13 September 2019
EMA/CHMP/502557/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Agenda for the meeting on 16-19 September 2019

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

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

17 September 2019, 08:30 – 19:30, room 1C

18 September 2019, 08:30 – 19:30, room 1C

19 September 2019, 08:30 – 19:30, room 1C

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 16-19 September 2019. See September 2019 CHMP minutes (to be published post October 2019 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 16-19 September 2019

1.3. Adoption of the minutes

CHMP minutes for 22-25 July 2019

CHMP minutes for August written procedure

CHMP ORGAM minutes for 09 September 2019

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

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

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

Scope: Oral explanation

Action: Oral explanation to be held on Monday, 16 September 2019 at time 11:00

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

2.1.2. fostamatinib - EMEA/H/C/005012

indicated for the treatment of thrombocytopenia

Scope: Possible oral explanation

Action: Possible oral explanation to be held on Thursday, 19 September 2019 at time 16:00

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

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

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

Scope: Possible oral explanation, SAG report from meeting held on 18 June 2019

Action: Possible oral explanation to be held on Tuesday, 17 September 2019 at time 14:00

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

2.1.4. siponimod - EMEA/H/C/004712

treatment of secondary progressive multiple sclerosis (SPMS)

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday, 18 September 2019 at time 16:00

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

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

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

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday, 18 September 2019 at time 14:00

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

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

Roche Registration GmbH; Treatment of mature B cell lymphomas

Scope: Oral explanation/opinion, SAG Report

List of experts to the SAG meeting was adopted via written procedure on 12 September 2019, Report from SAG held on 13 September 2019

Action: Oral explanation to be held on Monday, 16 September 2019 at time 14:00

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

See 3.1

2.1.7. netarsudil - EMEA/H/C/004583

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

Scope: Possible oral explanation

Action: Possible oral explanation to be held on Tuesday, 17 September 2019 at time 16:00

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

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

Daiichi Sankyo Europe GmbH; treatment of acute myeloid leukaemia

Scope: Oral explanation

Action: Oral explanation to be held on Tuesday 17 September 2019 at time 11:00

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

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

Accelerated assessment

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

Scope: Oral explanation

Action: Oral explanation to be held on Thursday 19 September 2019 at time 09:00

List of Questions adopted on 27.05.2019.

2.2. Re-examination procedure oral explanations

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

Emmaus Medical Europe Ltd; treatment of sickle cell disease

Scope: Oral Explanation

List of experts for the ad hoc expert group meeting was adopted via written procedure on 09 September 2019

Report from ad hoc expert group meeting held on 11 September 2019

Action: Oral explanation to be held on Wednesday, 18 September 2019 at time 11:00

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

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

2.3. Post-authorisation procedure oral explanations

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

GlaxoSmithKline (Ireland) Limited

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

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

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday, 18 September 2019 at time 9:00 (joint OE for WS1501 and WS1505)

Request for Supplementary Information adopted on 29.05.2019, 31.01.2019.

See 5.1

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

GlaxoSmithKline (Ireland) Limited

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

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

Scope: Oral explanation

Action: Oral explanation to be held on Wednesday, 18 September 2019 at time 9:00 (joint OE for WS1501 and WS1505)

Request for Supplementary Information adopted on 29.05.2019, 31.01.2019.

See 5.1

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

Pfizer Europe MA EEIG

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

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

Possible oral explanation

Action: Possible oral explanation to be held on Thursday, 19 September 2019 at time 11:00

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

See 4.2

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. arsenic trioxide - EMEA/H/C/005175

treatment of relapsed acute promyelocytic leukaemia (APL)

Scope: Opinion

Action: For adoption

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

3.1.2. bortezomib - EMEA/H/C/005074

treatment of multiple myeloma

Scope: Opinion

Action: For adoption

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

3.1.3. clofarabine - EMEA/H/C/005039

treatment of acute lymphoblastic leukaemia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 25.07.2019. List of Questions adopted on 31.01.2019.

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

Roche Registration GmbH; Treatment of mature B cell lymphomas

Scope: Possible oral explanation/opinion, SAG Report

Action: Possible oral explanation to be held on Monday, 16 September 2019 at time 14:00

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

See 2.1

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

- to improve glycaemic control when metformin with or without sulphonylurea (SU) does not provide adequate glycaemic control and where simultaneous addition of dapagliflozin and saxagliptin is considered necessary - 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.

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 29.05.2019. List of Questions adopted on 15.11.2018.

3.1.6. lidocaine / prilocaine - EMEA/H/C/005298

treatment of primary premature ejaculation

Scope: Opinion

Action: For adoption

List of Questions adopted on 25.07.2019.

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

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

indicated for the secondary prevention of atherothrombotic events

Scope: List of outstanding issues

Action: For adoption

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

3.2.2. deferasirox - EMEA/H/C/005156

treatment of chronic iron overload

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.03.2019.

3.2.3. dexmedetomidine - EMEA/H/C/005152

light to moderate sedation

Scope: List of outstanding issues, letter from third party

Action: For adoption

List of Questions adopted on 26.04.2019.

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

Accelerated assessment

Ebola Vaccine

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 25.06.2019.

3.2.5. alpelisib - EMEA/H/C/004804

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 29.05.2019.

3.2.6. delafloxacin - EMEA/H/C/004860

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

Scope: List of outstanding issues

Action: For adoption

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

3.2.7. upadacitinib - EMEA/H/C/004760

treatment of moderate to severe active rheumatoid arthritis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 29.05.2019.

3.2.8. tigecycline - EMEA/H/C/005114

treatment of soft tissue and intra-abdominal infections, - complicated skin and soft tissue infections, excluding diabetic foot infections, - complicated intra-abdominal infections, should be used only in situations where it is known or suspected that other alternatives are not suitable

Scope: List of outstanding issues

Action: For adoption

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

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

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 24.04.2019.

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

3.3.1. indacaterol / mometasone furoate - EMEA/H/C/005067

treatment of asthma

Scope: List of questions

Action: For adoption

3.3.2. cabazitaxel - EMEA/H/C/005178

treatment of adult patients with metastatic castration resistant prostate cancer previously

treated with a docetaxel-containing regimen

Scope: List of questions

Action: For adoption

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

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

Scope: List of questions

Action: For adoption

3.3.4. doxorubicin - EMEA/H/C/005194

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

Scope: List of questions

Action: For adoption

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

treatment of asthma and to reduce asthma exacerbations

Scope: List of questions

Action: For adoption

3.3.6. fingolimod - EMEA/H/C/005191

treatment of multiple sclerosis

Scope: List of questions

Action: For adoption

3.3.7. fingolimod - EMEA/H/C/005282

treatment of multiple sclerosis

Scope: List of questions

Action: For adoption

3.3.8. teriparatide - EMEA/H/C/005087

treatment of osteoporosis

Scope: List of questions

Action: For adoption

3.3.9. teriparatide - EMEA/H/C/005388

treatment of osteoporosis

Scope: List of questions

Action: For adoption

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

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

Scope: List of questions

Action: For adoption

3.3.11. semaglutide - EMEA/H/C/004953

treatment of type 2 diabetes mellitus

Scope: List of questions

Action: For adoption

3.3.12. isatuximab - Orphan - EMEA/H/C/004977

sanofi-aventis groupe; For the treatment of patients with multiple myeloma (MM)

Scope: List of questions

Action: For adoption

3.3.13. trastuzumab - EMEA/H/C/005066

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

Scope: List of questions

Action: For adoption

3.3.14. deferiprone - Orphan - EMEA/H/C/005004

Apotex B.V.; treatment of neurodegeneration with brain iron accumulation

Scope: List of questions

Action: For adoption

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

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

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

Scope: Letter from the applicant dated 20 August 2019 requesting an extension of clock stop to respond to the list of questions adopted in May 2019

Action: For adoption

List of Questions adopted on 29.05.2019.

3.4.2. rituximab - EMEA/H/C/005387

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

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

Action: For adoption

List of Outstanding Questions adopted on 27.06.2019.

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: Report from ad-hoc expert group meeting held on 3 September 2019

Action: For information

List of Outstanding Issues adopted on 27.06.2019, 14.09.2018, 25.05.2018. List of Questions adopted on 08.09.2017.

3.4.4. rituximab - EMEA/H/C/004807

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

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

Action: For adoption

List of Outstanding Questions adopted on 27.06.2019. List of Questions adopted on 18.10.2018.

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

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

Scope: Request by the applicant dated 25 August 2019 for an extension of clock stop to respond to the list of questions (adopted in May 2019) was adopted by written procedure

Action: For information

List of Questions adopted on 29.05.2019

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

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

Scope: Letter from the applicant dated 23 August 2019 requesting an extension of clock stop

to respond to the list of outstanding issues adopted in June 2019, SAG Report from the meeting held on 6 September 2019

Action: For adoption

List of outstanding issues adopted on 21.06.2019. List of Questions adopted on 22.02.2019.

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: Draft list of questions and draft list of experts to the ad-hoc expert group meeting, Letter from third party

Re-examination timetable

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.

3.6. Initial applications in the decision-making phase

3.6.1. Nuceiva - botulinum toxin type a - EMEA/H/C/004587

Evolus Pharma Limited; temporary improvement in the appearance of moderate to severe vertical lines between the eyebrows

Scope: Response from the European Commission to CHMP

Action: For information

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

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

4.1.1. Humalog - insulin lispro - EMEA/H/C/000088/X/0169

Eli Lilly Nederland B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: “Extension application to change process steps. The RMP is updated (version 9.3)

accordingly and in line with revision 2 of GVP module V on 'Risk management systems."

Action: For adoption

List of Questions adopted on 26.04.2019.

4.1.2. Liprolog - insulin lispro - EMEA/H/C/000393/X/0130

Eli Lilly Nederland B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: "Extension application to change process steps. The RMP is updated (version 9.3) accordingly and in line with revision 2 of GVP module V on 'Risk management systems."

Action: For adoption

List of Questions adopted on 26.04.2019.

4.1.3. Remsima - infliximab - EMEA/H/C/002576/X/0062

Celltrion Healthcare Hungary Kft.

Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension application to introduce a new pharmaceutical form (solution for injection), a new strength (120 mg) and a new route of administration (subcutaneous use).
The RMP (version 9.1) is updated in accordance."

Action: For adoption

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

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. Akynzeo - fosnetupitant / netupitant / palonosetron - EMEA/H/C/003728/X/0018

Helsinn Birex Pharmaceuticals Limited

Rapporteur: Peter Kiely, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: PRAC Rapporteur: Ilaria Baldelli

Scope: "Extension application to introduce the new pharmaceutical form 'powder for concentrate for solution for infusion' and a new strength for the fixed combination of fosnetupitant (pro-drug of netupitant) and palonosetron of 235 mg/0.25 mg, to be administered intravenously (new route of administration)."

Action: For adoption

List of Questions adopted on 28.03.2019.

4.2.2. Carbaglu - carglumic acid - Orphan - EMEA/H/C/000461/X/0038

Recordati Rare Diseases

Rapporteur: Fátima Ventura

Scope: “Extension application to introduce a new pharmaceutical form associated with 2 new strengths (200 mg and 800 mg soluble tablets).”

Action: For adoption

List of Questions adopted on 28.03.2019.

4.2.3. Pemetrexed Fresenius Kabi - pemetrexed - EMEA/H/C/003895/X/0009

Fresenius Kabi Deutschland GmbH

Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ghania Chamouni

Scope: “Extension application to introduce a new pharmaceutical form (concentrate for solution for infusion) associated with new strength 25 mg/ml.”

Action: For adoption

List of Questions adopted on 31.01.2019.

4.2.4. 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

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

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

4.3.1. Kymriah - tisagenlecleucel - Orphan - ATMP - EMEA/H/C/004090/X/0010

Novartis Europharm Limited

Rapporteur: Rune Kjeken, Co-Rapporteur: Dariusz Sladowski, CHMP Coordinators: Ingrid Wang and Ewa Balkowiec Iskra

Scope: “Extension application to introduce a new manufacturing process.”

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. Alunbrig - brigatinib / brigatinib - EMEA/H/C/004248/II/0003

Takeda Pharma A/S

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

Scope: “Extension of indication to include first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously untreated with an ALK inhibitor for Alunbrig.
The addition of a new indication is supported by data from study 301 (AP26113-13-301; ALTA 1L), a phase 3, randomized, open label, comparative, multicenter, international phase 3 study. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package leaflet and labelling are updated in accordance. The RMP version 5.1 has also been submitted. Minor editorial corrections are also proposed.”, Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

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

Merck Europe B.V.

Rapporteur: Filip Josephson, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Hans Christian Siersted

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

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019.

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

GlaxoSmithKline (Ireland) Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include patients aged 5 years and older in the current approved indication for Benlysta (belimumab powder for solution for infusion 120 mg/ml and 400 mg/ml) based on the results of the safety, efficacy and pharmacokinetics study in patients aged 5 years to 17 years (BEL114055). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated with safety and efficacy information.
Update of sections 4.2, 5.1 and 5.2 of the SmPC for Benlysta (belimumab, solution for injection in pre-filled pen and pre-filled syringe, 200 mg) to reflect the paediatric data available for the intravenous formulation. The Package Leaflet is updated accordingly.
The RMP version 28.0 is submitted to reflect the results of the study and to bring it in line with the GVP Module V RMP template version 2.0. In addition, the MAH took the opportunity to make some editorial changes in the product information and bring it in line with the latest QRD template version 10.0."

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019, 28.02.2019.

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

sanofi-aventis groupe

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

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

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019.

5.1.5. ECALTA - anidulafungin - EMEA/H/C/000788/II/0040

Pfizer Europe MA EEIG

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

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

Action: For adoption

5.1.6. Erleada - apalutamide - EMEA/H/C/004452/II/0001

Janssen-Cilag International N.V.

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Natalja Karpova, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension of indication to include the treatment of metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT) for Erleada based on the results of study 56021927PCR3002 (TITAN study), a randomised, double-blind, placebo-controlled phase 3 study comparing apalutamide plus ADT versus ADT in patients with mHSPC. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add a warning on ischaemic cardiovascular events and to reflect new safety and efficacy information. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to make editorial update to the SmPC and Labelling. The RMP version 2.0 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

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

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted

Scope: "Extension of indication to include the adjuvant treatment of adult patients with HER2-positive early breast cancer, as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Applicant took the opportunity to introduce editorial changes.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019.

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

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication to include 1st line treatment of locally advanced or metastatic non-small cell lung cancer tumours expressing PD-L1 with a ≥ 1% tumour proportion score (TPS), based on data from study KEYNOTE-042; an international, randomized, open-label Phase 3 study investigating Keytruda monotherapy compared to standard of care platinum-based chemotherapy in patients with locally advanced or metastatic PD-L1 positive (TPS ≥ 1%) NSCLC, and on supportive data from the final planned analysis of KEYNOTE-024; a Phase 3 randomized open-label study of Keytruda monotherapy compared to platinum-based chemotherapy in metastatic NSCLC with PD-L1 TPS ≥50%. As a result, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC have been updated. An updated RMP version 18.1 was provided as part of the application."

Action: For adoption

Request for Supplementary Information adopted on 28.03.2019, 18.10.2018.

5.1.9. 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 27.06.2019, 28.03.2019.

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

Merck Sharp & Dohme B.V.

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

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

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019.

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

Novartis Europharm Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

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

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019, 28.02.2019.

5.1.12. MabThera - rituximab - EMEA/H/C/000165/II/0168

Roche Registration GmbH

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

Scope: "Extension of indication in previously untreated, advanced stage paediatric B-cell Non-Hodgkin's Lymphoma (B-NHL)"

Action: For adoption

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

Celgene Europe BV

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

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

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019.

5.1.14. 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 29.05.2019, 31.01.2019.

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

Eli Lilly Nederland B.V.

Rapporteur: Martina Weise, PRAC Rapporteur: Ilaria Baldelli

Scope: "Extension of indication to include a new indication for Trulicity; "to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke), in adults with type 2 diabetes mellitus who have multiple cardiovascular

risk factors without established cardiovascular disease, and in adults with type 2 diabetes mellitus with established cardiovascular disease."
The data supporting this new indication is derived from study GBDJ (Researching Cardiovascular Events with a Weekly INcretin in Diabetes (REWIND)); a single pivotal Phase 3 long-term cardiovascular outcomes study, which assessed the efficacy and safety of treatment with once-weekly injection of dulaglutide 1.5 mg when added to glucose-lowering regimen of patients with type 2 diabetes (T2D), compared to the addition of a once weekly placebo injection. This study is a post-authorisation measure (PAM) (MEA 004) included in the dulaglutide RMP.
As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are being updated and the Package Leaflet is updated accordingly.
In addition, the MAH is taking the opportunity to update the wording of the existing indication in section 4.1 of the SmPC and to implement a minor change in section 5.1 of the SmPC, in the glycaemic control summary subsection, based on the results from the dulaglutide study as add-on to sodium-glucose co-transporter 2 inhibitor therapy which was assessed as part of II/25.
An updated RMP version 3.1 was provided as part of the application."

Action: For adoption

Request for Supplementary Information adopted on 25.07.2019.

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

GlaxoSmithKline (Ireland) Limited

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

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

Oral explanation

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019, 31.01.2019.

See 2.3

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

GlaxoSmithKline (Ireland) Limited

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

Scope: "Update of sections 4.1. and 5.1 of the SmPC in order to update the efficacy information regarding the benefit of umeclidinium and umeclidinium/vilanterol from the CTT116855 study (InforMing the PAthway of COPD Treatment [IMPACT]).

The Package Leaflet is updated in accordance."

Oral explanation

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019, 31.01.2019.

See 2.3

5.1.18. WS1542
Bretaris Genuair - aclidinium - EMEA/H/C/002706/WS1542/0040
Eklira Genuair - aclidinium - EMEA/H/C/002211/WS1542/0040

AstraZeneca AB

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

Scope: "Extension of indication to include reduction of COPD exarcerbations for Eklira Genuair and Bretaris Genuair; as a consequence, sections 4.1, 4.4, 4.8 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet for Bretaris Genuair and to implement minor editorial changes in sections 4.4, 4.6, 5.3 of the SmPC and section 2 of the PL for both Eklira Genuair and Bretaris Genuair."

Action: For adoption

Request for Supplementary Information adopted on 26.04.2019.

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

Aventis Pharma S.A.

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

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

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019.

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

Eli Lilly Nederland B.V.

Lead Rapporteur: Kristina Dunder

Scope: “Type II variation. B.IV.z. to introduce an additional prefilled pen presentation for Abasaglar, solution for injection (EU/1/14/944/007, EU/1/14/944/008, EU/1/14/944/012, EU/1/14/944/013), Humalog, solution for injection (EU/1/96/007/002, EU/1/96/007/004, EU/1/96/007/020, EU/1/96/007/021 EU/1/96/007/023), Humalog Kwikpen solution for injection (EU/1/96/007/031, EU/1/96/007/032, EU/1/96/007/039, EU/1/96/007/040, EU/1/96/007/041, EU/1/96/007/042) and Humalog Junior Kwikpen, solution for injection (EU/1/96/007/043, EU/1/96/007/044, EU/1/96/007/045). The pack contains 5 pre-filled pens. Type IAIN B. II.e.5.a.1 to request the 2x5 multipack.
As a consequence, the following sections were updated 1, 4.2, 4.4, 6.2, 6.4, 6.5, 6.6, 8 of the SmPC in order to add new pre-filled pen presentation; the Package Leaflet and Labelling are updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to make an editorial change (removing comma in SK address in the PL)

Action: For discussion

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

5.2.1. Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/II/0015

Pfizer Ireland Pharmaceuticals

Rapporteur: Bjorg Bolstad, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Rugile Pilviniene

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

Letter from the applicant dated 20 August 2019 requesting an extension of clock stop to respond to the request for supplementary information adopted in July 2019.

Action: For adoption

Request for Supplementary Information adopted on 25.07.2019

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

5.3.1. 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."

List of question to the SAG, list of experts for the SAG meeting

The Re-examination timetable was adopted via written procedure on 30 August 2019

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.

5.3.2. 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."

List of experts for the ad hoc expert group meeting

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.

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. monovalent, live, recombinant, replication-incompetent adenoviral serotype 26 (ad26)-vectored vaccine expressing the full length glycoprotein (gp) of the ebola virus (ebov) mayinga variant - H0005337

active immunisation for prevention of Ebola Viruses Disease caused by Zaire ebolavirus in adults => 18 years old

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

Action: For adoption

8.1.2. bulevirtide - Orphan - H0004854

MYR GmbH; treatment of hepatitis delta in patients with compensated liver disease

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

Action: For adoption

8.1.3. multivalent, live, recombinant, non-replicating in human cells, modified vaccinia ankara (mva)-vectored vaccine, expressing the ebov mayinga glycoprotein (gp), the sudan virus (sudv) gulu gp, the marburg virus (marv) musoke gp, and the taï forest vir - H0005343

active immunisation for prevention of Ebola Viruses Disease caused by Zaire ebolavirus in adults => 18 years old

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

Action: For adoption

8.1.4. pemigatinib - H0005266

Treatment of adult patients with previously treated, advanced/metastatic or surgically unresectable cholangiocarcinoma with FGFR2 fusions.

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

Action: For adoption

8.1.5. ivacaftor, tezacaftor, vx-445 - Orphan - H0005269

Vertex Pharmaceuticals (Ireland) Limited, indicated in a combination regimen with ivacaftor 150 mg tablet for the treatment of cystic fibrosis (CF) in patients aged 12 years and older who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

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. Aerivio Spiromax - fluticasone propionate / salmeterol - EMEA/H/C/002752

Teva B.V.

Rapporteur: John Joseph Borg, Co-Rapporteur: Ewa Balkowiec Iskra

Scope: Withdrawal of marketing authorisation

Action: For information

9.1.2. Blincyto - blinatumomab - Orphan - EMEA/H/C/003731

Amgen Europe B.V.

Rapporteur: Alexandre Moreau, Co-Rapporteur: Daniela Melchiorri

Scope: DHPC and communication plan in order to prevent a risk of premedication errors with dexamethasone in paediatric patients treated with Blincyto adopted on 23 August 2019 by written procedure

Action: For information

9.1.3. Increlex - mecasermin - EMEA/H/C/000704/II/0060

Applicant: Ipsen Pharma

Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.1, 4.2, 4.3, 4.4, 4.8 and 4.9 of the SmPC in order to update the safety information on benign or malignant neoplasia based on the EU registry study: the Ipsen global safety database and based on a literature review. The package leaflet and the RMP (version 11) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

DHPC and communication plan

Action: For adoption

9.1.4. 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 of conditional marketing authorisation

Action: For discussion

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

Biogen Netherlands B.V.

Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber

Scope: CHMP request for PRAC advice adopted via written procedure on 27 August 2019

Action: For information

9.1.6. Tresiba – insulin degludec – EMEA/H/C/002498

Novo Nordisk A/S

Rapporteur: Kristina Dunder, Co-Rapporteur: Sinan B. Sarac

Scope: Request for a LEG

Action: For adoption

10. Referral procedures

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

No items

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

10.2.1. Direct oral anticoagulants (DOAC) - EMEA/H/A-5(3)/1478

MAHs: various

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

Rapporteurs for involved CAPs:

Eliquis (APIXABAN):
Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bart van der Schueren;

Pradaxa (DABIGATRAN ETEXILATE):
Rapporteur: Mark Ainsworth, Co-Rapporteur: Jean-Michel Race;

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

Scope: List of outstanding issues

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

Action: For adoption

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

MAHs: various

Referral Rapporteur: TBC, Referral Co-Rapporteurs: TBC

Scope: As a consequence of lessons learnt from the Article 31 referral on sartans with a tetrazole ring, EMA together with the EU Network has continued the review to identify if there are any consequences for medicinal products outside the class of sartans. In addition EMA has been liaising with international partners.

The work that has been conducted so far has resulted in a common understanding that it would be appropriate as a means of precaution to ask all MAHs and manufacturers to review the potential risk for N-nitrosamines as part of the drug substance of all medicinal products containing chemically synthesised active pharmaceutical ingredients authorised in the EU and to ensure that their medicinal products are in line with the latest knowledge on the risk of formation of or contamination with nitrosamines.

Taking into account that nitrosamines have been found in sartans with a tetrazole ring and also in some batches of pioglitazone, it is foreseen that the CHMP's opinion is sought in accordance with Article 5(3) of Regulation (EC) No 726/2004 on the following to further investigate the issues at stake.

Action: For information

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

No items

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

No items

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

No items

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

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

MAH various

Rapporteur: Ondrej Slanar, Co-rapporteur: Janet Koenig

Scope: List of outstanding issues

Letter from third party

Action: For discussion

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

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

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

MAH various

Rapporteur: TBC, Co-rapporteur: TBC

Scope: Tests performed in a random selection of ranitidine API batches and finished products available in the EU have shown levels of NDMA which raise concerns.

Action: For information

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

September 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

No items

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on 02-05 September 2019

Action: For information

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

Action: For adoption

CHMP-PRAC Strategic Review and Learning Meeting (SRLM) under the Finnish presidency of the European Union (EU) Council – Helsinki, Finland, 21-23 October 2019

Action: For information

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 11-13 September 2019
Action: For information

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 23-25 September 2019

Action: For information

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at September 2019 PDCO

Action: For information

Report from the PDCO meeting held on 17-20 September 2019

Action: For information

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 10-12 September 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 September 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 02-05 September 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 22-25 July 2019.

Action: For adoption

Liposomal formulations - safety concerns linked to generic naming and applicability of recommendation issued in July to topical formulations

Questions from MAH

Action: For discussion

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP September 2019 meeting to CHMP for adoption:

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

Action: For adoption

14.3.4. Oncology Working Party (ONCWP)

Election of ONCWP Chair

Action: For election

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

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

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

Action: For information

14.9. Others

No items

15. Any other business

15.1. AOB topic

16. Explanatory notes

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

Oral explanations *(section 2)*

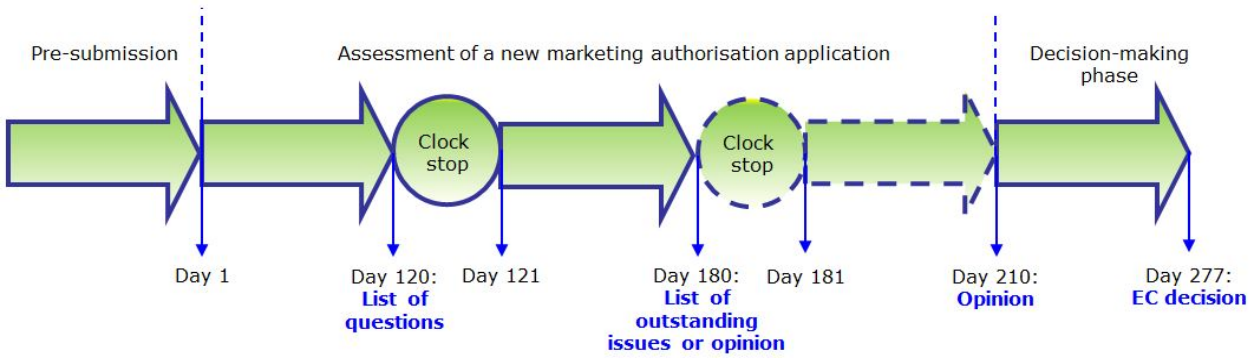
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

Initial applications *(section 3)*

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

Re-examination procedures *(section5.3)*

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

Withdrawal of application *(section 3.7)*

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

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

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

Pre-submission issues *(section 8)*

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

Post-authorisation issues *(section 9)*

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

Referral procedures *(section 10)*

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

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

Pharmacovigilance issues *(section 11)*

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

Inspections Issues *(section 12)*

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

Innovation task force *(section 13)*

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

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

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

Satellite groups / other committees *(section 14.2)*

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

Invented name issues *(section 14.3)*

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

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

13 September 2019
EMA/CHMP/502554/2019

Annex to 16-19 September 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 September 2019: **For adoption**

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

Final Outcome of Rapporteurship allocation for September 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

Kolbam - cholic acid -
EMEA/H/C/002081/S/0029, Orphan
Retrophin Europe Ltd, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Agni Kapou
Request for Supplementary Information adopted on 27.06.2019, 26.04.2019.

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Rixubis - nonacog gamma -
EMEA/H/C/003771/R/0029
Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski
Request for Supplementary Information adopted on 27.06.2019.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

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

Duavive - estrogens conjugated / bazedoxifene - EMEA/H/C/002314/R/0021
Pfizer Europe MA EEIG, Rapporteur: Martina Weise, Co-Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber
Request for Supplementary Information adopted on 27.06.2019.

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

Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/R/0033
Orexigen Therapeutics Ireland Limited, Rapporteur: Mark Ainsworth, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Martin Huber

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

SCENESSE - afamelanotide - EMEA/H/C/002548/R/0026, Orphan
Clinuvel Europe Limited, Rapporteur: Janet Koenig, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Martin Huber
Request for Supplementary Information adopted on 25.07.2019.

Sevelamer carbonate Winthrop - sevelamer carbonate - EMEA/H/C/003971/R/0022
Genzyme Europe BV, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Laurence de Fays
Request for Supplementary Information adopted on 25.07.2019.

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

Trevicta - paliperidone - EMEA/H/C/004066/R/0022
Janssen-Cilag International NV, Informed Consent of Xeplion, Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga
Request for Supplementary Information adopted on 27.06.2019.

Xydalba - dalbavancin - EMEA/H/C/002840/R/0028
Allergan Pharmaceuticals International Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Rugile Pilviniene
Request for Supplementary Information adopted on 25.07.2019.

B.2.3. Renewals of Conditional Marketing Authorisations

OCALIVA - obeticholic acid - EMEA/H/C/004093/R/0018, Orphan Intercept Pharma International Limited, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst	See agenda item 9.1

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 02-05 September 2019
PRAC:

Signal of ischaemic stroke:

Ibrutinib – IMBRUVICA

Action: For adoption

New information on the known association between SGLT2 inhibitors and diabetic ketoacidosis (DKA) in surgical patients:

Sodium-glucose co-transporter 2 (SGLT2) inhibitors: canagliflozin – INVOKANA; canagliflozin, metformin – VOKANAMET; dapagliflozin – EDISTRIDE; dapagliflozin – FORXIGA; dapagliflozin, metformin – EBYMECT; dapagliflozin, metformin – XIGDUO; empagliflozin – JARDIANCE; empagliflozin, metformin – SYNJARDY; empagliflozin, linagliptin – GLYXAMBI; ertugliflozin – STEGLATRO; ertugliflozin, metformin – SEGLUROMET; ertugliflozin, sitagliptin - STEGLUJAN; saxagliptin, dapagliflozin – QTERN

Action: For adoption

Signal of psoriasis:

Teriflunomide – AUBAGIO –

Action: For adoption

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

EMEA/H/C/PSUSA/00000871/201902
(collagenase clostridium histolyticum (treatment of Dupuytren's contracture and treatment of Peyronie's disease))
CAP:
Xiapex (EMEA/H/C/002048) (collagenase

clostridium histolyticum), Swedish Orphan Biovitrum AB (publ), Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, “From: 27/02/2018 To: 27/02/2019”

EMEA/H/C/PSUSA/00001295/201902
(etanercept (except for biosimilars))
CAP:
Enbrel (EMEA/H/C/000262) (etanercept), Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva Segovia, “From: 03/02/2018 To: 02/02/2019”

EMEA/H/C/PSUSA/00002162/201901
(nilotinib)
CAP:
Tasigna (EMEA/H/C/000798) (nilotinib), Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, “From: 01/02/2018 To: 31/01/2019”

EMEA/H/C/PSUSA/00002326/201901
(pegfilgrastim)
CAPs:
Fulphila (EMEA/H/C/004915) (pegfilgrastim), Mylan S.A.S, Rapporteur: Martina Weise
Neulasta (EMEA/H/C/000420) (pegfilgrastim), Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege
Pelgraz (EMEA/H/C/003961) (pegfilgrastim), Accord Healthcare S.L.U., Rapporteur: Sol Ruiz
Pelmeg (EMEA/H/C/004700) (pegfilgrastim), Mundipharma Biologics S.L., Rapporteur: Koenraad Norga
UDENYCA (EMEA/H/C/004413) (pegfilgrastim), ERA Consulting GmbH, Rapporteur: Martina Weise
Ziextenzo (EMEA/H/C/004802) (pegfilgrastim), Sandoz GmbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Menno van der Elst, “From: 31/01/2016 To: 31/01/2019”

EMEA/H/C/PSUSA/00002435/201902
(pirfenidone)
CAP:
Esbriet (EMEA/H/C/002154) (pirfenidone), Roche Registration GmbH, Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald, “27/02/2018 To: 27/02/2019”

EMEA/H/C/PSUSA/00010022/201901
(axitinib)
CAP:

Inlyta (EMEA/H/C/002406) (axitinib), Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: David Olsen, “From: 27/01/2018 To: 26/01/2019”

EMEA/H/C/PSUSA/00010035/201901
(ingenol mebutate)
CAP:
Picato (EMEA/H/C/002275) (ingenol mebutate), LEO Laboratories Ltd, Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Adam Przybylkowski, “31/07/2018 To: 31/01/2019”

EMEA/H/C/PSUSA/00010123/201901
(paclitaxel albumin)
CAP:
Abraxane (EMEA/H/C/000778) (paclitaxel), Celgene Europe BV, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, “From: 05/01/2016 To: 05/01/2019”

EMEA/H/C/PSUSA/00010140/201901
(vismodegib)
CAP:
Erivedge (EMEA/H/C/002602) (vismodegib), Roche Registration GmbH, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, “From: 29/01/2018 To: 29/01/2019”

EMEA/H/C/PSUSA/00010340/201902
(ospemifene)
CAP:
Senshio (EMEA/H/C/002780) (ospemifene), Shionogi B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Kirsti Villikka, “25/02/2018 To: 25/02/2019”

EMEA/H/C/PSUSA/00010405/201901
(evolocumab)
CAP:
Repatha (EMEA/H/C/003766) (evolocumab), Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola, “From: 17/07/2018 To: 17/01/2019”

EMEA/H/C/PSUSA/00010448/201901
(carfilzomib)
CAP:
Kyprolis (EMEA/H/C/003790) (carfilzomib), Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Nikica Mirošević Skvrce, “19/01/2018 To: 19/01/2019”

EMEA/H/C/PSUSA/00010452/201901
(etanercept (biosimilars))
CAP:
Benepali (EMEA/H/C/004007) (etanercept), Samsung Bioepis NL B.V., Rapporteur: Andrea Laslop
Erelzi (EMEA/H/C/004192) (etanercept), Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva Segovia, “From: 14/01/2018 To: 14/01/2019”

EMEA/H/C/PSUSA/00010476/201902
(ferric maltol)
CAP:
Feraccru (EMEA/H/C/002733) (ferric maltol), Norgine B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Adam Przybylkowski, “17/08/2018 To: 17/02/2019”

EMEA/H/C/PSUSA/00010578/201902
(baricitinib)
CAPS:
Olumiant (EMEA/H/C/004085) (baricitinib), Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski, “From: 12/08/2018 To: 12/02/2019”

EMEA/H/C/PSUSA/00010639/201902
(telotristat)
CAP:
Xermelo (EMEA/H/C/003937) (telotristat ethyl), Ipsen Pharma, Rapporteur: Martina Weise, PRAC Rapporteur: Adam Przybylkowski, “From: 28/08/2018 To: 27/02/2019”

B.4. EPARs / WPARs

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

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

Request for Supplementary Information adopted on 18.07.2019.

Afstyla - lonoctocog alfa - EMEA/H/C/004075/II/0023/G
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Alprolix - eftrenonacog alfa - EMEA/H/C/004142/II/0026, Orphan
Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop

Apealea - paclitaxel - EMEA/H/C/004154/II/0003/G
Oasmia Pharmaceutical AB, Rapporteur: Bart Van der Schueren
Request for Supplementary Information adopted on 25.07.2019, 26.04.2019.

Aripiprazole Mylan Pharma - aripiprazole - EMEA/H/C/003803/II/0012
Mylan S.A.S, Generic, Generic of Abilify, Rapporteur: Bjorg Bolstad

Atazanavir Mylan - atazanavir - EMEA/H/C/004048/II/0012
Mylan S.A.S, Generic, Generic of Reyataz, Rapporteur: Bjorg Bolstad
Request for Supplementary Information adopted on 11.07.2019.

Atriance - nelarabine - EMEA/H/C/000752/II/0047/G
Novartis Europharm Limited, Rapporteur: Sinan B. Sarac
Request for Supplementary Information adopted on 25.07.2019.

BeneFIX - nonacog alfa - EMEA/H/C/000139/II/0160
Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus
Request for Supplementary Information adopted on 06.06.2019.

Benlysta - belimumab - EMEA/H/C/002015/II/0068
GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder
Request for Supplementary Information adopted on 27.06.2019, 26.04.2019.

Betaferon - interferon beta-1b - EMEA/H/C/000081/II/0126/G

Bayer AG, Rapporteur: Martina Weise

Busulfan Fresenius Kabi - busulfan -
EMEA/H/C/002806/II/0014
Fresenius Kabi Deutschland GmbH, Generic, Generic of Busilvex, Rapporteur: John Joseph Borg

Buvidal - buprenorphine -
EMEA/H/C/004651/II/0002
Camurus AB, Rapporteur: Peter Kiely

Cinryze - C1 esterase inhibitor (human) -
EMEA/H/C/001207/II/0071/G
Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus

CRYSVITA - burosumab -
EMEA/H/C/004275/II/0007/G, Orphan
Kyowa Kirin Holdings B.V., Rapporteur: Kristina Dunder

Dupixent - dupilumab -
EMEA/H/C/004390/II/0018/G
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus
Request for Supplementary Information adopted on 25.07.2019.

Elaprase - idursulfase -
EMEA/H/C/000700/II/0082
Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege

Extavia - interferon beta-1b -
EMEA/H/C/000933/II/0099/G
Novartis Europharm Limited, Informed Consent of Betaferon, Rapporteur: Martina Weise

Eylea - aflibercept -
EMEA/H/C/002392/II/0053
Bayer AG, Rapporteur: Alexandre Moreau
Request for Supplementary Information adopted on 04.07.2019.

Hulio - adalimumab -
EMEA/H/C/004429/II/0010/G
Mylan S.A.S, Rapporteur: Bart Van der Schueren
Request for Supplementary Information adopted on 06.06.2019.

HyQvia - human normal immunoglobulin -
EMEA/H/C/002491/II/0051
Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus

Imfinzi - durvalumab -
EMEA/H/C/004771/II/0009
AstraZeneca AB, Rapporteur: Sinan B. Sarac

Keppra - levetiracetam -
EMEA/H/C/000277/II/0178/G
UCB Pharma S.A., Rapporteur: Koenraad Norga
Request for Supplementary Information adopted on 14.06.2019.

Lamzede - velmanase alfa -
EMEA/H/C/003922/II/0007, Orphan
Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege

Lonquex - lipegfilgrastim -
EMEA/H/C/002556/II/0053/G
Teva B.V., Rapporteur: Outi Mäki-Ikola

MVASI - bevacizumab -
EMEA/H/C/004728/II/0008
Amgen Europe B.V., Duplicate, Duplicate of KYOMARC, Rapporteur: Bjorg Bolstad

Nimenrix - meningococcal group a, c, w135 and y conjugate vaccine -
EMEA/H/C/002226/II/0092/G
Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad

Noxafil - posaconazole -
EMEA/H/C/000610/II/0059
Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau

Nucala - mepolizumab -
EMEA/H/C/003860/II/0025
GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely

Nucala - mepolizumab -
EMEA/H/C/003860/II/0026/G
GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely

OCALIVA - obeticholic acid -
EMEA/H/C/004093/II/0016/G, Orphan
Intercept Pharma International Limited, Rapporteur: Jorge Camarero Jiménez

Ocrevus - ocrelizumab -
EMEA/H/C/004043/II/0014/G
Roche Registration GmbH, Rapporteur: Mark Ainsworth

OPDIVO - nivolumab -
EMEA/H/C/003985/II/0067/G
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez
Request for Supplementary Information adopted on 25.07.2019.

Pelgraz - pegfilgrastim -
EMEA/H/C/003961/II/0011/G
Accord Healthcare S.L.U., Rapporteur: Sol Ruiz

Pemetrexed Hospira - pemetrexed -
EMEA/H/C/003970/II/0020/G
Pfizer Europe MA EEIG, Generic, Generic of Alimta, Rapporteur: Alar Irs

Prasugrel Mylan - prasugrel -
EMEA/H/C/004644/II/0003/G
Mylan S.A.S, Generic, Generic of Efient, Rapporteur: Alar Irs
Request for Supplementary Information adopted on 11.07.2019, 16.05.2019.

Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) -
EMEA/H/C/001104/II/0180/G
Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder

Repatha - evolocumab -
EMEA/H/C/003766/II/0036
Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege

RoActemra - tocilizumab -
EMEA/H/C/000955/II/0084/G
Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus

RotaTeq - rotavirus vaccine (live, oral) -
EMEA/H/C/000669/II/0079/G
MSD Vaccins, Rapporteur: Kristina Dunder

Skyrizi - risankizumab -
EMEA/H/C/004759/II/0002/G
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Peter Kiely
Request for Supplementary Information adopted on 18.07.2019.

SomaKit TOC - edotreotide -
EMEA/H/C/004140/II/0011, Orphan
Advanced Accelerator Applications, Rapporteur: Maria Concepcion Prieto Yerro

Tepadina - thiotepa - **EMEA/H/C/001046/II/0034, Orphan** ADIENNE S.r.l., Rapporteur: Alexandre Moreau	
Tepadina - thiotepa - **EMEA/H/C/001046/II/0035/G, Orphan** ADIENNE S.r.l., Rapporteur: Alexandre Moreau	
Tremfya - guselkumab - **EMEA/H/C/004271/II/0015** Janssen-Cilag International N.V., Rapporteur: Melinda Sobor	
Verzenios - abemaciclib - **EMEA/H/C/004302/II/0005** Eli Lilly Nederland B.V., Rapporteur: Filip Josephson	
Vizarsin - sildenafil - **EMEA/H/C/001076/II/0029** KRKA, d.d., Novo mesto, Generic, Generic of Viagra, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 27.06.2019, 28.02.2019, 22.11.2018.	
Voncento - human coagulation factor viii / human von willebrand factor - **EMEA/H/C/002493/II/0041/G** CSL Behring GmbH, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 18.07.2019.	
WS1524 **HyQvia-EMEA/H/C/002491/WS1524/0048** **Kiovig-EMEA/H/C/000628/WS1524/0090** Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 14.03.2019.	
WS1587/G **Abasaglar-EMEA/H/C/002835/WS1587/0028/G** **Humalog-EMEA/H/C/000088/WS1587/0178/G** Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder	See agenda 5.1 For discussion
WS1612/G **Herceptin-EMEA/H/C/000278/WS1612/0155/G** **Kadcyla-EMEA/H/C/002389/WS1612/0047/G**	

Roche Registration GmbH, Lead Rapporteur: Jan Mueller-Berghaus

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

WS1632/G
Brimica Genuair-EMEA/H/C/003969/WS1632/0027/G
Duaklir Genuair-EMEA/H/C/003745/WS1632/0027/G
AstraZeneca AB, Lead Rapporteur: Ewa Balkowiec Iskra

WS1644/G
Insulatard-EMEA/H/C/000441/WS1644/0076/G
Protaphane-EMEA/H/C/000442/WS1644/0075/G
Novo Nordisk A/S, Duplicate, Duplicate of Monotard (SRD), Ultratard (SRD), Lead Rapporteur: Sinan B. Sarac

WS1662
Nuwiq-EMEA/H/C/002813/WS1662/0031
Vihuma-EMEA/H/C/004459/WS1662/0013
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus

WS1674
Actraphane-EMEA/H/C/000427/WS1674/0079
Actrapid-EMEA/H/C/000424/WS1674/0073
Insulatard-EMEA/H/C/000441/WS1674/0077
Mixtard-EMEA/H/C/000428/WS1674/0080
Protaphane-EMEA/H/C/000442/WS1674/0076
Novo Nordisk A/S, Lead Rapporteur: Sinan B. Sarac

WS1678
Rixathon-EMEA/H/C/003903/WS1678/0027
Riximyo-EMEA/H/C/004729/WS1678/

0028
Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus

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

Advagraf - tacrolimus - EMEA/H/C/000712/II/0054
Astellas Pharma Europe B.V., Rapporteur: Jayne Crowe, "Update of section 4.2 of the SmPC to include a more clear statement for physicians regarding the potential risk of uncontrolled substitution between different tacrolimus formulations, even with those where BE has been proven, in order to minimise the risk of under or over exposure to tacrolimus."
Request for Supplementary Information adopted on 14.06.2019.

Brilique - ticagrelor - EMEA/H/C/001241/II/0045
AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC in order to add a new warning on interference with laboratories tests regarding platelet function tests to diagnose heparin induced thrombocytopenia (HIT) based on as safety review."
Request for Supplementary Information adopted on 29.05.2019.

Brinavess - vernakalant - EMEA/H/C/001215/II/0034
Correvio, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8 and 5.1 of the SmPC based on the final results from the non-interventional PASS SPECTRUM study, listed as a category 3 study in the RMP, in order to fulfil MEA 026.5; SPRECTRUM (6621-019) study is a prospective observational registry study to characterise normal conditions of use, dosing and safety following administration of vernakalant IV sterile concentrate."
Request for Supplementary Information adopted on 16.05.2019, 14.02.2019.

CellCept - mycophenolate mofetil - EMEA/H/C/000082/II/0146
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of sections 4.7 and 4.8 of the SmPC to update the safety information based on the reassessment of all available evidence from

clinical trials and post-marketing experience, in order to present adverse drug reactions (ADRs) rather than adverse events (AEs). Additionally, section 5.2 of the SmPC is updated based on current literature on the pharmacokinetics in geriatric patients. The Package Leaflet and Labelling are updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes throughout the PI and to bring the PI in line with the latest QRD template version 10."
Request for Supplementary Information adopted on 25.07.2019, 26.04.2019.

Cosentyx - secukinumab - EMEA/H/C/003729/II/0051
Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include additional dosing information for ankylosing spondylitis (AS) patients based on final results from study CAIN457F2314; this is a randomized, double-blind, double dummy, placebo controlled, parallel-group, Phase 3 multicenter study of secukinumab versus placebo to demonstrate efficacy at 16 weeks and to assess long-term efficacy up to Week 156 in patients with active AS; the Package Leaflet is updated accordingly."
Request for Supplementary Information adopted on 25.07.2019.

Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0003/G
Sanofi Pasteur, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Sonja Hrabcik, "C.I.13 grouping: Submission of the final report from studies CYD14 and CYD15 listed as category 3 studies in the RMP. These are the final results of the pivotal efficacy studies including amendments to long-term efficacy follow-up (to capture the full range of dengue disease in the study population prospectively i.e. return to active detection of all symptomatic dengue cases) and long-term safety monitoring. No changes to the PI or RMP identified are proposed at this stage. Minor updates of the RMP will follow."
Request for Supplementary Information adopted on 27.06.2019.

Edurant - rilpivirine -
EMEA/H/C/002264/II/0035

Janssen-Cilag International NV, Rapporteur: Paula Boudewina van Hennik, “Update of section 5.1 of the SmPC to reflect the week 240 results from the TMC278-TiDP38-C213(C213) study a phase II, open-label, single-arm trial to evaluate the pharmacokinetics, safety, tolerability, and antiviral activity of rilpivirine in antiretroviral-naïve HIV-1 infected adolescents and children aged ≥6 to <18 years, upon request by CHMP following the assessment of the paediatric study C213 submitted according to Art. 46 procedure (no. EMEA/H/C/2264/P46/028). In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.8 of the SmPC to indicate that no safety concerns were identified in the Week 240 analysis of the C213 trial in adolescents aged ≥12 to <18 years.”

Edurant - rilpivirine -
EMEA/H/C/002264/II/0036

Janssen-Cilag International NV, Rapporteur: Paula Boudewina van Hennik, “Update of section 4.6 of the SmPC based on the most recent data described in the ARV Pregnancy Registry (APR). In addition, the Marketing authorisation holder (MAH) took the opportunity to update the Package Leaflet to include information on the sodium excipient, as per the revised Annex to the European Commission guideline on ‘Excipients in the labelling and package leaflet of medicinal products for human use’ and the list of local representatives, as well as to make minor editorial changes in the SmPC and in the Package Leaflet.”

Eliquis - apixaban -
EMEA/H/C/002148/II/0064

Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, “Update of sections 4.2, 4.4, 4.5 and 5.1 of the SmPC in order to update the safety information based on the final results from study CV185316 (AUGUSTUS), an open-label, randomised, controlled clinical trial to evaluate the safety of apixaban in patients with atrial fibrillation and acute coronary syndrome and/or percutaneous coronary intervention.”

Elonva - corifollitropin alfa -

EMEA/H/C/001106/II/0046
Merck Sharp & Dohme B.V., Rapporteur: Paula Boudewina van Hennik, “Update of sections 4.3, 4.4 and 4.9 of the SmPC in order to revise the current text regarding Ovarian Hyperstimulation Syndrome (OHSS) to add clarity and remove clinical advice describing specific clinical interventions for reducing OHSS that have become outdated, based on post-marketing data and literature review. The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder included some editorial changes in the Package Leaflet.”
Request for Supplementary Information adopted on 14.06.2019.

Eurartesim - piperaquine tetraphosphate / artenimol - EMEA/H/C/001199/II/0036
Alfasigma S.p.A., Rapporteur: Janet Koenig, “Changes to sections 4.2, 4.4 and 4.6 of the SmPC with reference to the posology and the recommendation during pregnancy; sections 2 and 3 of the leaflet (PL) are amended accordingly and refrence to the pregnancy register deleted from Annex II.”

Eviplera - emtricitabine / rilpivirine / tenofovir disoproxil - EMEA/H/C/002312/II/0100
Gilead Sciences Ireland UC, Rapporteur: Johann Lodewijk Hillege, “Submission of the final study report for the drug utilisation study EDMS-ERI-139775027, an observational cohort study to assess rilpivirine utilisation according to the European SmPC, implemented using data from the EuroSIDA study cohort. The study is listed as a Category 3 study in the Eviplera RMP and submission of the final study report fulfils PAM MEA 011.5.”

Feraccru - ferric maltol - EMEA/H/C/002733/II/0022
Norgine B.V., Rapporteur: Maria Concepcion Prieto Yerro, “Update of sections 4.2, 4.4 and 5.2 of the SmPC to include information on patients with chronic kidney disease, following the submission of the final study report of study ST10-01-303.”

Fiasp - insulin aspart - EMEA/H/C/004046/II/0016
Novo Nordisk A/S, Rapporteur: Kristina Dunder,

“Update of the SmPC section 4.8 with data from an updated safety pool, further to assessment of the last PSUR assessment for insulin aspart (EMEA/H/C/PSUSA/00001749/201809). This update is based on 3 efficacy and safety studies: NN1218-3852 (52 week) – a study of Fiasp compared to insulin aspart both in combination with insulin detemir in adults with Type 1 Diabetes; NN1218-3854 a study of Continuous Subcutaneous Insulin Infusion of Fiasp compared to NovoRapid in adults with Type 1 Diabetes; NN1218-4131 a study of Fiasp compared to NovoRapid both in combination with insulin degludec in adults with Type 1 Diabetes. The patient leaflet has been updated accordingly. In addition, correction to the labelling for the FlexTouch and vial presentations, resulting in removal of information included in section 17 and 18 from the inner cartons for the multipack for both FlexTouch and vial presentation.”	
IBRANCE - palbociclib - EMEA/H/C/003853/II/0024 Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, “Submission of the final report from a non-clinical study (PD-0332991) evaluating the correlation of palbociclib response to RB1 status.”	
IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0027, Orphan CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, “Update of section 4.4 of the SmPC to update the warning with regards to inhibitor development. Section 4.8 of the SmPC and the PL have been updated accordingly.” Request for Supplementary Information adopted on 14.06.2019.	
Imnovid - pomalidomide - EMEA/H/C/002682/II/0036/G, Orphan Celgene Europe BV, Rapporteur: Jorge Camarero Jiménez, “Group of two type II variations to update sections 4.2, 4.4 and 4.8 of the SmPC and section 4 of the PL with information on anaphylaxis and section 4.8 of SmPC with hypothyroidism ADR following a safety review. This group also includes a type IB variation to update section 6.6 of the SmPC in order to include recommendations to minimize the risk of unintended occupational exposures in healthcare professionals. The MAH has also proposed minor updates to section 4.4 of the SmPC and Annex	

IID regarding the educational materials, prescribing and dispensing restrictions in order to provide more clarity about the recommended maximum duration of treatment."

Kisqali - ribociclib -
EMEA/H/C/004213/II/0014
Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC based on the final results of study MONALEESA-7 (CLEE011E2301), a randomized, double-blind, placebo-controlled, multicenter Phase III study of ribociclib or placebo in combination with an NSAI and goserelin or tamoxifen and goserelin in pre- or perimenopausal women with HR-positive, HER2-negative, advanced breast cancer who had received no prior hormonal therapy for advanced disease."

Kolbam - cholic acid -
EMEA/H/C/002081/II/0028, Orphan
Retrophin Europe Ltd, Rapporteur: Konstantinos Markopoulos, "Submission of the final report from study CAC-002-01, listed as a category 3 study in the RMP. This is a Phase 3, open-label, single arm, non-randomized study investigating cholic acid in the treatment of subjects with inborn errors of bile acid metabolism.
The study was a continuation study that included eligible subjects who had previously received cholic acid in studies CAC-91-10-10 or CAC-001-01 as well as newly diagnosed subjects."
Request for Supplementary Information adopted on 29.05.2019, 28.02.2019.

Kuvan - sapropterin -
EMEA/H/C/000943/II/0068, Orphan
BioMarin International Limited, Rapporteur: Peter Kiely, "Update of section 5.1 of the Summary Product Characteristics (SmPC) in order to reflect new paediatric information based on study PKU-015 evaluating the effect of Kuvan on neurocognitive function, maintenance of blood phenylalanine concentrations, safety, and population Pharmacokinetics in young Children with Phenylketonuria.
The study is listed as MEA-C-Clinical, category 3 in the RMP for Kuvan and submitted in accordance to article 46 of the paediatric regulation."

Kyprolis - carfilzomib - EMEA/H/C/003790/II/0038, Orphan

Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of section 6.6 of the SmPC with information regarding the handling and preparation of Kyprolis. The PL is updated accordingly."

Request for Supplementary Information adopted on 25.07.2019.

Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0024

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

Request for Supplementary Information adopted on 27.06.2019.

Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0007, Orphan

Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, "Update of sections 4.8 and 5.1 of the SmPC based on safety and efficacy data for paediatric patients with relapsed or refractory AML from a systematic literature review."

Request for Supplementary Information adopted on 25.07.2019.

Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0008, Orphan

Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, "Update the SmPC section 4.2 to specify the dose and schedule for the second induction. Furthermore, a statement in SmPC section 4.2 was added to increase awareness about the actual recommended (maximum) dose of Mylotarg and information regarding traceability added to section 4.4. In addition, the Marketing authorisation holder (MAH) took the opportunity to include minor editorial changes in sections 4.2, 4.4, 4.8 and 5.2 of the SmPC and to make minor updates to bring the PI in line with the latest QRD template version."

Request for Supplementary Information adopted on 25.07.2019.

Noxafil - posaconazole - EMEA/H/C/000610/II/0058

Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau, “Update of section 4.8 of the SmPC in order to include 'pseudoaldosteronism' as an adverse event in post-marketing experience, following a review of six case reports in the scientific literature of concurrent hypertension and hypokalemia in patients treated with posaconazole. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.”	
OPDIVO - nivolumab - EMEA/H/C/003985/II/0069 Bristol-Myers Squibb Pharma EEIG, Co-Rapporteur: Paula Boudewina van Hennik, “Update of sections 4.2, 5.1 and 6.6 of the SmPC in order to introduce a new dosing regimen and schedule for adjuvant treatment of melanoma based on population PK data and Exposure-Response (E-R) Efficacy analysis. The Package leaflet has been updated accordingly.” Request for Supplementary Information adopted on 25.07.2019.	
Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0118/G Boehringer Ingelheim International GmbH, Rapporteur: Mark Ainsworth, “Update of section 4.5 of the SmPC in order to add a warning regarding the interaction between Pradaxa and the fixed-dose combination of the P-gp inhibitors glecaprevir and pibrentasvir based on the phase I drug-drug interaction study results. The Package Leaflet was updated accordingly. Update of section 4.8 of the SmPC with new safety information regarding adverse reaction alopecia following the confirmation of signal “alopecia associated with dabigatran” by the EMA and the cumulative review of cases of alopecia and related terms that was provided in PSUR submitted by 27 May 2019. In addition small editorial corrections under "Adverse reaction" Table 2 were made additionally to highlight that information on some side effects was obtained from post-marketing data. The Package Leaflet was updated accordingly.” Request for Supplementary Information adopted on 12.09.2019.	Request for supplementary information adopted with a specific timetable.
Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) -	

EMEA/H/C/001104/II/0181
Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder, “Update of section 5.1 of the SmPC in order to update efficacy information based on results from a public health analysis and publication of data from the CAPiTA (Community-Acquired Pneumonia Immunization Trial in Adults), a double-blind, randomized, placebo-controlled efficacy trial of 13-valent pneumococcal conjugate vaccine (PCV13).”

Remicade - infliximab -
EMEA/H/C/000240/II/0223
Janssen Biologics B.V., Rapporteur: Kristina Dunder, “Update of section 4.8 of the SmPC and relevant section of the PL to include cerebrovascular accidents as rare undesirable effect.”

Repatha - evolocumab -
EMEA/H/C/003766/II/0033
Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, “Update of section 4.8 of the SmPC in order to update the safety information with regards to the adverse reaction “Influenza-like illness” with a frequency of Uncommon following the assessment of influenza-like illness with evolocumab in both the clinical database and postmarketing database. The Package Leaflet section 4 was updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement changes to the package leaflet section 2 subsequent to the revised Annex to the EC guideline on excipients in the labelling (EMA/CHMP/302620/2017) to update the wording for sodium.”
Request for Supplementary Information adopted on 29.05.2019.

Revlimid - lenalidomide -
EMEA/H/C/000717/II/0112/G, Orphan
Celgene Europe BV, Rapporteur: Alexandre Moreau, “Group of variations including one type II to update sections 4.2, 4.4 and 4.8 of the SmPC and section 4 of the PL with anaphylaxis following a safety review and a Type IB to update section 6.6 of the SmPC in order to include recommendations to minimize the risk of unintended occupational exposures. The MAH has also proposed minor updates to section 4.4 of the SmPC, the RMP and Annex IID regarding the

educational materials, prescribing and dispensing restrictions in order to provide more clarity about the recommended maximum duration of treatment. Finally the MAH took the opportunity to make editorial changes throughout the product information."	
RXULTI - brexpiprazole - EMEA/H/C/003841/II/0003 Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Daniela Melchiorri, "To update section 4.4 of the SmPC (paragraph "Impulse-control disorders") based on the Company Core Data Sheet of brexpiprazole. In addition, the applicant has taken the opportunity to update the section 4.2 of the SmPC requested by EMA (see annex to cover letter) and to perform additional changes, i.e. editorial changes in the SmPC and Package Leaflet."	
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0016 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of section 4.5 of the SmPC in order to update the information related to coadministration based on the final results from studies ZOSTER-035 and ZOSTER-042; these are immunogenicity and safety studies in which Shingrix was co-administered either with Merck's 23-valent pneumococcal polysaccharide vaccine (Pneumovax 23; ZOSTER-035) or with GSK's reduced-antigen-content diphtheria and tetanus toxoids and acellular pertussis (dTpa) vaccine (Boostrix; ZOSTER-042); the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 25.07.2019.	
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0017 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of section 4.5 of the SmPC in order to update the information on concomitant administration based on final results from study ZOSTER-048 (REC005); this is an immunogenicity and safety study of Shingrix in subjects previously vaccinated with Zostavax; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted	

on 25.07.2019.

SIMBRINZA - brinzolamide / brimonidine - EMEA/H/C/003698/II/0018/G

Novartis Europharm Limited, Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 5.1 of the SmPC in order to update the safety information with adjunctive use of BID Simbrinza with a PGA therapy based on final results from study CQVJ499A2401; this is a phase 4, multicentre, randomized, double-masked, parallel-group study.
Update of section 5.1 of the SmPC in order to update the safety information with adjunctive use of BID Simbrinza with a PGA/beta-blocker combination therapy. based on final results from study CQVJ499A2402; this is a phase 4, multicenter, randomized, double-masked, parallel-group study."

Symkevi - tezacaftor / ivacaftor - EMEA/H/C/004682/II/0012/G, Orphan

Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.5 and 5.2 of the SmPC in order to provide information on drug-drug interactions and pharmacogenetic data based on final results from two post-authorisation measures (PAMs) studies: VX18-661-011 (an open-label phase 1 study to examine the effects of combination of tezacaftor and ivacaftor on the pharmacokinetics and safety of pitavastatin in healthy subjects) and pharmacokinetics study P088 (pharmacogenetic study of TEZ and IVA exposure with respect to CYP3A4*22 genotype)."

TAGRISSO - osimertinib - EMEA/H/C/004124/II/0031

AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, "Update of section 4.8 of the SmPC to include onychalgia in the list of associated clustered terms for paronychia further to a MAH internal safety information review."

TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0061/G

Biogen Netherlands B.V., Rapporteur: Martina Weise, "7xC.I.13: Submission of non-clinical studies:
1) Study Rsch-2013-023: A receptor binding study of Dimethyl Fumarate and Monomethyl Fumarate
2) Study P00012-14-04: Dimethyl Fumarate: A

cardiovascular and respiratory assessment following oral administration to conscious, radiotelemetry-instrumented beagle dogs 3-4) Study P00012-05-03 and Study P00012-04-11: Amendments to two-year carcinogenicity study reports in mice and rats with DMF 5) Study P00012-12-02: A toxicity study of Dimethyl Fumarate when administered orally in juvenile male rats 6) Study P00012-13-07: Dimethyl Fumarate: Self-administration assessment in the male Sprague dawley rat 7) Study P00012-14-01: Dimethyl Fumarate: Drug discrimination assessment in the male Sprague dawley rat"	
Thalidomide Celgene - thalidomide - EMEA/H/C/000823/II/0061/G, Orphan Celgene Europe BV, Rapporteur: Alexandre Moreau, "Group of variations including one type II to update sections 4.2, 4.4 and 4.8 of the SmPC and section 4 of the PL with anaphylaxis following a safety review a and a Type IB v to update section 6.6 of the SmPC in order to include recommendations to minimize the risk of unintended occupational exposures in healthcare professionals. The MAH has also proposed minor updates to section 4.4 of the SmPC and Annex IID regarding the educational materials, prescribing and dispensing restrictions in order to provide more clarity."	
Tremfya - guselkumab - EMEA/H/C/004271/II/0010 Janssen-Cilag International N.V., Rapporteur: Melinda Sobor, "Update of sections 4.8 and 5.1 of the SmPC to add the long term 3-year clinical data from the two ongoing clinical studies CNTO1959PSO3001 (VOYAGE 1) and CNTO1959PSO3002 (VOYAGE 2) in subjects with plaque psoriasis." Request for Supplementary Information adopted on 20.06.2019, 02.05.2019, 14.03.2019.	
Tremfya - guselkumab - EMEA/H/C/004271/II/0014 Janssen-Cilag International N.V., Rapporteur: Melinda Sobor, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information based on final results from the phase 3 Eclipse study CNTO1959PSO3009, comparing	

guselkumab (Tremfya) and secukinumab (Cosentyx) for the treatment of moderate to severe plaque psoriasis."
Request for Supplementary Information adopted on 11.07.2019.

Truvada - emtricitabine / tenofovir disoproxil - EMEA/H/C/000594/II/0161
Gilead Sciences Ireland UC, Rapporteur: Bruno Sepodes, "Submission of the final clinical study report for the non-interventional study GS-US-276-0103, 'A Prospective, Observational Study of Individuals Who Seroconvert While Taking Truvada for Pre-Exposure Prophylaxis (PrEP)', listed as a Category 3 study in the Truvada RMP."

Verzenios - abemaciclib - EMEA/H/C/004302/II/0003
Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC in order to add a criterion for discontinuing abemaciclib in the event of specific hepatic changes based on available safety data.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make editorial changes to section 5.1 of the SmPC."
Request for Supplementary Information adopted on 25.07.2019, 29.05.2019.

Verzenios - abemaciclib - EMEA/H/C/004302/II/0006
Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to add interstitial lung disease (ILD)-like events (including pneumonitis) as a new adverse drug reaction. 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."

Vimpat - lacosamide - EMEA/H/C/000863/II/0082
UCB Pharma S.A., Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC in order to warn that Vimpat tablets must not be divided based on the results of safety Evaluation Report on 'chopped tablets'.
The Package Leaflet is updated accordingly."

Xaluprine - mercaptopurine - EMEA/H/C/002022/II/0022, Orphan

Nova Laboratories Ireland Limited, Rapporteur: Filip Josephson, “Update of sections 4.4, 4.8 and 4.9 of the SmPC to add further information on hepatic toxicity. The MAH took the oportunity to implement minor editoral changes to the SmPC and PIL.”

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

Ipsen Pharma, Rapporteur: Martina Weise, “To update sections 4.2 and 5.2 of the SmPC following final results from study LX1606-111; this is a Phase 1, open-label, parallel-group study to evaluate the single-dose pharmacokinetics of Telotristat Ethyl in Male and Female Subjects with Severe Hepatic Impairment and Matched Subjects with Normal Function; the Package Leaflet is updated accordingly.”
Request for Supplementary Information adopted on 11.07.2019.

Yondelis - trabectedin - EMEA/H/C/000773/II/0058, Orphan

Pharma Mar, S.A., Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, “Update of section 4.4 of the SmPC in order to add a warning based on results from study Cardiac Safety Report [Protocols ET743-SAR-3007, ET743-OVA-301, ET743-OVC-3006; Phase 3. JNJ-17027907; R270741 (trabectedin)] following the PSUSA procedure EMEA/H/C/PSUSA/00003001/201809; the Package Leaflet is updated accordingly.”

Zoely - nomegestrol acetate / estradiol - EMEA/H/C/001213/II/0050

Theramex Ireland Limited, Rapporteur: Jean-Michel Race, “Update of sections 4.3 and 4.4 of the SmPC in order to add a new contraindication and a new warning regarding meningioma, upon request by PRAC following the assessment of Post-authorisation measure “LEG 014”. The Package Leaflet is being updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in the Netherlands and Portugal in the Package Leaflet.”

WS1511/G
Advagraf-EMEA/H/C/000712/WS1511/0052/G
Modigraf-EMEA/H/C/000954/WS1511/0031/G

Astellas Pharma Europe B.V., Lead Rapporteur: Jayne Crowe, “Update of sections 4.5 and 4.8 of the SmPC to add the drug-drug interaction with letemovir and to add the febrile neutropenia with frequency unknown, based on the cumulative review of the MAH safety database.
Update of section 4.6 of the SmPC to add the information on pregnancy and lactation following the cumulative review of the cases reported in the MAH global safety database, published literature and the transplantation pregnancy exposure registry.
The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor editorial changes throughout the PI and to implement the wording from the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'.”
Request for Supplementary Information adopted on 14.06.2019, 14.03.2019.

WS1605
Lyrica-EMEA/H/C/000546/WS1605/0097
Pregabalin Pfizer-EMEA/H/C/003880/WS1605/0027
Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, “Addition in the SmPC section 4.5 of the wording on the risk of death, including in patients who are substance abusers.”
Request for Supplementary Information adopted on 23.05.2019.

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

WS1648
Docetaxel
Zentiva-EMEA/H/C/000808/WS1648/0060
Taxotere-EMEA/H/C/000073/WS1648/0133
Aventis Pharma S.A., Lead Rapporteur: Alexandre Moreau, “Update of sections 4.4 and 4.8 of the SmPC in order to add a warning about cases of severe cutaneous reactions and to add acute generalized exanthematous pustulosis as an undesirable effect, respectively. The Package

Leaflet is updated in accordance. In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet."	
WS1677 **Aluvia-EMEA/H/W/000764/WS1677/0110** **Kaletra-EMEA/H/C/000368/WS1677/0179** **Norvir-EMEA/H/C/000127/WS1677/0156** AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Jean-Michel Race, "To update sections 4.3 and 4.5 of the SmPC to include a new contraindication with apalutamide, a moderate to strong CYP3A4 inducer, as well as to update section 4.5 of the SmPC on the potential interaction with encorafenib following an update to the Kaletra and Aluvia (lopinavir/ritonavir) and Norvir (ritonavir) Company Core Data Sheets (CCDS). The Package Leaflet is also updated accordingly"	

B.5.3. CHMP-PRAC assessed procedures

Avastin - bevacizumab - EMEA/H/C/000582/II/0110 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, "Submission of the final report from study NEJ026 listed as an obligation in the Annex II of the Product Information. This is an open-label, randomized, Phase III study conducted in Japan to compare erlotinib + bevacizumab combination therapy versus erlotinib monotherapy as first-line therapies for patients with NSCLC with EGFR gene mutations (exon 19 deletion or exon 21 L858R substitution). The RMP version 30.0 has also been submitted. In addition, the Package leaflet is updated to reflect information on sodium content in compliance with the revised Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal products for human use"." Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
Avonex - interferon beta-1a - EMEA/H/C/000102/II/0182/G Biogen Netherlands B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, "2x type II (C.I.4):	A CHMP Request for PRAC Advice was adopted via written procedure on 27 August 2019

1) Update of sections 4.3 and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054). 2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles. The Package leaflet has been updated accordingly. This submission fulfils MEA 87.2 and 84." Request for Supplementary Information adopted on 29.05.2019, 28.02.2019.	
Betaferon - interferon beta-1b - EMEA/H/C/000081/II/0124/G Bayer AG, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "2x type II (C.I.4): 1) Update of sections 4.3 and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054). 2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles. The Package leaflet has been updated accordingly. This submission fulfils MEA 024.2 and 21. An updated RMP version 4.1 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes' and an update of the EU-RMP template (rev.2)." Request for Supplementary Information adopted on 29.05.2019, 28.02.2019.	A CHMP Request for PRAC Advice was adopted via written procedure on 27 August 2019
Brinavess - vernakalant - EMEA/H/C/001215/II/0035 Correvio, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information following updates to the Company Core Safety Datasheet (CCDS) based on the results of an	Request for supplementary information adopted with a specific timetable.

integrated safety analysis performed on data of existing clinical studies with a stronger emphasis on treatment-related ADRs and an incidence rate above one percent. The Package Leaflet was updated accordingly.
The RMP version 7.0 has also been submitted and incorporates the results from the new safety analysis. In addition the results from completed observational Cohort SPECTRUM study (A Prospective Observational Registry Study to Characterise Normal Conditions of Use, Dosing and Safety Following Administration of Vernakalant IV Sterile Concentrate: PASS Protocol 6621-049) currently under assessment within Brinavess II/34 were included in the updated RMP.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update sections 4.2, 4.4, 4.6, 4.7, 4.8, 5.1, 5.2, 5.3, 6.4 of the SmPC, Annex II, Labelling sections 3 and 5, Package Leaflet sections 2, 4, 5 and 6 to include editorial changes, to correct typographical errors and to bring the PI in line with the latest QRD template version 10 and well as to update statements related to the excipients in the SmPC and Package Leaflet in line with the EC Guideline on "Excipients in the Labelling and Package Leaflet of medicinal products for human use" of March 2018 and the EMA Annex to the EC Guideline of October 2017 (SANTE-2017-11668)."
Request for Supplementary Information adopted on 05.09.2019, 14.06.2019.

Defitelio - defibrotide - EMEA/H/C/002393/II/0043, Orphan
Gentium S.r.l., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga,
"Submission of the systematic literature analysis to fulfil a Specific Obligation (SOB) to provide comparative data on efficacy, including pooled outcomes of patients with veno-occlusive disease (VOD) treated with defibrotide; VOD incidence and outcomes in patients not treated with defibrotide. Consequently, the RMP v. 6.1 and Annex II of the Product Information have been revised.
Additionally, the due date of the observational DefiFrance study (Category 3 Study in the RMP) has been revised; the RMP has been aligned with the template of EU RMP rev. 2 and minor editorial

changes have been introduced."	
Extavia - interferon beta-1b - EMEA/H/C/000933/II/0096/G Novartis Europharm Limited, Informed Consent of Betaferon, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "2x type II (C.I.4): 1) Update of sections 4.3 and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054). 2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles. The Package leaflet has been updated accordingly. This submission fulfils MEA 022.2 and 019. An updated RMP version 4.1 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes' and an update of the EU-RMP template (rev. 2)." Request for Supplementary Information adopted on 29.05.2019, 28.02.2019.	A CHMP Request for PRAC Advice was adopted via written procedure on 27 August 2019
Iclusig - ponatinib - EMEA/H/C/002695/II/0051, Orphan Incyte Biosciences Distribution B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of the RMP to version 19.1, including deletion of previously agreed safety concerns; these deletions are proposed in line with the guideline on Good Pharmacovigilance Practices (GVP) Module V on RMP (revision 2 - dated on 31 March 2017). Other updates include: review of the categorisation of the posterior reversible encephalopathy syndrome (PRES) risk in the RMP in line with the request from PSUSA/00010128/201712; correction of the category (from Category 3 to 1) of the study AP24534-14-203, an imposed Annex II condition; revision of the due date for the submission of this study report to August 2021, as described in the Iclusig PI, and as agreed as part of procedure EMEA/H/C/002695/ANX/016. Additionally, The RMP and Annex II have been updated to remove the additional risk minimisation measures (Healthcare Professional	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Educational Brochure)." Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 14.06.2019.	
Increlex - mecasermin - EMEA/H/C/000704/II/0060 Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.1, 4.2, 4.3, 4.4, 4.8 and 4.9 of the SmPC in order to update the safety information on benign or malignant neoplasia based on the EU Registry Study, the Ipsen global safety database and literature review. The Package Leaflet is updated accordingly. The MAH also submitted the updated RMP version 11. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet"	
Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0048/G Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, "C.1.4: Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information on the risk of Left ventricular dysfunction (LVD) based on the final results from study BO39807 listed as a category 3 study in the RMP. This is an observational study of cardiac events in patients with HER2-positive metastatic breast cancer who have a Left Ventricular Ejection Fraction (LVEF) between 40%-49% prior to initiating treatment with Kadcyla; The RMP version 10.0 has also been submitted. C.I.13: Submission of the final report from study BO28408 listed as a category 3 study in the RMP addressing cardiac safety, safety in elderly patients, and immunogenicity. This is a randomised, multicenter, open-label, two-arm, phase III neoadjuvant study evaluating the efficacy and safety of trastuzumab emtansine plus pertuzumab compared with chemotherapy plus trastuzumab and pertuzumab for patients with HER2-Positive Breast Cancer." Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
Lokelma - sodium zirconium cyclosilicate - EMEA/H/C/004029/II/0013 AstraZeneca AB, Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Kirsti Villikka,	

“Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to update the clinical information based final results from study DIALIZE. This was a Phase 3b, multicentre, prospective, randomised, double-blind, placebo-controlled study to reduce incidence of pre-dialysis hyperkalaemia with sodium zirconium cyclosilicate. The Package Leaflet and Labelling are updated accordingly. The RMP version 2.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement the new excipient statement for sodium in section 4.4 of the SmPC, section 2 of Labelling and section 2 of the Package Leaflet. Furthermore, minor editorial changes were introduced in section 2 of the Package leaflet.”	
Lonsurf - trifluridine / tipiracil - EMEA/H/C/003897/II/0016 Les Laboratoires Servier, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Annika Folin, “Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update information on patients with severe renal impairment based on final results from study TO-TAS-102-107 (A Phase 1, Open-label Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of TAS-102 in Patients With Advanced Solid Tumors and Varying Degrees of Renal Impairment). The Package Leaflet is updated accordingly. The updated RMP version 6.3 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the RMP in line with the template revision 2 of the good Pharmacovigilance practice module V guideline.”	
Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0029/G Orexigen Therapeutics Ireland Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber, “Group of variations consisting of the: 2) C.I.3.b: to update section 4.8 on the list of adverse drug reactions and their corresponding frequencies following the PRAC outcome on PSUR procedure (PSUSA/10366/201709). 2) C.I.4: to update sections 4.2, 4.4 and 5.2 of the SmPC to add results from a phase I open label parallel study to evaluate the pharmacokinetics of a single oral dose of extended-release	

combination of naltrexone and bupropion in subjects with normal hepatic function or varying degrees of impaired hepatic function and remove the recommendation to not use naltrexone/bupropion in patients with mild hepatic impairment. The existing warning has also been updated accordingly. The warning related to contraindications has also been aligned to section 4.3 to add end-stage renal failure patients. Consequentially an updated RMP (version 11) has also been submitted. In addition, the MAH takes the opportunity to update the warning on lactose to be in accordance with EC guideline on Guideline on "Excipients in the labelling and package leaflet of medicinal products for human use".” Request for Supplementary Information adopted on 25.07.2019, 29.05.2019, 28.02.2019, 15.11.2018.	
NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0030/G Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Submisison of the Guardian 4 (NN7008-3809) Clinical Trial in Previously Untretaed Patients (PUPs) and the Guardian 9 (NN7008-4239) PK Clinical Trial. In addition, the MAH has updated the SmPC to align with the 'EMA Core SmPC for human plasma derived and recombinant coagulation factor VIII products, revision 3' and Annex to the European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use'. Further, some administrative updates have also been applied.” Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0002 Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, “C.I.13: Submission of the Final Study Report for, ANNEXA-4 Study ("Prospective, Open-Label Study of Andexanet Alfa in Patients Receiving a Factor Xa Inhibitor Who Have Acute Major Bleeding") listed as category 2 study in the RMP. This is an interventional non-randomized, multicentre, prospective, open-label, single-group study in patients with acute major	

bleeding. The results of ANNEXA-4 were requested to be submitted as Specific Obligation in the context of Conditional Marketing Authorisation. The RMP version 1.1 has also been submitted."	
Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0049 Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Rhea Fitzgerald, "Updated of section 4.8 of the SmPC with the safety data from the Phase 3, open-label, rollover study for Studies 109 and 011 Part B (Study 011B) designed to evaluate the long-term safety and tolerability of Orkambi treatment for 96 weeks in patients with cystic fibrosis, 6 years of age and older, homozygous for F508del." Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
Plegridy - peginterferon beta-1a - EMEA/H/C/002827/II/0052/G Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ulla Wändel Liminga, "2x type II (C.I.4): 1) Update of sections 4.3 and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054). 2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles. The Package leaflet has been updated accordingly. This submission fulfils MEA 8.2 and 002. An updated RMP version 4.1 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes' and an update of the EU-RMP template (rev. 2)." Request for Supplementary Information adopted on 29.05.2019, 28.02.2019.	A CHMP Request for PRAC Advice was adopted via written procedure on 27 August 2019
Rapiscan - regadenoson - EMEA/H/C/001176/II/0034/G GE Healthcare AS, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia,	Request for supplementary information adopted with a specific timetable.

"Grouping of variations: - Update of sections 4.4 and 4.8 of the SmPC regarding myocardial ischaemia (myocardial infarction, ventricular arrhythmias and cardiac arrest) based on a review of the safety database and CCDS update - Update of sections 4.4, 4.5, 4.8, 4.9 and 5.1 of the SmPC regarding co-administration with methylxanthines due to the risk of seizure and hypersensitivity including anaphylaxis based on a review of the safety database and CCDS update - Update of section 5.1 of the SmPC regarding the use of regadenoson in patients with inadequate stress test based on results from study 3606-CL-3004 and CCDS update. The RMP version (11.1) has also been submitted in order to fulfil LEG 016." Request for Supplementary Information adopted on 05.09.2019.	
Rebif - interferon beta-1a - EMEA/H/C/000136/II/0137/G Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "2x type II (C.I.4): 1) Update of sections 4.3, 4.6 and 5.3 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054). 2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles. The Package leaflet has been updated accordingly. This submission fulfils MEA 43.2 and 39. An updated RMP version 10.0 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes' and an update of the EU-RMP template (rev.2)." Request for Supplementary Information adopted on 29.05.2019, 28.02.2019.	A CHMP Request for PRAC Advice was adopted via written procedure on 27 August 2019
ReFacto AF - moroctocog alfa - EMEA/H/C/000232/II/0151 Pfizer Europe MA EEIG, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, "To update sections 4.8 Undesirable	

effects and 5.1 Pharmacodynamic effects of the SmPC based on the final results from study 3082B2-313 (B1831001 - "An Open-Label Study to Evaluate Prophylaxis Treatment, and to Characterize the Efficacy, Safety, and Pharmacokinetics of B-Domain Deleted Recombinant Factor VIII Albumin Free (Moroctocog Alfa [AF_CC]) in Children with Hemophilia A") listed as an additional pharmacovigilance activity in the Risk Management Plan (RMP; MEA 116). The RMP version 13.0 has also been submitted. In addition, the SmPC is being brought in line with the revised guidelines on core SmPC for human plasma derived and recombinant coagulation factor VIII products (Revision 3) in sections 4.2 Posology and Method of Administration, 4.4 Special warnings and special precautions for use, 4.8 Undesirable effects and 5.1 Pharmacodynamic effects." Request for Supplementary Information adopted on 29.05.2019.	
Spinraza - nusinersen - EMEA/H/C/004312/II/0014, Orphan Biogen Netherlands B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from Phase 2 Study SM202 (EMBRACE or CS7) listed as a category 3 study in the RMP. This is a Phase 2, randomized, double-blind, sham-procedure-controlled study to assess the safety and tolerability and explore the efficacy of ISIS 396443 (BIIB058) administered intrathecally in subjects with spinal muscular atrophy who are not eligible to participate in the clinical studies ISIS 396443-CS3B or ISIS 396443-CS4 due to age at screening and/or SMN2 copy number. Version 10.2 of the RMP was approved." Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 14.06.2019.	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Stayveer - bosentan - EMEA/H/C/002644/II/0028 Janssen-Cilag International NV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, "Update of section 4.2 of the SmPC in order to include that patients should be given the Package Leaflet and the Patient Alert Card which are included in the pack and update of annex II.D	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

to remove the Prescriber kit from the additional risk minimisation measures and also to remove the obligation to implement a formal "Controlled Distribution System" in EU countries following the assessment of LEG 10.2. The RMP version 11 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of the local representative in the UK, to bring the PI in line with the latest QRD template version 10, and with the guideline on Excipients in the labelling and package leaflet of medicinal products for human use (EMA/CHMP/302620/2017), and to implement some corrections to the Bulgarian translations."
Opinion adopted on 05.09.2019.

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

AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2 and 5.2 of the SmPC in order to reflect the outcome of study D5160C00035, an open-label, Phase I study to assess the pharmacokinetics, safety and tolerability of osimertinib following a single oral 80 mg dose to patients with advanced solid tumours and normal renal function or severe renal impairment. This study was a Category 3 study in the EU-RMP. The RMP version 13 has also been submitted."
Request for Supplementary Information adopted on 27.06.2019.

TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0062

Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Update of sections 4.4 and 4.8 of the SmPC to add a warning on the risk of herpes zoster based on cumulative review data submitted in the ongoing PSUSA/00010143/201903. The Package Leaflet is updated accordingly."

TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0063

Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Update of sections 4.4 and 4.8 of the SmPC to reflect PML in the setting of mild lymphopenia based on data submitted in the ongoing PSUSA/00010143/201903. The Package Leaflet

is updated accordingly. Additionally, the Product Information has been updated in line with QRD template (version 10.1)."	
Tracleer - bosentan - EMEA/H/C/000401/II/0092 Janssen-Cilag International NV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, "Update of section 4.2 of the SmPC in order to include that patients should be given the Package Leaflet and the Patient Alert Card which are included in the pack and update of annex II.D to remove the Prescriber kit from the additional risk minimisation measures and also to remove the obligation to implement a formal "Controlled Distribution System" in EU countries following the assessment of LEG 086.2. The RMP version 11 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of the local representative in the UK, to bring the PI in line with the latest QRD template version 10, and with the guideline on Excipients in the labelling and package leaflet of medicinal products for human use (EMA/CHMP/302620/2017), and to implement some corrections to the Bulgarian translations." Opinion adopted on 05.09.2019.	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Truberzi - eluxadoline - EMEA/H/C/004098/II/0009/G Allergan Pharmaceuticals International Ltd, Rapporteur: Martina Weise, PRAC Rapporteur: Adam Przybylkowski, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update the safety information based on results from PK study ELX-PK-01 listed as a category 3 study in the RMP; this is a Single-dose, Open-label, Pharmacokinetic study of Eluxadoline in Healthy Subjects with normal Renal Function and Patients with Renal Impairment. Update of sections 4.4 and 4.8 of the SmPC following Company Core Data Sheet (CCDS) update based on review of clinical safety data and post-marketing safety data. Section 4.3 has been updated to add clarification in line with section 4.4. and section 5.1 has been updated to add Pharmacotherapeutic Group and ATC code. The RMP version 3.0 has also been submitted. The Package Leaflet is updated accordingly. In addition, the MAH also took the opportunity to	

change “eluxadoline” to “Truberzi” when referring to the medicinal product throughout the SmPC.” Request for Supplementary Information adopted on 27.06.2019, 28.03.2019.	
UDENYCA - pegfilgrastim - EMEA/H/C/004413/II/0003 ERA Consulting GmbH, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, “To update section 4.6 of the SmPC to update the safety information based on feasability data regarding the pregnancy and lactation registry listed as a category 3 study in the RMP; this is a non-interventional registry. The Package Leaflet is updated accordingly. The updated RMP version 1.5 has also been submitted.” Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
Zelboraf - vemurafenib - EMEA/H/C/002409/II/0054 Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, “Update of sections 4.4 and 4.5 of the SmPC in order to add information and a precaution regarding concomitant strong CYP3A4 inhibitors based on final results from study GO29475 (MEA-011), a category 3 study in the RMP; the Package Leaflet is updated accordingly. The RMP version 12.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PL in line with the excipients guideline (EMA/CHMP/302620/2017) by adding information about the product's sodium content.” Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
Zydelig - idelalisib - EMEA/H/C/003843/II/0047 Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber, “Submission of the final clinical study report for study 101-09, A Phase 2 Study to Assess the Efficacy and Safety of Idelalisib in Subjects with Indolent B Cell non-hodgkin lymphomas refractory to rituximab and alkylating agents. This submission is an Annex II postauthorisation measure (ANX 002) and a category I commitment in the Zydelig Risk Management Plan (RMP). This submission also includes an update to the PI”	

WS1518 **Epclusa-EMEA/H/C/004210/WS1518/0034** **Harvoni-EMEA/H/C/003850/WS1518/0077** **Sovaldi-EMEA/H/C/002798/WS1518/0055** **Vosevi-EMEA/H/C/004350/WS1518/0025** Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, “Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC (Epclusa, Harvoni), sections 4.2, 4.4, 5.1 and 5.2 (Sovaldi) and 4.2, 4.8 and 5.2 (Vosevi) in order to add new information regarding the use of the sofosbuvir-containing products in patients with renal impairment, based on final results from studies GS-US-342-4062, GS-US-337-4063 and GS-US-334-0154, listed as a category 3 study in the RMP and study GS-US-338-1125. Study GS-US-342-4062 was a phase 2, multi-centre, open-label study to evaluate the efficacy and safety of sofosbuvir/velpatasvir for 12 Weeks in subjects with chronic HCV infection who are on dialysis for end stage renal disease. Study GS-US-337-4063 was a phase 2, multi-centre, open-label study to evaluate the efficacy and safety of ledipasvir/sofosbuvir in subjects with genotype 1, 4, 5 and 6 chronic HCV infection who are on dialysis for end stage renal disease. Study GS-US-334-0154 was a phase 2b, open label study of 200 mg or 400 mg Sofosbuvir+ribavirin for 24 Weeks in Genotype 1 or 3 HCV infected subjects with renal insufficiency. Study GS-US-338-1125 was a phase 1, open-label, parallel-group, single-dose study to evaluate the pharmacokinetics of voxilaprevir in subjects with normal renal function and severe renal impairment. The Package Leaflet is updated accordingly. The RMPs have also been submitted for each of the products in this work-sharing procedure.” Request for Supplementary Information adopted on 14.06.2019, 11.04.2019.	
WS1599 **Rixathon-EMEA/H/C/003903/WS1599/0020** **Riximyo-EMEA/H/C/004729/WS1599/0020**	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus, Lead PRAC Rapporteur: Hans Christian Siersted, “Submission of the final report from study (GP13-301) listed as a category 3 study in the RMP. This is a randomised, controlled double-blind Phase III trial to compare the efficacy, safety and pharmacokinetics of GP2013 plus cyclophosphamide, vincristine, prednisone vs MabThera plus cyclophosphamide, vincristine, prednisone, followed by GP2013 or MabThera maintenance therapy in patients with previously untreated advanced stage follicular lymphoma. The RMP version 4.1 has been agreed.” Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 16.05.2019.	

B.5.4. PRAC assessed procedures

PRAC Led **AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0025** sanofi-aventis groupe, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, “Submission of the patients and HCPs final survey reports to assess the effectiveness of the education materials; the survey reports are part of the additional pharmacovigilance activities in the RMP (category 3 studies). Within this submission the MAH is proposing a revised patient card with the following revisions: the patient card was restructured (general guidance, possible side effects, pregnancy), details related to the Accelerated Elimination Procedure were deleted and symptoms related to liver and infections are described.” Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0081** UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, “Submission of the final report from study (British Society for Rheumatology Biologics Register (BSRBR), RA0022) listed as a category 3 study in the RMP. This is a UK registry which aims to monitor the long term safety of TNF-α drugs and	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

other targeted therapies in rheumatoid arthritis patients. Submission of the interim report from study (RABBIT registry, RA0020) listed as a category 3 study in the RMP. This is a Germany biologic registry, long-term observational cohort study of the safety and effectiveness of biologic agent in rheumatoid arthritis." Opinion adopted on 05.09.2019.	
PRAC Led **Hemangiol - propranolol - EMEA/H/C/002621/II/0019** PIERRE FABRE DERMATOLOGIE, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Update of Package Leaflet in order to strengthen the warning on Hypoglycemia and Bronchospasm following completion of Drug Utilisation Study (DUS) performed in Germany and France to evaluate off-label use and effectiveness of RMM in a real-life clinical setting (MEA 002). In additions editorial changes have been introduced in section 4.4 of the SmPC as well as changes in the PL in accordance with QRD template 10.0. RMP version 3.1 has been submitted in order to updates the additional RMMs as a consequence of the results of the DUS." Request for Supplementary Information adopted on 05.09.2019, 16.05.2019, 14.02.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Kiovig - human normal immunoglobulin - EMEA/H/C/000628/II/0091** Baxter AG, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 9.0 in order to include the new indication chronic inflammatory demyelinating polyradiculoneuropathy [CIDP] and update the list of safety concerns (implementation of new specifications from GCP Module V (Rev 2)." Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 14.06.2019.	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Kisplyx - lenvatinib - EMEA/H/C/004224/II/0024** Eisai GmbH, Rapporteur: Bart Van der Schueren,	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Bjorg Bolstad, “Submission of an updated clinical study design of a PASS Study E7080-G000-218 (MEA 007) to change its design from phase 2 randomised, double-blind clinical trial to open label. The study assesses the Safety and efficacy of Lenvatinib at two different starting doses (18mg vs. 14mg QD) in Combination to Everolimus (5 mg QD) in Renal Cell carcinoma following one prior VEGF-Targeted treatment. This variation is a consequence of the post authorisation measure MEA 06.1. and the change is at CHMP's request. Consequently the RMP v.11.1 has been revised also additional minor administrative changes have been implemented.” Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 14.06.2019.	
PRAC Led **Luveris - lutropin alfa - EMEA/H/C/000292/II/0082** Merck Europe B.V., Rapporteur: Mark Ainsworth, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, “Submission of an updated RMP for Luveris 75 IU powder and solvent for injections version 3.1, 28 Nov 2018 in order to: - adapt the RMP template to Good Pharmacovigilance Practice (GVP) Module V, rev 2. - delete reference to Luveris 450 IU solution for injection in pre-filled pen, following the withdrawal of this presentation (EU/1/00/155/007). - removal of important identified risks “Ovarian Hyperstimulation Syndrome (OHSS)” and “Mild to severe hypersensitivity reactions including anaphylactic reactions and shock” and important potential risks “Thromboembolic (TE) events”, “Reproductive system cancer”, “Ectopic pregnancy”, “Multiple pregnancies”, “Congenital anomaly” and “off label use”). For the missing information of “Hypogonadotropic hypogonadal women with severe LH and FSH deficiency of advanced maternal age (older than 40 years)”, the advanced maternal age has been changed from 40 to 42 years. - amendment and update of the epidemiology and non-clinical sections of the RMP, as per the most recent data. The clinical trial section and	Request for supplementary information adopted with a specific timetable.

exclusion criteria in pivotal clinical studies section have been updated for recombinant human luteinizing hormone (rhLH). - update with the patient exposure data up to the data lock point (DLP) of 28 November 2018. - Other minor changes (e.g. reporting rates in RMP tables)" Request for Supplementary Information adopted on 05.09.2019.	
PRAC Led **Ozurdex - dexamethasone - EMEA/H/C/001140/II/0035** Allergan Pharmaceuticals Ireland, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "C.I.13: Submission of the final report from study CMO-EPI-EYE-0522 listed as a category 3 study in the RMP. This is an observational, cross-sectional study conducted in France, Germany, Spain, and the UK having as primary objective the assessment of the effectiveness of the educational material provided to the treating physicians. In consequence, the SmPC sections 4.2, 6.6 and Annex II of Product information were updated to reflect the conclusions of the assessment. Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder took the opportunity to include updates to local representative in SK." Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 14.06.2019.	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Selincro - nalmefene - EMEA/H/C/002583/II/0025** H. Lundbeck A/S, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of the Final Study Reports for the PASS 15649A: Use of Nalmefene (Selincro) in European databases: Cohort design using longitudinal electronic medical records or claims databases and PASS 14910A a non-interventional multicountry prospective cohort study to investigate the pattern of use of Selincro and frequency of selected adverse reactions in routine clinical practice." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 05.09.2019.	
PRAC Led **SIMBRINZA - brinzolamide / brimonidine - EMEA/H/C/003698/II/0019** Novartis Europharm Limited, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Submission of an updated RMP version 3.0 in order to remove metabolic acidosis/renal impairment as an important potential risk from the list of safety concerns and in addition update the Risk management plan to comply with the new GVP module V rev 2 RMP template." Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Slenyto - melatonin - EMEA/H/C/004425/II/0010** RAD Neurim Pharmaceuticals EEC SARL, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "The removal of "Delay of sexual maturation and development" as an "Important potential risk" from the EU-RMP." Request for Supplementary Information adopted on 05.09.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Tremfya - guselkumab - EMEA/H/C/004271/II/0013** Janssen-Cilag International N.V., Rapporteur: Melinda Sobor, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of RMP to remove exposure during lactation as missing information." Request for Supplementary Information adopted on 27.06.2019.	
PRAC Led **Votrient - pazopanib - EMEA/H/C/001141/II/0054** Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 17.0 in order to postpone CSR submission for the COMPARZ study and its substudy, to reflect PRAC recommendations for additional assessments of some risks, to revise the list of safety concerns and to adapt the RMP to the template of the	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

revised GVP module V guideline (rev 2)." Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 16.05.2019.	
PRAC Led **Xadago - safinamide - EMEA/H/C/002396/II/0031** Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Submission of an updated RMP version 6.1 in order to implement RMP rev 2 template and introduce changes to pre-clinical, clinical and post-marketing exposure information and update the due date of DUS Z7219N02 from July 2019 to 28 February 2020 ." Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 14.06.2019.	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1581** **Rasilez-EMEA/H/C/000780/WS1581/0123** **Rasilez HCT-EMEA/H/C/000964/WS1581/0093** Noden Pharma DAC, Lead Rapporteur: Daniela Melchiorri, Lead PRAC Rapporteur: Ilaria Baldelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of an updated RMP version 14 in order to update the template in line with GVP Module V Rev2 required, add new important potential risk of non-melanoma skin cancer (related to Rasilez HCT only), and remove several important risks and missing information items as per PRAC endorsement of PSUR 12." Opinion adopted on 05.09.2019. Request for Supplementary Information adopted on 16.05.2019.	Positive Opinion adopted by consensus on 05.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1655** **Aerius-EMEA/H/C/000313/WS1655/0091** **Azomyr-EMEA/H/C/000310/WS1655/0095** **Neoclarityn-EMEA/H/C/000314/WS1655/0089** Merck Sharp & Dohme B.V., Duplicate, Duplicate of Allex (SRD), Azomyr, Opulis (SRD), Lead Rapporteur: Koenraad Norga, Lead PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Bart Van der Schueren, "C.I.13:	Request for supplementary information adopted with a specific timetable.

Submission of the final report from study (EUPAS15038) listed as a category 3 study in the RMP. This is a non-interventional non-imposed PASS study designed to assess the potential risk of desloratadine exposure on seizures, supraventricular tachycardia, and atrial fibrillation or flutter."
Request for Supplementary Information adopted on 05.09.2019.

B.5.5. CHMP-CAT assessed procedures

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0011, Orphan, ATMP
Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang,
Request for Supplementary Information adopted on 19.07.2019.

Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0005/G, ATMP
CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder, "Update of the product information to reflect the study results of the 36-month follow up data for trial cod 16 HS 13 and the final study report with 60-month follow-up data for trial cod 16 HS 14.
Study cod 16 HS 13, is a Prospective, randomised, open label, multicentre Phase-III clinical trial to compare the efficacy and safety of the treatment with the autologous chondrocyte transplantation product co.don chondrosphere (ACT3D-CS) with microfracture in subjects with cartilage defects of the knee with a defect size between 1 and 4 cm^2.
Study cod 16 HS 14, is a Prospective, randomised, open label, multicentre Phase-II clinical trial to investigate the efficacy and safety of the treatment of large defects (4-10 cm^2) with three different doses of the autologous chondrocyte transplantation product co.don chondrosphere (ACT3D-CS) in subjects with cartilage defects of the knee."
Request for Supplementary Information adopted on 21.06.2019, 24.05.2019.

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

CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder,
Request for Supplementary Information adopted on 21.06.2019.

YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0008, Orphan, ATMP
Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus
Request for Supplementary Information adopted on 21.06.2019.

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

YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0012, Orphan, ATMP
Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

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

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

PRAC Led
Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0034, ATMP
Amgen Europe B.V., Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, “To update the RMP for Imlygic to version 7.0 in order

to add 2 category 3 studies (Studies 20180062 and 20180099), as well as an internal evaluation of managed distribution process metrics, to evaluate the effectiveness of additional risk minimization measures (aRMM)."
Request for Supplementary Information adopted on 19.07.2019.

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

WS1634
Advate-EMEA/H/C/000520/WS1634/0102
ADYNOVI-EMEA/H/C/004195/WS1634/0007
Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus

WS1643/G
Halimatoz-EMEA/H/C/004866/WS1643/0012/G
Hefiya-EMEA/H/C/004865/WS1643/0012/G
Hyrimoz-EMEA/H/C/004320/WS1643/0012/G
Sandoz GmbH, Lead Rapporteur: Milena Stain

WS1650
Olanzapine
Glenmark-EMEA/H/C/001085/WS1650/0031
Olanzapine Glenmark Europe-EMEA/H/C/001086/WS1650/0028
Olazax-EMEA/H/C/001087/WS1650/0024
Olazax Disperzi-EMEA/H/C/001088/WS1650/0025
Glenmark Arzneimittel GmbH, Generic, Generic of Olansek (SRD), Zyprexa, Zyprexa Velotab, Lead Rapporteur: Alexandre Moreau, "To updated section 4.8 of the SmPC to add "stuttering", section 5.2 of the SmPC to include new section with a sub heading 'Hepatic Impairment' and text related to smoking in line with PI text of the reference product. The PL has been updated accordingly. In addition the MAH has taken the opportunity to align the annexes with minor linguistic changes in line with the reference product."
Request for Supplementary Information adopted on 11.07.2019.

WS1656/G
Copalia-EMEA/H/C/000774/WS1656/

0108/G
Copalia HCT-EMEA/H/C/001159/
WS1656/0079/G
Dafiro-EMEA/H/C/000776/WS1656/0111/
G
Dafiro HCT-EMEA/H/C/001160/WS1656/
0081/G
Exforge HCT-EMEA/H/C/001068/WS1656/
0078/G
Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth

WS1658/G
Eucreas-EMEA/H/C/000807/WS1658/
0075/G
Galvus-EMEA/H/C/000771/WS1658/
0063/G
Icandra-EMEA/H/C/001050/WS1658/
0078/G
Jalra-EMEA/H/C/001048/WS1658/0065/
G
Xiliarx-EMEA/H/C/001051/WS1658/
0062/G
Zomarist-EMEA/H/C/001049/WS1658/
0077/G
Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder

WS1659/G
Silodosin Recordati-EMEA/H/C/004964/
WS1659/0001/G
Silodyx-EMEA/H/C/001209/WS1659/
0036/G
Urorec-EMEA/H/C/001092/WS1659/
0039/G
Recordati Ireland Ltd, Lead Rapporteur: Daniela Melchiorri

WS1665
Clopidogrel Zentiva-EMEA/H/C/000975/
WS1665/0065
Clopidogrel/Acetylsalicylic acid
Zentiva-EMEA/H/C/001144/WS1665/0053
DuoPlavin-EMEA/H/C/001143/WS1665/
0052
Iscover-EMEA/H/C/000175/WS1665/
0135
Plavix-EMEA/H/C/000174/WS1665/0132
Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, “To update SmPC section 4.5 “Interaction with other medicinal products and other forms of interaction” of the SmPC and the

corresponding section of the PL for the interaction between clopidogrel and morphine and other opioids. Furthermore a slight mistake about the number of patients for the TROPICAL-ACS study that was included in the SmPC section 5.1 in a different procedure is being corrected. The MAH has also taken the opportunity to update the Danish and Dutch local representatives in the PL of Plavix, Iscover, DuoPlavin and Clopidogrel/Acetylsalicylic acid Zentiva"	
WS1669 **Ryzodeg-EMEA/H/C/002499/WS1669/0035** **Tresiba-EMEA/H/C/002498/WS1669/0042** **Xultophy-EMEA/H/C/002647/WS1669/0032** Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder	
WS1672 **Mirapexin-EMEA/H/C/000134/WS1672/0092** **Sifrol-EMEA/H/C/000133/WS1672/0083** Boehringer Ingelheim International GmbH, Lead Rapporteur: Mark Ainsworth, "To delete the dosage strength of 1.1mg for Pramipexole tablets."	
WS1675 **Abseamed-EMEA/H/C/000727/WS1675/0085** **Binocrit-EMEA/H/C/000725/WS1675/0084** **Epoetin alfa Hexal-EMEA/H/C/000726/WS1675/0084** Sandoz GmbH, Lead Rapporteur: Alexandre Moreau, "To update sections 4.2, 4.4, 4.8 and 5.1 of the SmPC to align the PI with the NAP originator Eprex. The PL was updated accordingly. In addition, Annex II was updated following procedure EMEA/H/C/IG0970/G."	
WS1682 **Filgrastim Hexal-EMEA/H/C/000918/WS1682/0051** **Zarzio-EMEA/H/C/000917/WS1682/0052** Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "To update section 2 of the Package Leaflet in order to align the PI with its NAP originator Neupogen. Editorial chnages are	Positive Opinion adopted by consensus on 12.09.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

also proposed to the HU, IS, LT, PL and SV annexes."
Opinion adopted on 12.09.2019.

WS1688
Abseamed-EMEA/H/C/000727/WS1688/0086
Binocrit-EMEA/H/C/000725/WS1688/0085
Epoetin alfa Hexal-EMEA/H/C/000726/WS1688/0085
Sandoz GmbH, Lead Rapporteur: Alexandre Moreau

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

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

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

satralizumab - EMEA/H/C/004788, Orphan **Accelerated review**
Roche Registration GmbH, treatment of adult and adolescent patients from 12 years of age with neuromyelitis optica spectrum disorders (NMOSD)

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

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

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

Strensiq - asfotase alfa - EMEA/H/C/003794/S/0041, Orphan
Alexion Europe SAS, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Rhea Fitzgerald

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

Aripiprazole Mylan Pharma - aripiprazole - EMEA/H/C/003803/R/0013
Mylan S.A.S, Generic, Generic of Abilify, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ana Sofia Diniz Martins

EVOTAZ - atazanavir / cobicistat - EMEA/H/C/003904/R/0031
Bristol-Myers Squibb Pharma EEIG, Rapporteur:

Bruno Sepodes, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Adrien Inoubli

Keytruda - pembrolizumab - EMEA/H/C/003820/R/0081
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Menno van der Elst

Lumark - lutetium (177lu) chloride - EMEA/H/C/002749/R/0014
I.D.B. Holland B.V., Rapporteur: Jean-Michel Race, PRAC Rapporteur: Ronan Grimes

OPDIVO - nivolumab - EMEA/H/C/003985/R/0074
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski

Pregabalin Mylan - pregabalin - EMEA/H/C/004078/R/0014
Mylan S.A.S, Generic, Duplicate, Generic of Lyrica, Duplicate of Pregabalin Mylan Pharma, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Liana Gross-Martirosyan

Pregabalin Mylan Pharma - pregabalin - EMEA/H/C/003962/R/0012
Mylan S.A.S, Generic, Generic of Lyrica, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Liana Gross-Martirosyan

SIRTURO - bedaquiline - EMEA/H/C/002614/R/0035, Orphan
Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Voriconazole Hikma - voriconazole - EMEA/H/C/003737/R/0010
Hikma Farmaceutica (Portugal), S.A., Generic, Generic of Vfend, Rapporteur: Natalja Karpova, PRAC Rapporteur: Liana Gross-Martirosyan

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

Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0039/G

Biofrontera Bioscience GmbH, Rapporteur: Janet Koenig, Co-Rapporteur: Peter Kiely, “C.I.6.a - To modify the approved therapeutic indication to include the treatment of mild to severe actinic keratosis on extremities, trunk and neck. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC and sections 1 and 4 of the PL are updated accordingly. C.I.4 - To update section 5.1 of the SmPC based on follow-up data from study ALA-AK-CT009; this is a a randomized, observer-blind, intra-individual phase III study to evaluate the safety and efficacy of Ameluz in combination with daylight PDT (photodynamic therapy) in comparison with Metvix for the treatment of mild to moderate actinic keratosis.”	
Cosentyx - secukinumab - EMEA/H/C/003729/II/0053/G Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, PRAC Rapporteur: Eva A. Segovia, “Grouping of two variations: One type II variation II C.I.6.a: Extension of indication to include the treatment of Non-radiographic axial spondyloarthritis (nr-axSpA) / axial spondyloarthritis (axSpA) without radiographic evidence for Cosentyx. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 of the SmPC are amended. The package leaflet is amended in accordance. The updated RMP version 5.0 has also been submitted. One type IB C.I.11.z to change the due date of the Psoriasis Registry (category 3 study) within the RMP.”	
Fycompa - perampanel - EMEA/H/C/002434/II/0047 Eisai GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, “Extension of indication to include adjunctive treatment in paediatric patients from 2 to 11 years of age in Partial-Onset (focal) Seizures with or without secondary generalisation and Primary Generalised Tonic-Clonic Seizures with idiopathic generalised epilepsy for Fycompa; As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 4.3 has also been submitted.”	
Votubia - everolimus - EMEA/H/C/002311/II/0061, Orphan	

Novartis Europharm Limited, Rapporteur: Janet Koenig, “To modify the approved therapeutic indication (adjunctive treatment of patients aged 2 years and older whose refractory partial-onset seizures, with or without secondary generalisation, are associated with tuberous sclerosis complex, TSC) to include the new population of patients from 6 months to less than 2 years of age.
As a consequence, sections 4.1, 4.2, 5.1, 5.2 of the SmPC and sections 1 and 2 of the PL are updated accordingly.
Furthermore, the PI is brought in line with the latest QRD template version 10.1.”

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Eylea - aflibercept -
EMEA/H/C/002392/II/0055/G
Bayer AG, Rapporteur: Alexandre Moreau

Kalydeco - ivacaftor -
EMEA/H/C/002494/II/0080, Orphan
Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Maria Concepcion Prieto Yerro

LIBTAYO - cemiplimab -
EMEA/H/C/004844/II/0003
Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Sinan B. Sarac

Natpar - parathyroid hormone -
EMEA/H/C/003861/II/0020/G, Orphan
Shire Pharmaceuticals Ireland Limited, Rapporteur: Bart Van der Schueren

NeuroBloc - botulinum B toxin -
EMEA/H/C/000301/II/0104/G
Sloan Pharma S.a.r.l, Rapporteur: Bruno Sepodes

Palynziq - pegvaliase -
EMEA/H/C/004744/II/0002, Orphan
BioMarin International Limited, Rapporteur: Johann Lodewijk Hillege

Pelgraz - pegfilgrastim -
EMEA/H/C/003961/II/0013/G
Accord Healthcare S.L.U., Rapporteur: Sol Ruiz

Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) -
EMEA/H/C/000973/II/0141
GlaxoSmithkline Biologicals SA, Rapporteur:

Kristina Dunder

Xofigo - radium-223 -
EMEA/H/C/002653/II/0037
Bayer AG, Rapporteur: Janet Koenig

Zessly - infliximab -
EMEA/H/C/004647/II/0009/G
Sandoz GmbH, Rapporteur: Bjorg Bolstad

WS1700/G
Humalog-EMEA/H/C/000088/WS1700/0180/G
Liprolog-EMEA/H/C/000393/WS1700/0141/G
Eli Lilly Nederland B.V., Informed Consent of Humalog, Lead Rapporteur: Kristina Dunder

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

Dovato - dolutegravir / lamivudine -
EMEA/H/C/004909/II/0001
ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegavir. The SmPC is updated accordingly. The RMP is not submitted."

Faslodex - fulvestrant -
EMEA/H/C/000540/II/0067
AstraZeneca AB, Rapporteur: Filip Josephson, "To update a warning in section 4.6 of the SmPC following an overview of non-clinical data, clinical pharmacology simulation/modelling data, supporting documentation and safety data. The Package Leaflet is updated accordingly. In addition, the applicant has taken the opportunity to correct a minor mistake in the address of one of the manufacturers responsible for batch release in Annex II and PL."

Herceptin - trastuzumab -
EMEA/H/C/000278/II/0157

Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus

Juluca - dolutegravir / rilpivirine - EMEA/H/C/004427/II/0016

ViiV Healthcare B.V., Rapporteur: Janet Koenig, "Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegavir. The SmPC is updated accordingly. The RMP is not submitted."

Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0027

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Jean-Michel Race, "Submission of the final clinical study report from study M16-133, this is a phase 3b, single Arm, open label, multicenter study aimed to evaluate the efficacy and safety of glecaprevir (GLE)/pibrentasvir (PIB) in treatment of naïve adults with chronic Hepatitis C Virus (HCV) Genotypes 1 – 6 infection and aspartate aminotransferase to platelet ratio index (APRI) ≤ 1."

Mimpara - cinacalcet - EMEA/H/C/000570/II/0065

Amgen Europe B.V., Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to the new ADR 'chondrocalcinosis pyrophosphate' with a frequency of unknown. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1 and to implement a minor correction to the List of Excipients in section 6.1 of the SmPC."

Ongentys - opicapone - EMEA/H/C/002790/II/0020

Bial - Portela & Cª, S.A., Rapporteur: Martina Weise, "Update of sections 4.5 and 5.2 of the SmPC to add information on drug interaction and pharmacokinetic properties of opicapone based on final results from drug interaction studies

NBI-OPC-1708 and NBI-OPC-1707. Study NBI-OPC-1708 is a phase 1, open-label, one-sequence crossover, drug-interaction study to evaluate and compare the pharmacokinetics of repaglinide when administered alone and concomitantly with opicapone. Study NBI-OPC-1707 is a Phase 1, randomized, open-label, 2-period crossover drug interaction study of the effect of administration of single dose of quinidine on the pharmacokinetics of opicapone.
In addition, the marketing authorisation holder took the opportunity to delete the local representative for UK from the PL, according to the guidance provided on UK's withdrawal from the EU regarding medicinal products for human and veterinary use within the framework of the Centralised Procedure"

OPDIVO - nivolumab - EMEA/H/C/003985/II/0073
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, "To update sections 4.8 and 5.1 of the SmPC based on the final results from two studies: CA209017 Open-label Randomized Phase III Trial comparing Nivolumab Versus Docetaxel in Previously Treated Advanced or Metastatic Squamous Cell Non-small Cell Lung Cancer and CA209057 Open-label Randomized Phase III Trial comparing Nivolumab Versus Docetaxel in Previously Treated Metastatic Non-Squamous Non-small Cell Lung Cancer."

Resolor - prucalopride - EMEA/H/C/001012/II/0049/G
Shire Pharmaceuticals Ireland Limited, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to update the safety information following the final results from study SHP555-802 (a cohort Study of the Relative Incidence of Major Cardiovascular Events) and based on an analysis of all potential major adverse cardiovascular events (MACE) from completed Phase 2/4 clinical studies in adult subjects. In addition, the Marketing authorisation holder (MAH) took the opportunity to update typographical errors in sections 4.4 and 5.1"

Rezolsta - darunavir / cobicistat - EMEA/H/C/002819/II/0035
Janssen-Cilag International NV, Rapporteur:

Johann Lodewijk Hillege, “C.I.4 Update of sections 4.8 and 5.1 of the SmPC to update the efficacy and safety information of Rezolsta following results from study TMC114FD2HTX3001 (AMBER); this is an ongoing Phase 3, randomized, active-controlled, double-blind study to evaluate efficacy and safety of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) once daily fixed dose combination (FDC) regimen versus a regimen consisting of darunavir/cobicistat (DRV/COBI) FDC co-administered with emtricitabine/tenofovir disoproxil fumarate FDC in antiretroviral treatment-naïve human immunodeficiency virus type 1 infected subjects.
The applicant takes the opportunity to update section 4.5 to remove the interaction with simeprevir, following the withdrawal of Olysio Marketing Authorization. In addition, the MAH has implemented some minor administrative updates throughout the Product Information.
The Package Leaflet is updated accordingly.”

Sivextro - tedizolid phosphate - EMEA/H/C/002846/II/0032

Merck Sharp & Dohme B.V., Rapporteur: Bruno Sepodes, “To update the Marketing Authorization for Sivextro with the final report from Phase 3 study for the treatment of Hospital-Acquired Bacterial Pneumonia and Ventilator-Associated Bacterial Pneumonia (HABP/VABP) MK-1986-002; protocol TR701-132.”

Tivicay - dolutegravir - EMEA/H/C/002753/II/0052

ViiV Healthcare B.V., Rapporteur: Filip Josephson, “Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegavir. The SmPC is updated accordingly. The RMP is not submitted.”

Triumeq - dolutegravir / abacavir /

lamivudine - EMEA/H/C/002754/II/0069
ViiV Healthcare B.V., Rapporteur: Filip Josephson, “Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the DTG-containing regimens based on interim analysis from Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegavir. The SmPC is updated accordingly. The RMP is not submitted.”

XALKORI - crizotinib - EMEA/H/C/002489/II/0064
Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, “Update of section 5.1 of the SmPC in order to reflect updated efficacy data from Study A8081001 in patients with ROS1-positive NSCLC. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1.”

WS1701
Epclusa-EMEA/H/C/004210/WS1701/0040
Vosevi-EMEA/H/C/004350/WS1701/0032
Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, “Update of section 4.8 of the SmPC in order to add new safety information on rash and angioedema following a cumulative review of hypersensitivity with Epclusa and Vosevi, prompted by routine pharmacovigilance and signal detection activities. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes throughout the Product Information.”

WS1705
Aluvia-EMEA/H/W/000764/WS1705/0111
Kaletra-EMEA/H/C/000368/WS1705/0180
AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Jean-Michel Race, “Change of section 4.8 of the SmPC to update the safety information of Kaltera and Aluvia following a cumulative safety review of the incidence rate of Stevens-Johnson syndrome, erythema

multiforme and jaundice during clinical trials according to LEG 110 (from EMEA/H/C/000368/R/107). The Package Leaflet is updated accordingly."

B.6.10. CHMP-PRAC assessed procedures

Odomzo - sonidegib -
EMEA/H/C/002839/II/0024
Sun Pharmaceutical Industries Europe B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Željana Margan Koletić, "To submit the final report of study CLDE225X2116, listed as a category 3 study in the RMP. This is an interventional Phase Ib/II, open-label, multi-center, dose-finding study to assess the safety and efficacy of the oral combination of LDE225 and INC424 (ruxolitinib) in subjects with myelofibrosis. The RMP version 7.1 has also been submitted."

Raxone - idebenone -
EMEA/H/C/003834/II/0018, Orphan
Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli, "C.I.11z for SOB studies: Submission of the final report from study SNT-EAP-001 listed as a Specific Obligation (SOB11, former SOB4) in the Annex II of the Product Information. This is a follow-up study of patients in the Expanded Access Program (SNT-EPA-001) for Raxone in the treatment of patients with Leber's Hereditary Optic Neuropathy (LHON). The goal is to collect further long-term real-world efficacy and safety data. Annex II is modified accordingly. Submission of an updated RMP version 1.9 accordingly."

B.6.11. PRAC assessed procedures

PRAC Led
Adempas - riociguat -
EMEA/H/C/002737/II/0030, Orphan
Bayer AG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Tuomo Lapveteläinen, "Submission of the final report from risk management plan (RMP) category 3 study 16657, EXPERT (EXPosurE Registry RiociguaT in patients with pulmonary hypertension) to collect information about the long term use of Adempas in real clinical

practice.The RMP version 7.1 has also been submitted."

PRAC Led

Colobreathe - colistimethate sodium - EMEA/H/C/001225/II/0044/G

Teva B.V., Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Adam Przybylkowski, PRAC-CHMP liaison: Ewa Balkowiec Iskra, "Submission of the final Post-authorisation safety study report for CLB-MD-05: An observational safety study of Colobreathe (colistimethate sodium dry powder for inhalation) compared with other inhaled anti-pseudomonal antibiotics in cystic fibrosis patients using cystic fibrosis registries. The MAH is also providing an updated RMP, reflecting results from CLB-MD-05 but also the results form CLB-MD-08 that had been provided previously."

PRAC Led

Cubicin - daptomycin - EMEA/H/C/000637/II/0074

Merck Sharp & Dohme B.V., PRAC Rapporteur: Pernille Harg, PRAC-CHMP liaison: Bjorg Bolstad, "Submission of an updated RMP version 11.1 in order to delete all risks and additional risk minimisation measures in line with GVP module V revision 2. Annex II of the Product Information is updated accordingly. In addition, the MAH took the opportunity to align the Product Information with the QRD template version 10.1 and update the list of local representatives."

PRAC Led

Invokana - canagliflozin - EMEA/H/C/002649/II/0045/G

Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the final report from 3 non-interventional studies (listed as category 3 studies in the RMP):
- Study RRA-21410, an Epidemiology Study to characterize the risk of LLA in subjects in the overall T2DM population and in a subpopulation with established CVD.
- NAP4001, a Meta-Analysis from CANVAS, CANVAS-R and CREDENCE Studies to characterize the risk of LLA in subjects at high risk for CV events and/or progression of kidney disease .
- Meta-Analysis from CANVAS, CANVAS-R and

CREDENCE to evaluate the incidence of bladder cancer in the canagliflozin group compared to the placebo group."

PRAC Led

Praluent - alirocumab -

EMEA/H/C/003882/II/0050/G

sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 5.0 in order to amend the list of safety concerns (removing 'cataract (in the context of very low LDL-C)' as important potential risk; 'long-term use (>5years)' and 'clinical impact of very low LDL-C for extended period of time' as missing information; and consequentially to remove the following additional Pharmacovigilance activities (category 3 studies in the RMP) from the RMP: study R727-CL-1609 (MEA 016), study OBS14697 (MEA 019) and study ALIROC07997 (MEA 017) based on a review of data since the MA was granted including the 1st interim report for study OBS14697, a drug utilisation study (DUS) of alirocumab in Europe to assess the effectiveness of the dosing recommendation to avoid very low LDL-C levels, in order to fulfil MEA 019.4."

PRAC Led

VELCADE - bortezomib -

EMEA/H/C/000539/II/0093

Janssen-Cilag International NV, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of an updated RMP version 30.1 in order to revise the list of safety concerns. This revision has been triggered by the PRAC recommendation received in outcome of the EU-PSUR covering the period from 26 April 2017 to 25 April 2018. As a consequence, the Annex II of the PI has been updated to reflect the removal of the additional risk minimisation activities. In addition, the applicant took the opportunity to update the list of local representatives in the PL. Furthermore, the PI is being brought in line with the latest QRD template (version 10.1)."

PRAC Led

Vokanamet - canagliflozin / metformin -

EMEA/H/C/002656/II/0050/G

Janssen-Cilag International NV, Rapporteur:

Martina Weise, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of the final report from 3 non-interventional studies (listed as category 3 studies in the RMP):
- Study RRA-21410, an Epidemiology Study to characterize the risk of LLA in subjects in the overall T2DM population and in a subpopulation with established CVD.
- NAP4001, a Meta-Analysis from CANVAS, CANVAS-R and CREDENCE Studies to characterize the risk of LLA in subjects at high risk for CV events and/or progression of kidney disease.
- Meta-Analysis from CANVAS, CANVAS-R and CREDENCE to evaluate the incidence of bladder cancer in the canagliflozin group compared to the placebo group.”

PRAC Led

WS1654

Enbrel-EMEA/H/C/000262/WS1654/0228

LIFMIOR-EMEA/H/C/004167/WS1654/0022

Pfizer Europe MA EEIG, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, “C.I.13: Submission of the final report from study (B1801311 - BADDIR) listed as a category 3 study in the RMP. This is a prospective cohort study that compared patients treated with biologic interventions (etanercept, adalimumab, and ustekinumab) and patients with similar disease characteristics but exposed only to conventional non-biologic systemic therapies.”

B.6.12. CHMP-CAT assessed procedures

Alofisel - darvadstrocel - EMEA/H/C/004258/II/0009, Orphan, ATMP

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

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0014, Orphan, ATMP

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

B.6.13. CHMP-PRAC-CAT assessed procedures

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0013/G, Orphan, ATMP

Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang, PRAC Rapporteur: Brigitte Keller-Stanislawski,, "Group of variations consisting of:
1) C.I.4: a type II to update sections 4.4, 4.8, 5.1 and 5.2 of the SmPC with the long-term efficacy and safety of Kymriah in relapsed/refractory DLBCL based on the 24 months follow-up results from study CCTL019C2201.
2) C.I.4: a type II to update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC based on interim results from study CCTL019B2202.
3) C.I.4: a type II to update section 5.2 of the SmPC based on interim results from study CCTL019B2205J.
The Annex II and the Package Leaflet are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to clarify the wording of the indication in order to reflect that patients of 25 years of age are being included and to introduce some minor editorial corrections throughout the SmPC and the Package Leaflet. The RMP version 2.0 has also been submitted."

B.6.14. PRAC assessed ATMP procedures

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

WS1661/G
Entresto-EMEA/H/C/004062/WS1661/0026/G
Neparvis-EMEA/H/C/004343/WS1661/0025/G

Novartis Europharm Limited, Lead Rapporteur: Johann Lodewijk Hillege

WS1706
Enurev Breezhaler-EMEA/H/C/002691/WS1706/0030
Seebri Breezhaler-EMEA/H/C/002430/WS1706/0030
Tovanor Breezhaler-EMEA/H/C/002690/WS1706/0034

Novartis Europharm Limited, Duplicate, Duplicate of Seebri Breezhaler, Lead Rapporteur: Mark

Ainsworth, “To introduce a modification of the Instructions for Use (IFU) for the Breezhaler devices affecting the labeling (SmPC and PL) through simplification of its content and layout - condensing textual instructions, optimizing illustrations, and clustering of content to aid comprehension of the procedure of use. In addition both the packaging and IFU in the SmPC and PL have included device-specific information in precise locations in order to meet the MDR requirements. This is because the device does not have its own packaging or leaflet.”	
WS1708 **Hirobriz Breezhaler-EMEA/H/C/001211/ WS1708/0055** **Onbrez Breezhaler-EMEA/H/C/001114/ WS1708/0053** **Oslif Breezhaler-EMEA/H/C/001210/ WS1708/0053** Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth, “To introduce a modification of the Instructions for Use (IFU) for the Breezhaler devices affecting the labeling (SmPC and PL) through simplification of its content and layout - condensing textual instructions, optimizing illustrations, and clustering of content to aid comprehension of the procedure of use. In addition both the packaging and IFU in the SmPC and PL have included device-specific information in precise locations in order to meet the MDR requirements. This is because the device does not have its own packaging or leaflet. Finally, as notified to the Agency, the MAH took this opportunity to remove unnecessary details from the quality module 3.2.P.7 currently registered for Onbrez/ Hirobriz/ Oslif Breezhaler.”	

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.

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

G. ANNEX G

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

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

G.2. PRIME

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

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