important potential risks varicella-like or herpes zoster-like rashes, potential central nervous system events, potential transmission of varicella vaccine virus strain, exposure of immunocompromised individuals, hypersensitivity including anaphylaxis and injection-site reactions are also removed. - Additionally, secondary transmission of Oka/Merck vaccine virus strain in susceptible high-risk individuals leading to severe clinical consequences is included. - The important missing information 'categories exposure during pregnancy' and 'safety and immunogenicity in patients less than 9 months' of age is also removed." Opinion adopted on 03.10.2019. Request for Supplementary Information adopted on 16.05.2019.	
PRAC Led **Rebetol - ribavirin -** **EMEA/H/C/000246/II/0086** Merck Sharp & Dohme B.V., PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Jean-Michel Race, "Submission of an updated RMP version 6.0 in order to revise safety concerns for ribavirin based on GVP module V (rev. 2) guidance. In addition, the MAH took the opportunity to revise the safety concerns of ribavirin in light of the current era of IFN free regimen, as requested in a previous PSUSA procedure (EMEA/H/C/PSUSA/00010007/201707)." Opinion adopted on 03.10.2019. Request for Supplementary Information adopted on 11.07.2019.	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Sutent - sunitinib -** **EMEA/H/C/000687/II/0073** Pfizer Europe MA EEIG, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of an updated RMP version 17.2 in order to review the list of safety concerns to make it more risk proportionate based on available safety data. The updates are in line	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

with the new GVP Module V (Rev 2) guideline and new RMP template." Opinion adopted on 03.10.2019. Request for Supplementary Information adopted on 16.05.2019, 17.01.2019.	
PRAC Led **Tysabri - natalizumab - EMEA/H/C/000603/II/0114** Biogen Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of the RMP (version 25.0) with data on extended interval dosing, including an update to part II, Part VI and Annex 6. In order to align with the changes in the RMP, the MAH also submitted PI with changes in the annex I and II. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and add some QRD V10.1 requirement such as a statement on batch traceability in annex I and III (PL)." Opinion adopted on 03.10.2019. Request for Supplementary Information adopted on 11.07.2019.	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1586** **Anoro Ellipta-EMEA/H/C/002751/WS1586/0028** **Laventair Ellipta-EMEA/H/C/003754/WS1586/0031** GlaxoSmithKline (Ireland) Limited, Lead Rapporteur: Peter Kiely, Lead PRAC Rapporteur: Ilaria Baldelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of an updated RMP version 8.0 following the renewal procedures (EMEA/H/C/4002751/R/0022 and EMEA/H/C/003754/R/0025) commitments to remove the important identified risks of 'hypersensitivity' and 'paradoxical bronchospasm' from the list of safety concerns and to update all relevant sections of the RMP in line with revision 2 of GVP module V on 'Risk management systems' and revision 2 of the guidance on the format of the RMP in the EU (template). In addition, the important potential risks of 'narrow angle glaucoma' and 'bladder outflow obstruction and urinary retention' are removed; as well as the missing information on 'safety in pregnancy and lactation', 'safety in	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

long-term use' and 'safety in severe hepatic impairment'." Opinion adopted on 03.10.2019. Request for Supplementary Information adopted on 16.05.2019.	
PRAC Led **WS1614** **Enbrel-EMEA/H/C/000262/WS1614/0227** **LIFMIOR-EMEA/H/C/004167/WS1614/0021** 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 final report for the PURPOSE study, a category 3 study in the RMP. PURPOSE was a non-interventional, multi-centre, prospective, observational, cohort study to evaluate the long-term safety and effectiveness of etanercept prescribed by dermatologists to paediatric patients for the treatment of plaque psoriasis." Opinion adopted on 03.10.2019.	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1651** **Idacio-EMEA/H/C/004475/WS1651/0003** **Kromeya-EMEA/H/C/005158/WS1651/0003** Fresenius Kabi Deutschland GmbH, Lead PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "To update the risk management plans (RMP) for Idacio and Kromeya in order to align it with the parent product Humira one. The Risk Minimization Measures in Annex II.D of the PI are also updated. Minor linguistic changes/corrections to the Product Information in German, French, Hungarian (Idacio only) and Slovenian have been included." Opinion adopted on 03.10.2019.	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1663/G** **Exviera-EMEA/H/C/003837/WS1663/0046/G** **Viekirax-EMEA/H/C/003839/WS1663/0055/G** AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

liaison: Maria Concepcion Prieto Yerro, “C.I.13 To submit the final report from study P15-421, listed as a category 3 study in the RMP. This was a prospective, observational cohort study utilizing the Hepatitis C Therapeutic Registry and Research Network (HCV-TARGET) data to evaluate the clinical impact and real world frequency of Grade 3+ ALT elevations in patients being treated for Hepatitis C with paritaprevir with ritonavir (paritaprevir/r), ombitasvir and dasabuvir (3-DAA regimen) or paritaprevir/r and ombitasvir (2-DAA regimen) with or without ribavirin for Hepatitis C Infection (HCV). C.I.11.Z (Type IB): To change the final due date for the prospective safety study report in order to evaluate the recurrence of hepatocellular carcinoma associated with Viekirax and Exviera from Q2 2021 to Q2 2023. Annex II of the Product Information is updated accordingly. An updated RMP version 5.0 has also been submitted in order to convert the RMP to the new format and to remove some safety concerns and activities from the PhV Plan that have already been finalised.” Opinion adopted on 03.10.2019.	
PRAC Led **WS1671** **Afinitor-EMEA/H/C/001038/WS1671/0063** **Votubia-EMEA/H/C/002311/WS1671/0059** Novartis Europharm Limited, Lead Rapporteur: Janet Koenig, Lead PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, “To update the RMP for Afinitor and Votubia to version 14.0 to change the safety concerns, to reflect the completion of pharmacovigilance studies [CRAD001Y2201 (Afinitor II/0058), CRAD001M2304 (Votubia II/0051), CRAD001J2301 (Afinitor II/0051/G), CRAD00W2301 (Afinitor II/0051/G)] and to implement the latest GVP module V rev.2 template; the change has been agreed by the PRAC in the outcome of a PSUR assessment (EMEA/H/C/PSUSA/00010268/201703).” Opinion adopted on 03.10.2019.	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1680** **Actos-EMEA/H/C/000285/WS1680/0082** **Competact-EMEA/H/C/000655/WS1680/**	Request for supplementary information adopted with a specific timetable.

0074 **Glubrava-EMEA/H/C/000893/WS1680/0060** **Glustin-EMEA/H/C/000286/WS1680/0081** **Tandemact-EMEA/H/C/000680/WS1680/0060** Takeda Pharma A/S, Lead Rapporteur: Peter Kiely, Lead PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, "Submission of an updated RMP (version 27) in order to update and consolidate within a single RMP the RMPs for Pioglitazone, Pioglitazone/Metformin fixed dose combination (FDC) and Pioglitazone/Glimepiride FDC. The list of safety concerns has also been reviewed and consolidated RMP version updated with information agreed/approved as part of the PSUR procedure (EMEA/H/C/PSUSA/00002417/201807) with regards to discontinuation of pioglitazone aRMMs." Request for Supplementary Information adopted on 03.10.2019.	

B.5.5. CHMP-CAT assessed procedures

YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0011, Orphan, ATMP Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus Request for Supplementary Information adopted on 13.09.2019.	
Zynteglo - autologous cd34+ cell enriched population that contains hematopoietic stem cells transduced with lentiglobin bb305 lentiviral vector encoding the beta-a-t87q-globin gene - EMEA/H/C/003691/II/0001/G, Orphan, ATMP bluebird bio (Netherlands) B.V, Rapporteur: Carla Herberts, CHMP Coordinator: Paula Boudewina van Hennik Request for Supplementary Information adopted on 13.09.2019.	See 9.1

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/0022, 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, from a prospective to a retrospective study. Following additional minor changes to the RMP are also included: Update of the RMP in line with EMA Rev.2.0.1 template; update of the RMP to make the necessary amendments to the name of the MAH following the MAH transfer; update of the data in the RMP in line with the updated data lock point; update of timelines for the STRIM-001 study."	

B.5.7. PRAC assessed ATMP procedures

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

WS1645 **Exelon-EMEA/H/C/000169/WS1645/0123** **Prometax-EMEA/H/C/000255/WS1645/0124** Novartis Europharm Limited, Lead Rapporteur: Alexandre Moreau Opinion adopted on 03.10.2019. Request for Supplementary Information adopted on 25.07.2019.	Positive Opinion adopted by consensus on 03.10.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1676/G **Exelon-EMEA/H/C/000169/WS1676/0124/G** **Prometax-EMEA/H/C/000255/WS1676/0125/G** Novartis Europharm Limited, Lead Rapporteur: Alexandre Moreau Opinion adopted on 26.09.2019.	Positive Opinion adopted by consensus on 26.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1681 **Esperoct-EMEA/H/C/004883/WS1681/0001**	

NovoEight-EMEA/H/C/002719/WS1681/0032
Novo Nordisk A/S, Lead Rapporteur: Jan Mueller-Berghaus

WS1687
Fiasp-EMEA/H/C/004046/WS1687/0017
NovoMix-EMEA/H/C/000308/WS1687/0100
NovoRapid-EMEA/H/C/000258/WS1687/0130
Ryzodeg-EMEA/H/C/002499/WS1687/0037
Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder

WS1697
Ebymect-EMEA/H/C/004162/WS1697/0040
Xigduo-EMEA/H/C/002672/WS1697/0051
AstraZeneca AB, Lead Rapporteur: Kristina Dunder

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

Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0054/G Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez Request for Supplementary Information adopted on 26.04.2019, 14.02.2019.	The MAH withdrew the procedure on 23.09.2019.

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

WS1524 **HyQvia-EMEA/H/C/002491/WS1524/0048** **Kiovig-EMEA/H/C/000628/WS1524/0090** Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 19.09.2019, 14.03.2019.	Request for an extension to the clock stop to respond to the Request for Supplementary Information adopted in September 2019.

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

abiraterone acetate - EMEA/H/C/005408
treatment of metastatic prostate cancer

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.

lenalidomide - EMEA/H/C/005306
treatment of multiple myeloma

pegfilgrastim - EMEA/H/C/005085
treatment of neutropenia

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

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

IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/X/0035, Orphan
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, “Extension application to add a new strength of 3500 IU (700 IU/ml) for albutrepenonacog alfa powder and solvent for solution for injection. The RMP version 3.1 was updated in accordance.
In addition, the applicant took the opportunity to update sections 3.2.S.4, 3.2.P.1-2-3-5-8 with editorial changes and align the dossier.”

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)”

Velphoro - iron - EMEA/H/C/002705/X/0020/G
Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Kimmo Jaakkola, “Extension

application to add a new pharmaceutical form with a new strength - powder for oral suspension 125 mg, and extension of indication to add indication to use Velphoro for the control of serum phosphorus levels in paediatric patients 2 years of age and older with CKD stages 4-5 (defined by a glomerular filtration rate <30 mL/min/1.73 m2) or with CKD on dialysis, based on the results from an open-label, randomised, active-controlled, parallel group, multicentre, phase 3 study investigating the safety and efficacy of Velphoro and calcium acetate in paediatric and adolescent CKD patients with hyperphosphataemia (Study PA-CL-PED-01). As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 7.0 has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.1." Request for 1 year of data exclusivity for a new indication (Article 10(5) of Directive 2001/83/EC)	

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

IBRANCE - palbociclib - EMEA/H/C/003853/X/0018 Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, "Extension application to introduce a new pharmaceutical form (film-coated tablets) associated with new strengths." List of Questions adopted on 25.07.2019.	
Pemetrexed Fresenius Kabi - pemetrexed - EMEA/H/C/003895/X/0009 Fresenius Kabi Deutschland GmbH, Generic, Generic of Alimta, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ghania Chamouni, "Extension application to introduce a new pharmaceutical form (concentrate for solution for infusion) associated with new strength 25 mg/ml." List of Outstanding Issues adopted on 19.09.2019. List of Questions adopted on 31.01.2019.	
rituximab - EMEA/H/C/004696 treatment of Non-Hodgkin's lymphoma (NHL),	

Chronic lymphocytic leukaemia (CLL) and
Rheumatoid arthritis
List of Questions adopted on 13.12.2018.

isatuximab - EMEA/H/C/004977, Orphan
sanofi-aventis groupe, For the treatment of
patients with multiple myeloma (MM)
List of Questions adopted on 19.09.2019.

lifitegrast - EMEA/H/C/004653
treatment of moderate to severe dry eye disease
in adults for whom prior artificial tears has not
been sufficient
List of Questions adopted on 26.04.2019.

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

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

Natpar - parathyroid hormone -
EMEA/H/C/003861/R/0022, Orphan
Shire Pharmaceuticals Ireland Limited,
Rapporteur: Bart Van der Schueren, PRAC
Rapporteur: Rhea Fitzgerald

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

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Apidra - insulin glulisine -
EMEA/H/C/000557/II/0082/G
Sanofi-Aventis Deutschland GmbH, Rapporteur:
Mark Ainsworth

Cimzia - certolizumab pegol -
EMEA/H/C/001037/II/0085/G
UCB Pharma S.A., Rapporteur: Kristina Dunder

Coagadex - human coagulation factor X -
EMEA/H/C/003855/II/0023, Orphan
BPL Bioproducts Laboratory GmbH, Rapporteur:
Andrea Laslop

Esperoct - turoctocog alfa pegol -
EMEA/H/C/004883/II/0002, Orphan

Novo Nordisk A/S, Rapporteur: Andrea Laslop

Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0008
Seqirus Netherlands B.V., Rapporteur: Sol Ruiz

Fulphila - pegfilgrastim - EMEA/H/C/004915/II/0005/G
Mylan S.A.S, Rapporteur: Martina Weise

Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0037, Orphan
Roche Registration GmbH, Rapporteur: Sinan B. Sarac

Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0111/G
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Ilumetri - tildrakizumab - EMEA/H/C/004514/II/0010/G
Almirall S.A, Rapporteur: Jan Mueller-Berghaus

Inflectra - infliximab - EMEA/H/C/002778/II/0081/G
Pfizer Europe MA EEIG, Duplicate, Duplicate of Remsima, Rapporteur: Outi Mäki-Ikola

Kyprolis - carfilzomib - EMEA/H/C/003790/II/0040, Orphan
Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez

NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0033/G
Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus

OPDIVO - nivolumab - EMEA/H/C/003985/II/0076/G
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez

OPDIVO - nivolumab - EMEA/H/C/003985/II/0078
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez

Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0053/G
Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Daniela Melchiorri

Pheburane - sodium phenylbutyrate -

EMEA/H/C/002500/II/0025
Eurocept International B.V., Rapporteur: Jayne Crowe

Posaconazole AHCL - posaconazole - EMEA/H/C/005028/II/0001
Accord Healthcare S.L.U., Generic, Generic of Noxafil, Rapporteur: Kolbeinn Gudmundsson

Remsima - infliximab - EMEA/H/C/002576/II/0075/G
Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola

Somavert - pegvisomant - EMEA/H/C/000409/II/0091
Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race

Symtuza - darunavir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004391/II/0020
Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege

Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0020/G
Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege

WS1726
Nuwiq-EMEA/H/C/002813/WS1726/0033
Vihuma-EMEA/H/C/004459/WS1726/0015
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus

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

Bydureon - exenatide - EMEA/H/C/002020/II/0066
AstraZeneca AB, Rapporteur: Kristina Dunder, “Update of section 4.8 of the SmPC to include information about the new ADR drug-induced thrombocytopenia (DITP) based on spontaneous reports post-marketing. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes in line with the latest QRD template.”

BYETTA - exenatide - EMEA/H/C/000698/II/0071

AstraZeneca AB, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC to include information about the new ADR drug-induced thrombocytopenia (DITP) based on spontaneous reports post-marketing. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes in line with the latest QRD template."

Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/II/0082

Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, "Update of section 5.3 of the SmPC in order to add new information on ledipasvir carcinogenicity based on final results from study TX-256-2016; this was a 104-week oral gavage carcinogenicity study in rats."

Jivi - damoctocog alfa pegol - EMEA/H/C/004054/II/0004

Bayer AG, Rapporteur: Sinan B. Sarac, "Submission of the final Clinical Study Report PH-40657 for the pharmacokinetic study (study 19096) comparing pharmacokinetic parameters of Jivi vs. Elocta."

Lorviqua - lorlatinib - EMEA/H/C/004646/II/0002

Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, "Update of section 4.5 of the SmPC in order to further reflect the induction potential of lorlatinib on CYP2C9, P-gp, CYP2B6 and UGT1A1 substrates based on the results from the drug-drug interaction sub-study of B7461001. Furthermore, the MAH corrected information regarding ADRs in sections 4.4 and 4.8 of the SmPC and clarification regarding linearity/non-linearity of lorlatinib PK in section 5.2 of the SmPC. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1."

Portrazza - necitumumab - EMEA/H/C/003886/II/0017

Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Rugile Pilviniene, "Submission of the exploratory biomarker analysis from 4 clinical studies (I4X-MC-JFCU, I4X-MC-JFCQ, I4X-MC-JFCP, I6A-MC-CBBE) listed as a category 3 measure in the RMP. The RMP version 8.1 has also been submitted."

Praluent - alirocumab -
EMEA/H/C/003882/II/0051
sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, “Update of section 4.4 of the SmPC to add a new warning on angioedema and update of section 4.8 of the SmPC to add ‘angioedema’ as a new adverse drugs reaction, based on safety review of post-marketing cases and cases from study EFC11570 (OUTCOMES study); the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make some formatting changes throughout the product information.”

PREVYMIS - letermovir -
EMEA/H/C/004536/II/0014, Orphan
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, “Update of section 4.5 of the SmPC in order to update the safety information with regard to the drug interaction information following the results from study MK-8228-039, a clinical pharmacology trial entitled “A Study to Assess the Effect of P-gp/BCRP Inhibition, following Multiple Oral Doses of Itraconazole, on the Steady-State Pharmacokinetics of MK-8228 in Healthy Adult Subjects” listed as a category 3 study in the RMP. The RMP version has not been submitted.
In addition, the Marketing authorisation holder (MAH) took the opportunity to submit the protein binding report as part of the rifampin study MK-8228-038 as it was requested within the previous type II variation (EMEA/H/C/004536/II/0011) .”

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

from 31 May 2020 to 31 May 2021."

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."

Revatio - sildenafil -
EMEA/H/C/000638/II/0086
Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 5.1 of the SmPC based on the final results from study A1481316; this is a multi-centre, randomised, placebo-controlled, double-blind, two-armed, parallel group study to evaluate efficacy and safety of iv sildenafil in the treatment of neonates with persistent pulmonary hypertension of the newborn (PPHN) or hypoxic respiratory failure and at risk for PPHN, with a long-term follow-up investigation of developmental progress 12 and 24 months after completion of study treatment. In addition some minor editorial updates to the Product Information are being proposed."

Soliris - eculizumab -
EMEA/H/C/000791/II/0107, Orphan
Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez"Submission of the final report from study ECU-MG-302, a phase III, open-label, extension trial of ECU-MG-301 to evaluate the safety and efficacy of eculizumab in subjects with refractory generalized myasthenia gravis (EudraCT 2013-002191-41)."

Strensiq - asfotase alfa -
EMEA/H/C/003794/II/0043/G, Orphan
Alexion Europe SAS, Rapporteur: Daniela Melchiorri, "Type IB B.II.f.1.z. – To extend the time out of refrigeration (TOR) of the Strensiq vials from 1 to 3 hours.
Section 6.3 of the SmPC and the Package Leaflet are updated accordingly. In addition, the MAH took the opportunity to align the annexes with the latest QRD template v. 10.1 and to update the Package Leaflet section "How to inject Strensiq" with the clarification of the steps for injection, in order to align the instructions for injection with the EU RMP educational materials."

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.”

Verzenios - abemaciclib - EMEA/H/C/004302/II/0008
Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, “Update of section 5.1 of the SmPC to include the results of the interim OS analysis from study MONARCH 2, a randomised, double-blind, placebo-controlled, phase 3 study of fulvestrant with or without abemaciclib, for women with hormone receptor positive, HER2 negative locally advanced or metastatic breast cancer.”

Xagrid - anagrelide - EMEA/H/C/000480/II/0086
Shire Pharmaceuticals Ireland Limited, Rapporteur: Alexandre Moreau, “Update of section 4.8 of the SmPC to include the adverse drug reaction Prinzmetal angina with a frequency not known. The PIL is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes throughout the product information.”

Zessly - infliximab - EMEA/H/C/004647/II/0011
Sandoz GmbH, Rapporteur: Bjorg Bolstad, “Submission of the final CSR for the efficacy and safety study GP11-301; the report includes results from treatment period 3, where all subjects continued to receive open-label Zessly treatment for an additional 24 weeks (Week 54 until Week 78).”

WS1689
Leganto-EMEA/H/C/002380/WS1689/0031
Neupro-EMEA/H/C/000626/WS1689/0085
UCB Pharma S.A., Lead Rapporteur: Bruno Sepodes, “Update of section 4.8 of the SmPC in order to include “Rhabdomyolysis” as undesirable effect with frequency “not known” and widen the scope of an existing undesirable effect “increased CPK” based on new pharmacovigilance data. The Package Leaflet is updated accordingly.

In addition, the Worksharing applicant took the opportunity to correct some minor editorial discrepancies found within the package leaflets of Germany, Italy, France and Sweden."	
WS1702 **Fertavid-EMEA/H/C/001042/WS1702/0046** **Puregon-EMEA/H/C/000086/WS1702/0104** Merck Sharp & Dohme B.V., Lead Rapporteur: Peter Kiely, "To update of section 4.4 of the SmPC in order to revise the safety information regarding Ovarian Hyperstimulation Syndrome (OHSS) to replace clinical advice describing specific interventions with the recommendation to follow current clinical practice for reducing the risk of OHSS during Assisted Reproductive Technology (ART), based on post-marketing data and literature review. The package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet and made some editorial changes in the Product Information."	
WS1714 **OPDIVO-EMEA/H/C/003985/WS1714/0077** **Yervoy-EMEA/H/C/002213/WS1714/0073** Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.2 and 4.4 of the SmPC in order to update the safety information on myocarditis management for nivolumab monotherapy or for nivolumab in combination with ipilimumab therapy."	
WS1722 **OFEV-EMEA/H/C/003821/WS1722/0029** **Vargatef-EMEA/H/C/002569/WS1722/0028** Boehringer Ingelheim International GmbH, Lead Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to add alopecia with a frequency uncommon for Ofev and very common for Vargatef; and headache with a frequency of common for both Ofev and Vargatef as new adverse drug reactions based on an overall assessment of the safety data for the nintedanib products. The Package Leaflet is updated	

accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to include the latest renewal date for Vargatef."

B.6.10. CHMP-PRAC assessed procedures

AJOVY - fremanezumab - EMEA/H/C/004833/II/0003

TEVA GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Kirsti Villikka, "Update of section 4.8 of the SmPC in order to update the safety information based on final results from study TV48125-CNS-30051 listed as a category 3 study in the RMP; A Multicenter, Randomized, Double-Blind, Parallel-Group Study Evaluating the Long-Term Safety, Tolerability, and Efficacy of Subcutaneous Administration of TEV-48125 for the Preventive Treatment of Migraine. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted."

Benlysta - belimumab - EMEA/H/C/002015/II/0073

GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from study BEL116027 listed as a category 3 study in the RMP. This is a multi-centre, open-label, non-randomized, efficacy and safety study to evaluate treatment holidays and rebound phenomenon after treatment with belimumab 10 mg/kg in subjects with low SLE disease activity. The RMP version 34 has also been submitted."

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

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

Gazyvaro - obinutuzumab -
EMEA/H/C/002799/II/0036, Orphan
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Annika Folin, "Update of sections 4.8 and 5.1 of the SmPC based on data from the final CSR of the pivotal study GA04753g/GO01297/GADOLIN to fulfill a Category 3 [MEA] PAM. The PL and RMP are updated accordingly."

Orencia - abatacept -
EMEA/H/C/000701/II/0134
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, "As a result of the outcome of the Article 46 P64, update of sections 4.8 and 5.1 of the SmPC for Orencia solution for injection in pre-filled syringe based on the final 24-month results from Study IM101301; this is an open-label study to assess pharmacokinetics (PK), safety, and efficacy of SC abatacept in pJIA with no formal hypothesis testing.
Update of section 4.8 of the SmPC for Orencia powder for concentrate for solution for infusion based on the final 24-month results from Study IM101301.
The package leaflet for Orencia solution for injection in pre-filled syringe has been updated to reflect the removal of the IFU booklet as requested by the CHMP as part of the procedure X/117G.
The RMP version 27.0 has also been submitted.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the Annex II and to update Section 4.4 of the SmPC in line with the latest QRD template version 10.1 for all registered presentations. In addition, the list of local representatives in the Package Leaflet has been updated."

Zoely - nomegestrol acetate / estradiol -
EMEA/H/C/001213/II/0051
Theramex Ireland Limited, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Adrien Inoubli, "To update the RMP to version 9.1, as a result of the outcome of PRAC assessment of the article 107o procedure. The updated RMP includes the reformatting to the new RMP version and several changes including the due date for the PASS study (changed from 30 June 2020 to 30 April 2021). Annex II of the Product Information was updated as a consequence.

The MAH also took the opportunity to update the Annex IIIB (Package Leaflet) of the Product Information containing the list of local representatives in The Netherlands and Portugal."	
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."	

B.6.11. PRAC assessed procedures

PRAC Led **BLINCYTO - blinatumomab -** **EMEA/H/C/003731/II/0033, Orphan** Amgen Europe B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Eva Jirsová, PRAC-CHMP liaison: Ondřej Slanař, "Submission of an updated RMP version 11 in line with the guideline on Good Pharmacovigilance Practices (GVP) Module V on RMP. In accordance with the RMP update, the protocol for Category 1 PASS 20150136 has been updated and the enrolment period for the study has been extended by 1 year. The milestones in the RMP were updated accordingly. In addition, the RMP includes a proposed update to the milestone of the Category	

3 PASS 20180138."

PRAC Led

Constella - linaclotide -

EMEA/H/C/002490/II/0043

Allergan Pharmaceuticals International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the final report from study "Linaclotide Utilization Study in Selected European Populations" listed as a category 3 study in the RMP. This is a rug Utilisation Study (DUS) address following safety concerns
- The potential for off-label use and abuse/excessive use
- Extent of use in pregnancy and lactation, and male patients
- Assess the extent of off-label use and the extent of use in males and in pregnant females"

PRAC Led

Darzalex - daratumumab -

EMEA/H/C/004077/II/0033, Orphan

Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, PRAC-CHMP liaison: Bruno Sepodes, "Submission of final study results of a non-interventional PASS to investigate the effectiveness of Darzalex' educational materials concerning the potential risk of daratumumab to interfere with blood typing analysis. This commitment was requested as PAM-001. An updated RMP (v.5.4) to reflect the completion of the study is included in the submission."

PRAC Led

Daxas - roflumilast -

EMEA/H/C/001179/II/0038

AstraZeneca AB, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Amendment of safety concerns and removal of additional risk minimisation measures. Minor changes are implemented in section 4.4 of SmPC and PL according to QRD template."

PRAC Led

Iclusig - ponatinib -

EMEA/H/C/002695/II/0053, Orphan

Incyte Biosciences Distribution B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin,

PRAC-CHMP liaison: Filip Josephson, “Submission of an updated RMP version 20 in order to remove the study AP24534-14-401, a Postmarketing Observational Registry to Evaluate the Incidence of and Risk Factors for Vascular Occlusive Events Associated With Iclusig (ponatinib) in Routine Clinical Practice in the US (OMNI) from the Pharmacovigilance plan. In addition, in the framework of variation type II/51, it was considered that the distribution of the educational material was not needed anymore. The MAH is therefore also taking the opportunity to amend the RMP to remove reference to these measures.”

PRAC Led

Inflectra - infliximab - EMEA/H/C/002778/II/0079

Pfizer Europe MA EEIG, Duplicate, Duplicate of Remsima, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, “Submission of the final clinical study report for C1231002 (PERSIST) study, an observational cohort study designed to evaluate real life drug persistence in biologic naive rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis patients receiving CT-P13 or those switched to CT-P13 from stable treatment with Remicade (reference medicinal product).”

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.”

PRAC Led

Instanyl - fentanyl -
EMEA/H/C/000959/II/0052
Takeda Pharma A/S, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 19.2 in order to update information relating to educational material."

PRAC Led
Kisplyx - lenvatinib -
EMEA/H/C/004224/II/0030
Eisai GmbH, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Bjorg Bolstad, "Submission of an updated RMP version 11.3 as a result of interim analysis and updated final report submission dates added for study E7080-G000-307. The protocol for study E7080-G000-307 has been updated to version 06, dated 10 September 2019, to include an interim analysis for progression-free survival and overall survival."

PRAC Led
M-M-RVAXPRO - measles, mumps and rubella vaccine (live) -
EMEA/H/C/000604/II/0096
MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP (version 4.1) in order to
- Align to the new EU RMP template and EMA guideline on good pharmacovigilance practices (GVP) Module V (Rev. 2);
- Remove the important potential risk "a potential change in the safety profile related to the replacement of human serum albumin (HAS) with recombinant human albumin (rHA)";
- Remove the missing information related to "exposure during pregnancy"."

PRAC Led
Mavenclad - cladribine -
EMEA/H/C/004230/II/0009
Merck Europe B.V., Rapporteur: Mark Ainsworth, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, PRAC-CHMP liaison: Bruno Sepodes, "Submission of the final CSR for the PREMIERE registry (EMR700568-012) which is a category 3 study in the RMP. The PREMIERE study is a prospective, observational, long-term

safety registry of Multiple Sclerosis patients who have participated in cladribine clinical studies. It collected long-term safety data from patients previously participating in 1 out of 5 clinical trials (protocol numbers: 25643, 26593, 27820, 27967 and 28821)."

PRAC Led

Qarziba - dinutuximab beta - EMEA/H/C/003918/II/0015, Orphan

EUSA Pharma (Netherlands) B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "To update the RMP for Qarziba to version 9.0 to remove from the RMP as missing information Drug-drug interaction, Use in adolescents, adults and elderly, Use in patients with an ethnic origin other than Caucasian, Use in patients with hepatic and renal impairment and Potential harm from overdose."

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."

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 naive rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis patients receiving CT-P13 or those switched to

CT-P13 from stable treatment with Remicade (reference medicinal product)."

PRAC Led

WS1711

Aluvia-EMEA/H/W/000764/WS1711/0112

Kaletra-EMEA/H/C/000368/WS1711/0181

AbbVie Deutschland GmbH & Co. KG, Lead PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Jean-Michel Race, "To update the RMP for Kaletra and Aluvia (LPV/r) to version 9.0 in order to comply with the current revision 2 of the template. At the same time, the MAH took the opportunity to review the safety information contained in the RMP, removed an important potential risk of drug interaction with telaprevir and boceprevir (HCV protease inhibitors) and missing information regarding use of LPV/r in elderly patients.
In addition, the MAH has added information regarding the requirement for a pharmacovigilance (PV) cohort as part of LEG 121 to the RMP."

B.6.12. CHMP-CAT assessed procedures

Alofisel - darvadstrocel - EMEA/H/C/004258/II/0010/G, Orphan, ATMP

Takeda Pharma A/S, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

WS1667/G

Corbilta-EMEA/H/C/002785/WS1667/0019/G

Levodopa/Carbidopa/Entacapone Orion-EMEA/H/C/002441/WS1667/0028/G

Stalevo-EMEA/H/C/000511/WS1667/0089/G

Orion Corporation, Lead Rapporteur: Outi Mäki-Ikola

WS1684/G

Infanrix hexa-EMEA/H/C/000296/

WS1684/0264/G
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1692/G
Edistride-EMEA/H/C/004161/WS1692/0033/G
Forxiga-EMEA/H/C/002322/WS1692/0052/G
AstraZeneca AB, Lead Rapporteur: Kristina Dunder

WS1712
Blitzima-EMEA/H/C/004723/WS1712/0028
Ritemvia-EMEA/H/C/004725/WS1712/0028
Truxima-EMEA/H/C/004112/WS1712/0031
Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz

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.

Qualification of Biomarkers:

HTA:

G.2. Ongoing procedures

G.3. PRIME

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

G.3.1. List of procedures concluding at 14-17 October 2019 CHMP plenary

G.3.2. List of procedures starting in October 2019 for November 2019 CHMP adoption of outcomes

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