18 May 2020
EMA/CHMP/147656/2020 Corr[1]
Human Medicines Division

Committee for medicinal products for human use (CHMP)

Agenda for the meeting on 23-26 March 2020

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

23 March 2020, 09:00 – 18:00, 1C/Adobe Connect

24 March 2020, 08:30 – 18:00, 1C/Adobe Connect

25 March 2020, 08:30 – 18:00, 1C/Adobe Connect

26 March 2020, 08:30 – 16:00, 1C/Adobe Connect

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).

[1] Correction in B.4 (Annex)

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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 23-26 March 2020. See March 2020 CHMP minutes (to be published post April 2020 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 23-26 March 2020

1.3. Adoption of the minutes

CHMP minutes from the meeting held on 24-27 February 2020.

ORGAM minutes from the meeting held on 17 February 2020.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

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

treatment of asthma and to reduce asthma exacerbations

Scope: Oral explanation

Action: Oral explanation to be held on Tuesday, 24 March 2020 at 14:00

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

2.1.2. ozanimod - EMEA/H/C/004835

Treatment of multiple sclerosis

Scope: Possible oral explanation

Updated list of experts for the SAG Neurology meeting held on 16.03.2020 was adopted via written procedure on 13.03.2020

SAG report

Action: Possible oral explanation to be held on Tuesday, 24 March 2020 at 11:00

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

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

treatment of asthma and to reduce asthma exacerbations

Scope: Oral explanation

Action: Oral explanation to be held on Tuesday, 24 March 2020 at 14:00

List of Outstanding Issues adopted on 30.01.2020.

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

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

Takeda Pharma A/S

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

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

List of experts for SAG Oncology meeting scheduled on 05.03.2020 was adopted via written procedure on 04.03.2020

SAG Report, Oral explanation

Action: Oral explanation to be held on Wednesday, 25 March 2020 at 11:00

Request for Supplementary Information adopted on 30.01.2020, 17.10.2019.

See 5.1

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

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

treatment of asthma

Scope: Opinion

Action: For adoption

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

19.09.2019.

3.1.2. indacaterol / mometasone furoate - EMEA/H/C/005516

treatment of asthma

Scope: Opinion

Action: For adoption

3.1.3. cabazitaxel - EMEA/H/C/005178

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

Scope: Opinion

Action: For adoption

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

3.1.4. influenza vaccine (surface antigen, inactivated) - Article 28 - EMEA/H/C/004993

Active immunisation against influenza in the elderly (65 years of age and older) and in children 6 months to less than 6 years of age.

Scope: Opinion

Action: For adoption

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

3.1.5. etanercept - EMEA/H/C/004711

Rheumatoid arthritis, Juvenile idiopathic arthritis, Psoriatic arthritis, Axial spondyloarthritis, Ankylosing spondylitis, Non-radiographic axial spondyloarthritis, Plaque psoriasis, Paediatric plaque psoriasis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 25.07.2019, 29.05.2019. List of Questions adopted on 20.09.2018.

3.1.6. pretomanid - Orphan - EMEA/H/C/005167

FGK Representative Service GmbH; treatment of tuberculosis

Scope: Opinion

Action: For adoption

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

25.07.2019.

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

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 27.02.2020, 12.12.2019. List of Questions adopted on 19.09.2019.

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

AveXis EU Ltd; treatment of spinal muscular atrophy (SMA)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 06.12.2019, 21.06.2019. List of Questions adopted on 22.02.2019.

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

3.2.1. aripiprazole - EMEA/H/C/005062

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 25.07.2019.

3.2.2. apixaban - EMEA/H/C/005358

prevention of venous thromboembolic events (VTE)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 17.10.2019.

3.2.3. bevacizumab - EMEA/H/C/005106

treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer.
First-line treatment of patients with unresectable advanced, metastatic or recurrent non-

small cell lung cancer.
First line treatment of patients with advanced and/or metastatic renal cell cancer.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 14.11.2019.

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

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

Scope: List of outstanding issues, SAG report from meeting held on 05.03.2020

Action: For adoption

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

3.2.5. erlotinib - EMEA/H/C/005071

treatment of lung and pancreatic cancers

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.

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

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 27.06.2019.

3.2.7. bulevirtide - Orphan - EMEA/H/C/004854

Accelerated assessment

MYR GmbH; indicated for the treatment of chronic hepatitis delta virus (HDV) infection in adult patients with compensated liver disease.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.01.2020.

3.2.8. melphalan - EMEA/H/C/005173

used alone or in combination with other cytotoxic drugs and/or total body irradiation is indicated in the treatment of: multiple myeloma, malignant lymphoma (Hodgkin, non-Hodgkin lymphoma), acute lymphoblastic and myeloblastic leukaemia, childhood neuroblastoma, ovarian adenocarcinoma, mammary adenocarcinoma.
In combination with other cytotoxic drugs and/or total body irradiation, in adult and pediatric population, is indicated as conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (HSCT) in haematological diseases.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 25.07.2019.

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

is indicated as an aid for the enhanced visualization and detection of colorectal lesions in adult patients undergoing screening / surveillance colonoscopy for colorectal cancer.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 27.06.2019.

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

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 17.10.2019.

3.2.11. doxorubicin - EMEA/H/C/005320

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 17.10.2019.

3.2.12. pexidartinib - Orphan - EMEA/H/C/004832

Daiichi Sankyo Europe GmbH; treatment of adult patients with symptomatic tenosynovial giant cell tumour (TGCT), also referred to as giant cell tumour of the tendon sheath (GCT-TS) or pigmented villonodular synovitis (PVNS)

Scope: List of outstanding issues, SAG report from meeting held on 04.03.2020

Action: For adoption

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

3.2.13. lefamulin - EMEA/H/C/005048

treatment of community-acquired pneumonia (CAP)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 17.10.2019.

3.2.14. lifitegrast - EMEA/H/C/004653

treatment of moderate to severe dry eye disease in adults for whom prior artificial tears has not been sufficient

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 12.12.2019. List of Questions adopted on 26.04.2019.

3.2.15. trastuzumab - EMEA/H/C/005209

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 17.10.2019.

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

3.3.1. autologous CD34+ cell enriched population that contains hematopoietic stem and progenitor cells transduced ex vivo using a lentiviral vector encoding the human arylsulfatase A gene - Orphan - ATMP - EMEA/H/C/005321

Accelerated assessment

Orchard Therapeutics (Netherlands) BV; treatment of metachromatic leukodystrophy (MLD)

Scope: List of questions

Action: For information

3.3.2. potassium - Orphan - EMEA/H/C/005407

Advicenne Pharma S.A.; treatment of distal renal tubular acidosis (dRTA) in patients aged 6

months and older.

Scope: List of questions

Action: For adoption

3.3.3. icosapent ethyl - EMEA/H/C/005398

indicated to reduce cardiovascular risk as an adjunct to statin therapy.

Scope: List of questions

Action: For adoption

3.3.4. baloxavir marboxil - EMEA/H/C/004974

Treatment of influenza in patients aged 12 and above, including patients at high risk of developing influenza-related complications and for post-exposure prophylaxis of influenza in individuals aged 12

Scope: List of questions

Action: For adoption

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

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

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

Scope: Letter from the applicant dated 16 March 2020 requesting an extension of clock-stop to respond to the list of outstanding issues adopted in June 2019.

Action: For adoption

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 13.12.2018.

3.4.2. insulin aspart - EMEA/H/C/004965

treatment of diabetes mellitus

Scope: Letter from the applicant dated 17 March 2020 requesting an extension of clock-stop to respond to the list of questions adopted in February 2020.

Action: For adoption

List of Questions adopted on 27.02.2020.

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

Agios Netherlands B.V.; Treatment of adult patients (≥ 18 years old) with relapsed or refractory acute myeloid leukaemia (AML) with an isocitrate dehydrogenase-1 (IDH1) R132 mutation

Scope: Letter from the applicant dated 09 March 2020 requesting an extension of clock-stop to respond to the list of outstanding issues adopted in February 2020.

Action: For adoption

List of Outstanding Questions adopted on 27.02.2020. List of Questions adopted on 29.05.2019.

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

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

Scope: Letter by the applicant dated 10 March 2020 requesting an extension of the clock stop to respond to the list of questions adopted on 19.09.2019

Action: For adoption

List of Questions adopted on 19.09.2019.

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

No items

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. doxorubicin - EMEA/H/C/005194

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

Scope: Withdrawal of initial marketing authorisation application

Action: For information

List of Outstanding Issues adopted on 27.02.2020, 12.12.2019. List of Questions adopted on 19.09.2019.

3.7.2. rituximab - EMEA/H/C/005387

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

Scope: Withdrawal of initial marketing authorisation application

Action: For information

Oral explanation held on 27.02.2020. List of Outstanding Issues adopted on 12.12.2019, 27.06.2019.

3.7.3. rituximab - EMEA/H/C/004807

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

Scope: Withdrawal of initial marketing authorisation application

Action: For information

Oral explanation held on 27.02.2020. List of Outstanding Issues adopted on 12.12.2019, 27.06.2019. List of Questions adopted on 18.10.2018.

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

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

4.1.1. Jorveza - budesonide - Orphan - EMEA/H/C/004655/X/0007/G

Dr. Falk Pharma GmbH

Rapporteur: Martina Weise, Co-Rapporteur: Tomas Radimersky, PRAC Rapporteur: Zane Neikena

Scope: "Extension application to add a new strength of 0.5 mg for budesonide orodispersible tablets, grouped with:
- A type II variation (C.I.6) - Extension of indication to include the maintenance of remission for Jorveza (0.5 mg and 1 mg orodispersible tablets); as a consequence, sections 4.2, 4.8 and 5.1 of the SmPC are updated to reflect the recommended daily dose and duration of treatment of Jorveza for the maintenance of remission, to update the list of adverse reactions and the clinical efficacy and safety information based on the results of the phase III clinical study BUL-2/EER. The relevant sections of the PL are updated accordingly. In addition, a revised RMP (version 2.0) has been submitted to reflect the results of this study and to align with the GVP Module V (rev 2) template. The MAH also took the opportunity to bring the product information in line with the latest QRD template (version 10.1).
- A type IB variation (B.II.e.5.a.2)"

Action: For adoption

List of Questions adopted on 12.12.2019.

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

Janssen-Cilag International NV

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

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

Action: For adoption

List of Questions adopted on 12.12.2019.

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

4.3.1. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/X/0083/G

Vertex Pharmaceuticals (Ireland) Limited

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

Scope: "Extension application to add a new strength of 75 mg film-coated tablets of ivacaftor to enable administration to patients aged 6 to less than 11 years.
C.II.6.a - To update sections 4.1, 4.2 and 6.5 the SmPC, and sections 1 and 2 of the PL for the 150 mg film-coated tablet presentations to extend the indication for use in children aged 6 to less than 11 years old in combination with tezacaftor/ivacaftor and to bring it in line with the new dosage form (75 mg film-coated tablets of ivacaftor). The RMP (version 8.6) is updated in accordance. In addition, the MAH took the opportunity to implement minor updates in the Product Information."

Action: For adoption

4.3.2. Lacosamide Accord - lacosamide - EMEA/H/C/004443/X/0007

Accord Healthcare S.L.U.

Rapporteur: John Joseph Borg, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to introduce a new pharmaceutical form (solution for infusion), a new strength (10mg/ml) and a new route of administration (intravenous use)."

Action: For adoption

4.3.3. Praluent - alirocumab - EMEA/H/C/003882/X/0054/G

sanofi-aventis groupe

Rapporteur: Johann Lodewijk Hillege

Scope: "Grouping of:
• Extension application to introduce a new strength of 300 mg solution for injection in pre-filled pen (in a pack of 1 and 3 pens, EU/1/15/1031/019-20)
• B.II.b.3.z
• B.II.d.2.a
• B.II.e.5.a.1
• B.II.e.5.a.1
• B.II.e.5.a.1
• B.II.e.5.a.1
• B.II.e.5.a.1
• B.II.e.6.b
• B.IV.1.c
Update of sections 1, 2, 4.2, 6.3, 6.5 and 8 of the SmPC; the Labelling and Package Leaflet are updated accordingly.
In addition, the applicant has taken the opportunity to update the contact details of the Maltese local representative in the Package Leaflet, to bring the PI in line with the latest QRD template (v. 10.1) and to introduce editorial changes."

Action: For adoption

4.3.4. Symkevi - tezacaftor / ivacaftor - Orphan - EMEA/H/C/004682/X/0015/G

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Extension application to add a new strength of 50/75 mg film-coated tablets of tezacaftor/ivacaftor to enable administration to patients aged 6 to less than 11 years.
C.II.6.a - To update sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.1 of the SmPC, and sections 2, 3 and 6 of the PL for the 100/150 mg film-coated tablet presentations to extend the indication for use in children aged 6 to less than 11 years old in combination with ivacaftor and to bring it in line with the new dosage form (50/75mg film-coated tablets tezacaftor/ivacaftor). The RMP (version 2.1) is updated in accordance.
In addition, the MAH took the opportunity to implement minor updates and formatting changes in the Product Information."

Action: For adoption

4.3.5. Tepadina - thiotepa - Orphan - EMEA/H/C/001046/X/0036

ADIENNE S.r.l.

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension application to introduce a new pharmaceutical form associated with new strength (400 mg powder and solvent for solution for infusion)."

Action: For adoption

4.3.6. Trimbow - beclometasone dipropionate / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004257/X/0008/G

Chiesi Farmaceutici S.p.A.

Rapporteur: Janet Koenig, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Jan Neuhauser

Scope: "Extension application to introduce a new strength (172 µg / 5 µg / 9 µg) grouped with a type II variation (C.I.6.a) to add a new indication (asthma). The RMP (version 6.1) is updated in accordance." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

4.3.7. Trulicity - dulaglutide - EMEA/H/C/002825/X/0045

Eli Lilly Nederland B.V.

Rapporteur: Martina Weise, PRAC Rapporteur: Ilaria Baldelli

Scope: "Extension application to introduce two new strengths of 3 mg and 4.5 mg solution for injection."

Action: For adoption

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

No items

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

No items

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

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

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

Takeda Pharma A/S

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

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

List of experts for SAG Oncology meeting scheduled on 05 March 2020 was adopted via written procedure on 04 March 2020

SAG Report, Oral explanation

Action: For adoption

Request for Supplementary Information adopted on 30.01.2020, 17.10.2019.

See 2.3

5.1.2. Cosentyx - secukinumab - EMEA/H/C/003729/II/0053/G

Novartis Europharm Limited

Rapporteur: Tuomo Lapveteläinen, PRAC Rapporteur: Eva A. Segovia

Scope: "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."

Action: For adoption

Request for Supplementary Information adopted on 12.12.2019.

5.1.3. Intelence - etravirine - EMEA/H/C/000900/II/0058

Janssen-Cilag International NV

Rapporteur: Jean-Michel Race, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Adrien Inoubli

Scope: "To extend the approved therapeutic indication of Intelence in order to include patient population from 2 to 6 years of age based on the 48 week study results from study TMC125-C234/P1090 (A Phase I/II, Open-label Trial to Evaluate the Safety, Tolerability, Pharmacokinetics and Antiviral Activity of Etravirine (ETR) in Antiretroviral (ARV) Treatment-experienced HIV-1 Infected Infants and Children, Aged ≥2 Months to <6 Years). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC and sections 1, 2 and 3 of the PL are updated accordingly. The updated RMP version 13.1 has also been submitted. The RMP (version 13.1) of the product has been updated to remove the completed additional pharmacovigilance activities (TMC125-C234/P1090 (Week 48) and TMC125-EPPICC) from the pharmacovigilance plan of the RMP). The RMP has also been updated to meet the requirements and updated definitions in the European Medicines Agency (EMA) Guideline on good pharmacovigilance practices (GVP) Module V Revision 2 (EMA/838713/2011; Rev 2) and Guidance on the format of the RMP in the European Union (EMA/164014/2018 Rev 2.0.1) including proposed removal of safety concerns.
The MAH took the opportunity to include some typographic changes in Annex II C and D."

Action: For adoption

Request for Supplementary Information adopted on 30.01.2020.

5.1.4. Kineret - anakinra - EMEA/H/C/000363/II/0070

Swedish Orphan Biovitrum AB (publ)

Rapporteur: Mark Ainsworth, Co-Rapporteur: Fátima Ventura, PRAC Rapporteur: Hans Christian Siersted

Scope: "Extension of indication to include the treatment of Familial Mediterranean Fever (FMF) for Kineret, to be given in combination with colchicine, if appropriate; as a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 5.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 30.01.2020.

5.1.5. Latuda - lurasidone - EMEA/H/C/002713/II/0029

Aziende Chimiche Riunite Angelini Francesco S.p.A.

Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication for the treatment of schizophrenia in adolescent from 13 to less than 18 years. As a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) takes the opportunity to update the PI according to the excipient guideline and update the list of local representatives in the Package Leaflet. The RMP version 8 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

5.1.6. Lynparza - olaparib - EMEA/H/C/003726/II/0035

AstraZeneca AB

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

Scope: "Extension of indication to include the use of Lynparza tablets in combination with bevacizumab for the maintenance treatment of adult patients with advanced (FIGO stages III and IV) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy with bevacizumab. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the SmPC are updated. The PL is updated accordingly. In addition, sections 4.4 and 4.8 of the SmPC for Lynparza hard capsules are revised based on updated safety data analysis. Furthermore, the PI is brought in line with the latest QRD template version 10.1. The RMP version 19 has also been submitted."

Action: For adoption

5.1.7. Lynparza - olaparib - EMEA/H/C/003726/II/0036

AstraZeneca AB

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

Scope: "Extension of indication to include the use of Lynparza tablets as monotherapy for the treatment of adult patients with metastatic castration-resistant prostate cancer and homologous recombination repair gene mutations (germline and/or somatic) who have progressed following a prior new hormonal agent. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC are updated. The PL is updated accordingly. In addition, sections 4.4 and 4.8 of the SmPC for Lynparza hard capsules are revised based on updated safety data analysis. The RMP version 20 has also been submitted."

Action: For adoption

5.1.8. Ofev - nintedanib - Orphan - EMEA/H/C/003821/II/0027

Boehringer Ingelheim International GmbH

Rapporteur: Peter Kiely, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication to include new indication for OFEV for the treatment of other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype based on the results of pharmacology studies and the double-blind, randomised, placebo-controlled phase III trial (INBUILD). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to reflect the use of Ofev in the new indication. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to introduce minor formatting changes in the PI. Furthermore, the PI is brought in line with the latest QRD template version 10.1. The RMP version 9.0 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

Request for Supplementary Information adopted on 12.12.2019.

5.1.9. Olumiant - baricitinib - EMEA/H/C/004085/II/0016

Eli Lilly Nederland B.V.

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension of indication to include a new indication in the treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy for Olumiant; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Minor editorial changes were brought to the Labelling. Furthermore, the Annex II is brought in line with the latest QRD template version 10.1. The RMP version 8.1 has also been submitted." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

5.1.10. Ruconest - conestat alfa - EMEA/H/C/001223/II/0053/G

Pharming Group N.V

Rapporteur: Andrea Laslop, PRAC Rapporteur: Jan Neuhauser

Scope: "Update of indication to include children in the treatment of acute angioedema attacks with hereditary angioedema (HAE) due to C1 esterase inhibitor deficiency. This is based from Study C1 1209 in children. In addition final efficacy and safety data from the OLE phases of Studies C1 1304 and 1205 and the completed Study C1 1310 are submitted together with final study results of Studies C1 1207 and 3201, concerning prophylactic treatment of HAE patients. Consequently the product information has been updated. Furthermore, the company is requesting an extension for the completion of registry Study C1 1412. The current RMP (V 18.0) states that completion of the final study report for Study C1 1412 is anticipated 31 March 2020. Although patient enrolment has increased, the study will not be completed on time. The MAH would therefore like to request an extension of the study completion date to submit the final report date for Study C1 1412 of 30 June 2022. In addition, as mentioned below, the RMP has also been aligned to RMP template version 2.0.1.
The product information has also been updated to align with the most recent QRD template, version 10.1."

Action: For adoption

Request for Supplementary Information adopted on 30.01.2020.

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

Eli Lilly Nederland B.V.

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

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

Action: For adoption

Request for Supplementary Information adopted on 12.12.2019.

5.1.12. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0033

Roche Registration GmbH

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

Scope: "Extension of indication to include the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumours express PD-L1 for Tecentriq based on the results of the pivotal study GO29431 (IMpower110), comparing atezolizumab monotherapy to platinum-based chemotherapy. As a consequence, sections 4.1, 4.2, 4.8

and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. The RMP version 12.0 has also been submitted."

Action: For adoption

5.1.13. Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0013

Pfizer Europe MA EEIG

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jean-Michel Dogné

Scope: "Extension of indication for Trumenba to include active immunisation of children 1-9 years old. Sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated in parallel based on the results from the two pivotal studies B1971017 and B1971035. The Package Leaflet is updated in accordance. The RMP version 2.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to submit a corrected version of the final report of study B1971016, which was included in the initial marketing authorisation application."

Action: For adoption

Request for Supplementary Information adopted on 14.11.2019, 25.07.2019, 28.02.2019.

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

Alexion Europe SAS

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

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

Action: For adoption

Request for Supplementary Information adopted on 14.11.2019.

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

Pfizer Ireland Pharmaceuticals

Rapporteur: Bjorg Bolstad, Co-Rapporteur: Simona Stankeviciute, 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 to SmPC sections 2 and 4.4 and PL section 2 and the volumes of distribution of ceftazidime and avibactam in SmPC section 5.2. Furthermore, the MAH is also introducing a correction in the Czech SmPC to add missing values in the table in SmPC section 5.1. The RMP version 3.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 25.07.2019.

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

Astellas Pharma Europe B.V.

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

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

revised timetable

Action: For discussion

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

No items

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. idecabtagene vicleucel - H0004662

Treatment of adult patients with multiple myeloma who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody

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

Action: For adoption

8.1.2. trastuzumab deruxtecan - H0005124

Treatment of HER2-positive breast cancer and HER2-positive gastric cancer. DS-8201a as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received 2 or more prior anti-HER2 therapies

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. Desloratadine ratiopharm - desloratadine - EMEA/H/C/002404/II/0023/G

ratiopharm GmbH

Rapporteur: Koenraad Norga, Co-Rapp: Peter Kiely, PRAC Rapporteur: Jean-Michel Dogné

Scope: "C.I.5.b - Change in the legal status of desloratadine ratiopharm from 'medicinal product subject to medical prescription' to 'medicinal product not subject to medical prescription' in view of the safety profile of desloratadine ratiopharm and the post-marketing experience already available with other medicinal products containing similar long acting histamine antagonists. The RMP version 1.0 has also been submitted. In addition, the MAH also took the opportunity to bring the PI in line with the latest QRD template (version 10.1), to update the list of local representatives in the package leaflet and to make editorial changes.
C.I.6.b - To delete the therapeutic indication in adolescents aged 12 years and older for the relief of symptoms associated with allergic rhinitis and urticaria. Section 4.1 of the SmPC and section 1 of the PL are updated accordingly."

Action: For discussion

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

Recordati Ireland Ltd

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

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

Action: For discussion

Request for Supplementary Information adopted on 12.12.2019.

9.1.3. Kanuma - sebelipase alfa - EMEA/H/C/004004/II/0026/G, Orphan

Alexion Europe SAS

Rapporteur: Bart Van der Schueren, Co-Rapporteur: Fátima Ventura

Scope: Grouped variations consisting of
1) update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the clinical information based on the pooled safety and efficacy analysis of already submitted studies (namely study LAL-CL04: an open label multicentre extension study to evaluate the long-term safety, tolerability, and efficacy of sebelipase alfa (SBC-102) in adult subjects with liver dysfunction due to lysosomal acid lipase deficiency (LAL-D) who previously received treatment in study LAL-CL01; study LAL-CL03: an open label, multicentre, dose escalation study to evaluate the safety, tolerability, efficacy, pharmacokinetics, and pharmacodynamics of SBC-102 in children with growth failure due to LAL-D; study LAL-CL06: a multicentre, open-label study of sebelipase alfa in patients with LAL-D; study LAL-CL08: a phase 2, open label, multicentre study to evaluate the safety, tolerability, efficacy, and pharmacokinetics of sebelipase alfa in infants with rapidly progressive LAL-D; study LAL-CL02: a multicentre, randomized, placebo-controlled study of SBC-102 in patients with LAL-D) and updated population pharmacokinetic (PK) analyses in children and adults. The package leaflet and the RMP (version 4.0) are updated accordingly. Annex II is also updated to remove the obligation related to the provision of study LAL-CL08;
2) submission of the final report from study LAL-EA01: an open-label study with sebelipase alfa 1 mg/kg every other week for up to 78 weeks or until drug commercialisation in the United States (US) patients who did not otherwise qualify for an active sebelipase alfa trial (expanded access protocol)

Action: For adoption

9.1.4. Lokelma - sodium zirconium cyclosilicate - EMEA/H/C/004029/II/0013

AstraZeneca AB

Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Kirsti Villikka

Scope: "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."

Action: For discussion

Request for Supplementary Information adopted on 12.12.2019, 19.09.2019.

9.1.5. PD1/PD-L1 targeting agents

Scope: LEG procedure, Response from the Biostatistics Working Party

Action: For discussion

9.1.6. Tyverb - lapatinib - EMEA/H/C/000795/II/0059

Novartis Europharm Limited

Rapporteur: Filip Josephson

Scope: "Update of section 5.1 of the SmPC in order to update Table 8 based on updated/corrected results from study EGF114299/LAP016A2307, an interventional study with progression free survival rate as primary objective, original report submitted during procedure EMEA/H/C/00795/II/0051."

Action: For adoption

Request for Supplementary Information adopted on 14.11.2019, 26.04.2019.

10. Referral procedures

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

No items

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

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: Opinion

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: Martina Weise, Referral Co-Rapporteurs: Kristina Dunder

Scope: Report from the ad-hoc expert group meeting scheduled on 27-28 February 2020,

QWP, SWP, PRAC and BWP responses to CHMP lists of questions

Action: For discussion

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

No items

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

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

MAH: Sun Pharmaceutical Industries Europe B.V.

Referral Rapporteur: Johann Lodewijk Hillege, Referral Co-Rapporteur: Giuseppa Pistritto

Scope: Opinion

Action: For adoption

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

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

MAH: Laboratorios Tillomed Spain S.L.U

Referral Rapporteur: TBC, Referral Co-Rapporteur: TBC

Scope: Start of procedure, timetable, appointment of Rapporteurs

Action: For adoption

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

10.4.3. Ibuprofen Kabi – EMEA/H/A-29(4)/1498

MAH: Fresenius Kabi Deutschland GmbH

Referral Rapporteur: TBC, Referral Co-Rapporteur: TBC

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

Action: For adoption

Summary: Decentralised Procedure number: DE/H/6040/001/DC, notification by the German Agency notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC.

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

MAHs: various

Referral Rapporteur: Ondrej Slanar, Referral Co-Rapporteur: Janet Koenig

Scope: Opinion

Action: For adoption

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

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

10.6.2. Gadolinium-containing contrast agents (GdCA): Gadobutrol (NAP); gadodiamide (NAP); gadopentetic acid (NAP); gadoteric acid (NAP); gadoteridol (NAP); gadoxetic acid (NAP) - EMEA/H/A-31/1097; Optimark (withdrawn) – gadoversetamide - EMEA/H/C/000745/ANX/014.12

Applicant: various

Referral Rapporteur: Johann Lodewijk Hillege

Scope: Final analysis report of long-term effects Study ALS-Gd64/001 (“Bone study”) on gadolinium accumulation in the bone for gadoversetamide, gadoteric acid, gadobutrol, gadoxetic acid, gadopentetic acid and gadodiamide containing medicinal products.

Timetable

Action: For adoption

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

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

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

Scope: Opinion

Action: For adoption

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

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

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

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

Action: For information

13.2. Innovation Task Force briefing meetings

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Rules of procedures

Amendments to the existing Rules of procedures of EMA's scientific committees

Action: For adoption

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 09-12 March 2020

Action: For information

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

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 18-20 March 2020

Action: For information

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 02-04 March 2020

Action: For information

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at March 2020 PDCO

Action: For information

Report from the PDCO meeting held on 24-27 March 2020

Action: For information

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 17-19 March 2020

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 24-26 March 2020

Action: For information

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

14.3.1. Ad-hoc Influenza Working Group

Scope EU Strain selection for the Influenza Vaccines for the Season 2020/2021: Report from the Ad Hoc Influenza working group to the BWP

Action: For adoption

Postponed from February.

Scope: EU Recommendation for the Seasonal Influenza Vaccine Composition for the Season 2020/2021

Action: For adoption

14.3.2. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP March 2020 meeting to CHMP for adoption:

- 10 reports on products in scientific advice and protocol assistance
- 7 reports on products in pre-authorisation procedures
- 1 report on products in plasma master file

Action: For adoption

14.3.3. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 25-26 March 2020.

Action: For adoption

14.3.4. Pharmacokinetics Working Party (PKWP)

Chair: Henrike Potthast

Election of PKWP vice chair

Previous vice chair Henrike Potthast has now become the chair of PKWP.

Action: For election

14.3.5. Quality Working Party (QWP)

Chair: Blanka Hirschlerova

Election of new QWP vice chair

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

Action: For election

14.3.6. Safety Working Party (SWP)

Chair: Jan Willem Van der Laan

CMDh question to SWP - Determination of acceptable intake levels of chlorobutanol as excipient

Action: For adoption

14.3.7. Scientific Advice Working Party (SAWP)

Chair: Anja Schiel

Report from the SAWP meeting held on 09-12 March 2020. Table of conclusions

Action: For information

Scientific advice letters:

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

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

2020 initial marketing authorisation application submissions with eligibility request to central procedure

Action: For information

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Update on COVID-19

Action: For information

16. Explanatory notes

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

Oral explanations *(section 2)*

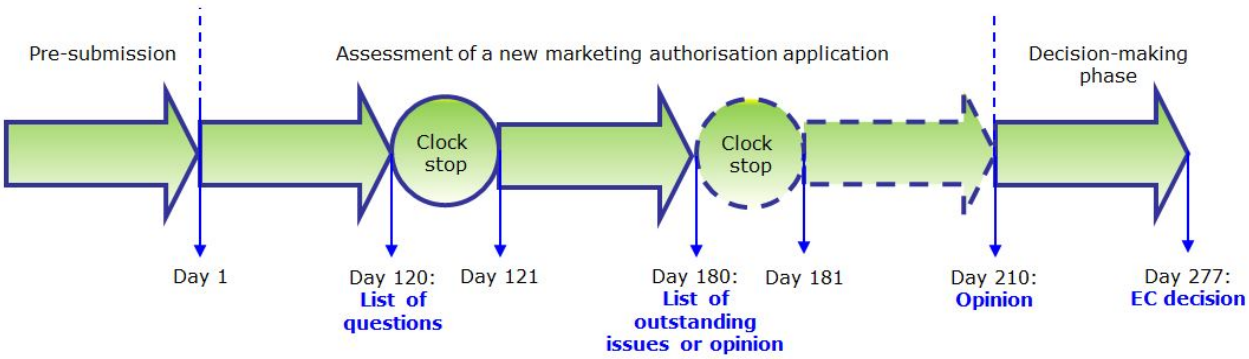
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

Initial applications *(section 3)*

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

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

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



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

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

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

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

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

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

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

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

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

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

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

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

Re-examination procedures *(section5.3)*

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

Withdrawal of application *(section 3.7)*

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

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

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

Pre-submission issues *(section 8)*

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

Post-authorisation issues *(section 9)*

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

Referral procedures *(section 10)*

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

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

Pharmacovigilance issues *(section 11)*

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

Inspections Issues *(section 12)*

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

Innovation task force *(section 13)*

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

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

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

Satellite groups / other committees *(section 14.2)*

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

Invented name issues *(section 14.3)*

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

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

18 May 2020
EMA/CHMP/158294/2020 Corr[1]

Annex to 23-26 March 2020 CHMP Agenda

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[1] Correction in B.4

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A. PRE-SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

Final Outcome of Rapporteurship allocation for March 2020: **For adoption**

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

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

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

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

Kolbam - cholic acid -
EMEA/H/C/002081/S/0031, Orphan
Retrophin Europe Ltd, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Agni Kapou

Lojuxta - lomitapide -
EMEA/H/C/002578/S/0036
Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 30.01.2020, 14.11.2019.

Myalepta - metreleptin -
EMEA/H/C/004218/S/0009, Orphan
Aegerion Pharmaceuticals B.V., Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Adam Przybylkowski
Request for Supplementary Information adopted on 30.01.2020.

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

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Brinavess - vernakalant -
EMEA/H/C/001215/R/0037
Correvio, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst

Daxas - roflumilast -
EMEA/H/C/001179/R/0039
AstraZeneca AB, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Maria del Pilar Rayon
Request for Supplementary Information adopted on 30.01.2020.

Intuniv - guanfacine -
EMEA/H/C/003759/R/0022
Shire Pharmaceuticals Ireland Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Maria del Pilar Rayon

Praluent - alirocumab -
EMEA/H/C/003882/R/0055
sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Brigitte Keller-Stanislawski

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Aripiprazole Sandoz - aripiprazole -
EMEA/H/C/004008/R/0014
Sandoz GmbH, Generic, Generic of Abilify, Rapporteur: John Joseph Borg, PRAC Rapporteur: Ana Sofia Diniz Martins

Aripiprazole Zentiva - aripiprazole -
EMEA/H/C/003899/R/0012
Zentiva, k.s., Generic, Generic of Abilify, Rapporteur: John Joseph Borg, PRAC Rapporteur: Ana Sofia Diniz Martins
Request for Supplementary Information adopted on 30.01.2020.

Cresemba - isavuconazole - EMEA/H/C/002734/R/0027, Orphan
Basilea Pharmaceutica Deutschland GmbH, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Adam Przybylkowski

Duloxetine Zentiva - duloxetine - EMEA/H/C/003935/R/0009
Zentiva k.s., Generic, Generic of Cymbalta, Yentreve, Rapporteur: Kristina Dunder, PRAC Rapporteur: Maria del Pilar Rayon

Ivabradine Anpharm - ivabradine - EMEA/H/C/004187/R/0014
ANPHARM Przedsiebiorstwo Farmaceutyczne S.A., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 30.01.2020.

Lenvima - lenvatinib - EMEA/H/C/003727/R/0031
Eisai GmbH, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin
Request for Supplementary Information adopted on 12.12.2019.

Odomzo - sonidegib - EMEA/H/C/002839/R/0028
Sun Pharmaceutical Industries Europe B.V., Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Željana Margan Koletić
Request for Supplementary Information adopted on 30.01.2020.

Pemetrexed Lilly - pemetrexed - EMEA/H/C/004114/R/0011
Eli Lilly Nederland B.V., Generic, Generic of Alimta, Rapporteur: Alar Irs, PRAC Rapporteur: Ghania Chamouni

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

Pregabalin Zentiva - pregabalin - EMEA/H/C/003900/R/0021
Zentiva k.s., Generic, Generic of Lyrica,

Rapporteur: Alar Irs, PRAC Rapporteur: Liana Gross-Martirosyan
Request for Supplementary Information adopted on 30.01.2020.

Raxone - idebenone -
EMEA/H/C/003834/R/0020, Orphan
Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Amelia Cupelli

VPRIV - velaglucerase alfa -
EMEA/H/C/001249/R/0045, Orphan
Shire Pharmaceuticals Ireland Limited, Rapporteur: Martina Weise, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Martin Huber

Zalviso - sufentanil -
EMEA/H/C/002784/R/0016
Grunenthal GmbH, Rapporteur: Milena Stain, PRAC Rapporteur: Adam Przybylkowski

B.2.3. Renewals of Conditional Marketing Authorisations

LIBTAYO - cemiplimab -
EMEA/H/C/004844/R/0006
Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Sinan B. Sarac, Co-Rapporteur: Tuomo Lapveteläinen, PRAC Rapporteur: Menno van der Elst

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 09-12 March 2020
PRAC:

Signal of tuberculosis:
Immune checkpoint inhibitors - TECENTRIQ, BAVENCIO, LIBTAYO, IMFINZI, YERVOY, OPDIVO, KEYTRUDA

PRAC recommendation on a variation

Action: For adoption

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

EMEA/H/C/PSUSA/00002660/201907
(romiplostim)

CAPS:
Nplate (EMEA/H/C/000942) (romiplostim), Amgen Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "Period Covered From: 30/07/2016 To: 30/07/2019"

EMEA/H/C/PSUSA/00009305/201908
(teduglutide)
CAPS:
Revestive (EMEA/H/C/002345) (teduglutide), Shire Pharmaceuticals Ireland Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Hans Christian Siersted, "Period Covered From: 29/08/2018 To: 29/08/2019"

EMEA/H/C/PSUSA/00010025/201908
(linaclotide)
CAPS:
Constella (EMEA/H/C/002490) (linaclotide), Allergan Pharmaceuticals International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Period Covered From: 28/08/2018 To: 28/08/2019"

EMEA/H/C/PSUSA/00010081/201908
(cobicistat)
CAPS:
Tybost (EMEA/H/C/002572) (cobicistat), Gilead Sciences Ireland UC, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ana Sofia Diniz Martins, "Period Covered From: 27/08/2018 To: 26/08/2019"

EMEA/H/C/PSUSA/00010403/201909
(pembrolizumab)
CAPS:
Keytruda (EMEA/H/C/003820) (pembrolizumab), Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Menno van der Elst, "Period Covered From: 03/09/2018 To: 03/09/2019"

EMEA/H/C/PSUSA/00010409/201908
(panobinostat)
CAPS:
Farydak (EMEA/H/C/003725) (panobinostat), Secura Bio Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sofia Trantza, "Period Covered From: 23/08/2018 To: 22/08/2019"

EMEA/H/C/PSUSA/00010715/201908

(patisiran) CAPS: **Onpattro** (EMEA/H/C/004699) (patisiran), Alnylam Netherlands B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Rhea Fitzgerald, "Period Covered From: 08/02/2019 To: 08/08/2019"	

B.4. EPARs / WPARs

Fetcroja - cefiderocol - EMEA/H/C/004829 Shionogi B.V., treatment of infections due to aerobic Gram-negative bacteria, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Rituximab Mabion Duplicate - rituximab - EMEA/H/C/005387 Mabion Spolka Akcyjna, treatment of Non-Hodgkin's lymphoma (NHL), Chronic lymphocytic leukaemia (CLL), Duplicate, Duplicate of Rituximab Mabion, Similar biological application (Article 10(4) of Directive No 2001/83/EC) **WPAR**	For information only. Comments can be sent to the PL in case necessary.
Rituximab Mabion - rituximab - EMEA/H/C/004807 Mabion Spolka Akcyjna, treatment of Non-Hodgkin's lymphoma (NHL), Chronic lymphocytic leukaemia (CLL) and Rheumatoid arthritis, Similar biological application (Article 10(4) of Directive No 2001/83/EC) **WPAR**	For information only. Comments can be sent to the PL in case necessary.
Tigecycline Accord - tigecycline - EMEA/H/C/005114 Accord Healthcare S.L.U., 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, Generic, Generic of Tygacil, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Afstyla - lonoctocog alfa - EMEA/H/C/004075/II/0029/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus	
Alprolix - eftrenonacog alfa - EMEA/H/C/004142/II/0028, Orphan Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop Opinion adopted on 12.03.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Bexsero - meningococcal group B vaccine (recombinant, component, adsorbed) - EMEA/H/C/002333/II/0087 GSK Vaccines S.r.l, Rapporteur: Kristina Dunder Opinion adopted on 12.03.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cometriq - cabozantinib - EMEA/H/C/002640/II/0037, Orphan Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
Delstrigo - doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746/II/0012/G Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson Opinion adopted on 05.03.2020. Request for Supplementary Information adopted on 30.01.2020.	Positive Opinion adopted by consensus on 05.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Erelzi - etanercept - EMEA/H/C/004192/II/0024/G Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 12.03.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Eylea - aflibercept - EMEA/H/C/002392/II/0055/G Bayer AG, Rapporteur: Alexandre Moreau Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 12.12.2019, 07.11.2019.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Fiasp - insulin aspart - EMEA/H/C/004046/II/0018/G Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin Opinion adopted on 12.03.2020. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 16.01.2020.	
Flixabi - infliximab - EMEA/H/C/004020/II/0053 Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus	
GONAL-f - follitropin alfa - EMEA/H/C/000071/II/0148 Merck Europe B.V., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 23.01.2020.	
Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0111/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 19.03.2020, 12.12.2019.	Request for supplementary information adopted with a specific timetable.
Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0112/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
HyQvia - human normal immunoglobulin - EMEA/H/C/002491/II/0054 Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 12.03.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
ILARIS - canakinumab - EMEA/H/C/001109/II/0068/G Novartis Europharm Limited, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 19.03.2020.	Positive Opinion adopted by consensus on 19.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kanuma - sebelipase alfa - EMEA/H/C/004004/II/0023, Orphan Alexion Europe SAS, Rapporteur: Bart Van der Schueren Opinion adopted on 19.03.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 19.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0084 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri Opinion adopted on 05.03.2020. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 05.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 30.01.2020.	
Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0080/G Genzyme Europe BV, Co-Rapporteur: Koenraad Norga Opinion adopted on 12.03.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Nivestim - filgrastim - EMEA/H/C/001142/II/0059 Pfizer Europe MA EEIG, Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 30.01.2020.	
Nulojix - belatacept - EMEA/H/C/002098/II/0065/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
Obizur - susoctocog alfa - EMEA/H/C/002792/II/0027 Baxalta Innovations GmbH, Rapporteur: Andrea Laslop	
Ogivri - trastuzumab - EMEA/H/C/004916/II/0011/G Mylan S.A.S, Rapporteur: Koenraad Norga Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
Omnitrope - somatropin - EMEA/H/C/000607/II/0062/G Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 12.03.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Onpattro - patisiran - EMEA/H/C/004699/II/0011/G, Orphan Alnylam Netherlands B.V., Rapporteur: Kristina Dunder Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 06.02.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ovaleap - follitropin alfa - EMEA/H/C/002608/II/0032 Theramex Ireland Limited, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 12.03.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pifeltro - doravirine - EMEA/H/C/004747/II/0010/G	Positive Opinion adopted by consensus on 05.03.2020. The Icelandic and Norwegian CHMP

Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson Opinion adopted on 05.03.2020. Request for Supplementary Information adopted on 30.01.2020.	Members were in agreement with the CHMP recommendation.
Remsima - infliximab - EMEA/H/C/002576/II/0080/G Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola Opinion adopted on 12.03.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Rizmoic - naldemedine - EMEA/H/C/004256/II/0005/G Shionogi B.V., Rapporteur: Mark Ainsworth Opinion adopted on 05.03.2020. Request for Supplementary Information adopted on 23.01.2020.	Positive Opinion adopted by consensus on 05.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Silapo - epoetin zeta - EMEA/H/C/000760/II/0056 STADA Arzneimittel AG, Rapporteur: Martina Weise	
Spectrila - asparaginase - EMEA/H/C/002661/II/0015/G medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 16.01.2020.	
Starlix - nateglinide - EMEA/H/C/000335/II/0036/G Novartis Europharm Limited, Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 16.01.2020.	
TAKHZYRO - lanadelumab - EMEA/H/C/004806/II/0012/G, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
Trazimera - trastuzumab - EMEA/H/C/004463/II/0011 Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 05.03.2020. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 05.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 16.01.2020.	
Ziextenzo - pegfilgrastim - EMEA/H/C/004802/II/0004 Sandoz GmbH, Rapporteur: Andrea Laslop Opinion adopted on 19.03.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 19.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1758 **Infanrix hexa-** **EMEA/H/C/000296/WS1758/0270** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 12.03.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Abilify Maintena - aripiprazole - EMEA/H/C/002755/II/0035 Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Bruno Sepodes, "update of the PI to add an alternate initiation regimen"	
Ambirix - hepatitis A (inactivated) and hepatitis B (rDNA) vaccine (adsorbed) - EMEA/H/C/000426/II/0105 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of sections 4.2 and 5.1 of the Ambirix SmPC in order to reflect information on the long-term antibody persistence and immune memory up to 15 years after primary immunisation of adolescents, based on data from the Phase IV study HAB-084 EXT Y11-15 (An open, long-term follow-up study to evaluate long-term antibody persistence and immune memory between 11 and 15 years after the primary study HAB-084). The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1 and make some minor editorial changes. Furthermore, the MAH took the opportunity to update Annex II with regards to PSUR requirements." Request for Supplementary Information adopted on 30.01.2020.	
Benlysta - belimumab - EMEA/H/C/002015/II/0077	

GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder, "Update of section 4.2 of the SmPC in order to update the information on elderly patients based on the interim results from study BEL116559 listed as a category 3 study in the RMP; this is a meta-analysis to assess efficacy and safety in elderly subjects treated in selected belimumab studies."

CABOMETYX - cabozantinib - EMEA/H/C/004163/II/0012

Ipsen Pharma, Rapporteur: Bjorg Bolstad, "Update of section 4.4 of the SmPC to include the risk of Osteonecrosis as a warning. Update of section 4.8 of the SmPC based on the Company Core Safety Information:
- to remove Anaemia, Oral pain and Dry mouth from the list of adverse reactions (ADRs), - to add Dysphagia and Hyperkeratosis to the existing ADR, - to replace Peripheral sensory neuropathy by Peripheral neuropathy in order to reflect the broader medical concept and to add DVT (Deep vein thrombosis) to the existing ADR venous thrombosis in order to alert prescribers to the most frequently reported type of venous thrombosis. Changes to the frequency categorisation of some ADRs are also proposed based on new pooled data. The Package Leaflet is updated accordingly. The MAH took the opportunity to align the product Information with the QRDv10.1 and update the local representative information of Hungary."
Request for Supplementary Information adopted on 23.01.2020.

Cometriq - cabozantinib - EMEA/H/C/002640/II/0035, Orphan

Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.2 to introduce a clarification in alignment with Cabometyx; update of section 4.4 of the SmPC to include the addition of the risk of diarrhoea and additional test to the existing risks of thromboembolic events, haemorrhage, wound complications and RPLS (Reversible posterior leukoencephalopathy syndrome). Update of section 4.8 of the SmPC, based on the Company Core Safety Information, to remove oropharyngeal pain from the list of adverse reactions (ADRs) and to add DVT (Deep vein thrombosis) to the existing ADR venous thrombosis in order to alert prescribers to the most frequently reported type of venous

thrombosis. Changes to the frequency categorisation of some ADRs are also proposed based on new pooled data. The Package Leaflet is updated accordingly. The MAH took the opportunity to align the product Information with the QRDv10.1 and update the local representative information of Hungary." Request for Supplementary Information adopted on 23.01.2020.	
Cometriq - cabozantinib - EMEA/H/C/002640/II/0036, Orphan Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, "Submission of PK results from the clinical study ADVL1211 (an open-label trial to evaluate toxicity, tolerability, pharmacokinetics and pharmacodynamics of cabozantinib in children with refractory or relapsed malignant solid tumours (MEA 019))." Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
Darzalex - daratumumab - EMEA/H/C/004077/II/0035, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, "C.I.4 - Update of section 5.1 of the SmPC in order to update efficacy information based on interim results from phase III studies of 3 approved combination treatments of daratumab (D) in relapsed or refractory MM patients MMY3003 (DRd vs Rd) and MMY3004 (DVd vs Vd) and in newly diagnosed MM patients MMY3007 (DVd vs Vd). In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet ."	
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."
Request for Supplementary Information adopted on 12.12.2019, 14.11.2019.

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."
Request for Supplementary Information adopted on 30.01.2020, 19.09.2019.

Emgality - galcanezumab - EMEA/H/C/004648/II/0009
Eli Lilly Nederland B.V., Rapporteur: Daniela Melchiorri, "Update of sections 4.2 and 5.1 of the SmPC following final results from a CONQUER study (A Randomized, Double-Blind, Placebo-Controlled Study of Galcanezumab in Adults with Treatment-Resistant Migraine); the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct Slovakian contact information in the Package Leaflet."
Request for Supplementary Information adopted on 30.01.2020.

EVRA - ethinylestradiol / norelgestromin - EMEA/H/C/000410/II/0046/G
Janssen-Cilag International NV, Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.5 and 4.8 of the SmPC in order to add drug-drug interaction information on use with cobicistat and to add anaphylactic reaction to the list of adverse drug reactions (ADRs) with frequency rare, following the update of the company's core data sheet (CCDS) due to new data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.1."

Fexinidazole Winthrop - fexinidazole - EMEA/H/W/002320/II/0002 sanofi-aventis groupe, Rapporteur: Fátima Ventura, "Update of section 4.5 of the SmPC with data on pharmacokinetic interactions, based on results obtained from five in vitro pharmacokinetics study reports and the Drug Drug Interaction phase I study (INT15307), the latter mentioned in the RMP as "other study" in post-opinion development plan." Opinion adopted on 12.03.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Glivec - imatinib - EMEA/H/C/000406/II/0117 Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, "Update of section 4.6 of the SmPC to include that women of childbearing potential must be advised to use effective contraception for at least 15 days after stopping treatment with imatinib, based on a company review of the company Core Data Sheet. The PL has been updated accordingly." Request for Supplementary Information adopted on 30.01.2020, 10.10.2019.	
IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0034, Orphan CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, "Submission of a variation to update the dosing regimen as follows: -21-day prophylaxis regimen with rIX-FP at a dose of 100 IU/kg body weight for patients ≥ 12 years who are well controlled on a 14-day prophylaxis regimen. -10- or 14-day prophylaxis regimen with rIX-FP at a dose of 75 IU/kg body weight for patients < 12 years who are well controlled on a 7-day prophylaxis regimen. This submission also updates the existing population PK model with additional intravenous and subcutaneous (SC) data from the PTPs in the PTP arm of study CSL654_3003 and re-evaluates the covariates that are possible determinants of PK variability." Request for Supplementary Information adopted on 14.11.2019.	
Juluca - dolutegravir / rilpivirine - EMEA/H/C/004427/II/0016 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." Request for Supplementary Information adopted on 12.12.2019, 14.11.2019.	
Kalydeco - ivacaftor - EMEA/H/C/002494/II/0084, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 5.1 of the SmPC in order to include the information based on results from study VX14-661-110, which is a Phase 3, multicenter, open label, rollover study for Studies 103, 106, 107, 108, 109, 111, 112, and 114 designed to evaluate the long-term safety and tolerability of TEZ/IVA treatment in combination with ivacaftor for 96 weeks in cystic fibrosis (CF) subjects 12 years and older, homozygous or heterozygous for the F508del CFTR mutation." Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
Kisqali - ribociclib - EMEA/H/C/004213/II/0018 Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 5.2 of the SmPC to include updated information about the use of Kisqali in patients with mild or moderate renal impairment based on the results of Study CLEE011A2116 Part II and additional data from breast cancer patients with mild or moderate renal impairment." Request for Supplementary Information adopted on 14.11.2019.	
Obizur - susoctocog alfa - EMEA/H/C/002792/II/0030 Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, "Update of sections 4.4 and 4.8 of the SmPC to add information on anamnesic reaction	

and to list it with the frequency unknown."	
Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0123 Boehringer Ingelheim International GmbH, Rapporteur: Mark Ainsworth, "Update of section 4.8 of the SmPC in order to update the safety information regarding neutropenia and agranulocytosis following update to the Pradaxa Company Core Data Sheet. The Package Leaflet are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make Minor Linguistic Changes to the several language versions of the Product Information." Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
Praluent - alirocumab - EMEA/H/C/003882/II/0053 sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Submission of the final report from study DFI14223, listed as a category 3 study in the RMP in order to fulfil MEA 029. The submission serves also to comply with article 46 of the regulation (EC) N° 1901/2006 (as amended). This is an 8-week open label, sequential, repeated dose-finding study to evaluate the efficacy, safety and PK profile of alirocumab in children and adolescents with heterozygous familial hypercholesterolemia followed by an extension phase." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pravafenix - fenofibrate / pravastatin sodium - EMEA/H/C/001243/II/0028/G Laboratoires SMB s.a., Rapporteur: Jean-Michel Race, "Grouping of variations following a request from PRAC as part of PSUSA/00001363/201804: - Update of section 4.8 of the SmPC to add 'dermatomyosis', 'lichenoid eruption' and 'erythematous lupus syndrome' as new adverse drug reactions. - Update of sections 4.4 and 4.5 of the SmPC to include a new warning regarding the concomitant use with glecaprevir/pibrentasvir - Update of sections 4.4 and 4.5 of the SmPC to amend the current warning regarding co-administration with fusidic acid and the risk of	Positive Opinion adopted by consensus on 19.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

rhabdomyolysis. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include 'hepatitis' as an adverse drug reaction in section 4.8 of the SmPC as it is already included in section 4 of the Package Leaflet and to bring the PI in line with version 10 and 10.1 of the QRD template." Opinion adopted on 19.03.2020.	
PREVYMIS - letermovir - EMEA/H/C/004536/II/0016/G, Orphan Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "C.I.4 (type II) – Update of sections 4.4 and 6.6 of the SmPC to include the recommendation to use an in-line filter at the point of administration for finished product Prevymis 240 mg and 480 mg concentrate for solution for infusion (EU/1/17/1245/003-004). The package leaflet and labelling are updated accordingly. B.II.d.1.z (type IB) C.1.11.z (type IB) - Change in the due date of the Annex II condition for the medicinal product Prevymis 240 mg and 480 mg concentrate for solution for infusion (EU/1/17/1245/003-004) from 31 May 2020 to 31 May 2021." Request for Supplementary Information adopted on 12.12.2019.	
Qutenza - capsaicin - EMEA/H/C/000909/II/0049 Grunenthal GmbH, Rapporteur: Bruno Sepodes, "Update of section 4.8 of the SmPC in order to update the safety information on adverse reactions frequencies based on latest clinical data pooling; the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version." Request for Supplementary Information adopted on 19.03.2020.	Request for supplementary information adopted with a specific timetable.
SonoVue - sulphur hexafluoride - EMEA/H/C/000303/II/0040 Bracco International B.V., Rapporteur: Alexandre Moreau, "Update of annex II.D to amend the description and due date of study BR1-145 (ANX 002), an observational study of SonoVue/Lumason- enhanced urosonography in paediatric subjects with known or suspected	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

vesicoureteral reflux to assess subject management decision and changes during a follow-up period of at least 12-months among children undergoing SonoVue/Lumason-enhanced Voiding Urosonography (VUS) (VUS group) in comparison with children undergoing Voiding cystourethrography (VCUG) (VCUG group) for assessment of VUR, following the adoption of the final draft protocol by CHMP. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement some formatting changes (hyperlink on Appendix V) in the SmPC and in the Package Leaflet." Opinion adopted on 12.03.2020.	
SonoVue - sulphur hexafluoride - EMEA/H/C/000303/II/0041 Bracco International B.V., Rapporteur: Alexandre Moreau, "Update of section 4.8 of the SmPC to add 'Kounis symdrome' as a new adverse drug reaction based on a review of post-marketing cases and of the literature. The Package Leaflet is updated accordingly." Opinion adopted on 12.03.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
TAGRISSO - osimertinib - EMEA/H/C/004124/II/0033 AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, "Update of section 5.1 of the SmPC in order to reflect the final Overall Survival (OS) analysis from study D5160C00007 (FLAURA) as recommended by the CHMP in the context of procedure No EMEA/H/C/004124/II/0019. In addition, results from a biomarker analysis from FLAURA study has also been provided as recommended by the CHMP. The MAH also took the opportunity of this variation to add the respective strength and pharmaceutical form to the correspondent Marketing Authorisation Number in the SmPC and Labelling." Opinion adopted on 12.03.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0036 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Submission of the final report from study GO28915 (OAK) listed as a category 3 study in the RMP. This is a Phase III, open-label multicenter, randomized study to investigate the efficacy and safety of atezolizumab (anti−PD-L1 antibody) compared with docetaxel in patients with NSCLC after failure with	Request for supplementary information adopted with a specific timetable.

platinum-containing chemotherapy. In addition, the MAH submitted integrated analyses of the potential relationship of ADA and safety we based on studies IMvigor210, IMvigor211, OAK, POPLAR, IMpower150, IMpower130, IMpower131, IMpower132, IMpower133 and IMpassion130 as recommended by the CHMP." Request for Supplementary Information adopted on 12.03.2020.	
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0037 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to amend the information regarding immunogenicity further to the assessment of the effect of atezolizumab neutralising antibodies on the pharmacokinetics and efficacy endpoints including OS, PFS and ORR on the NSCLC studies POPLAR, OAK, IMpower 150, IMpower 130, IMPower 131 and IMpower 132 as well as on studies IMvigor 211 (UC), IMmotion 151 (RCC), IMpower 133 (SCLC) and IMpassion 130 (TNBC), as recommended by the CHMP." Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
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." Request for Supplementary Information adopted on 12.12.2019, 14.11.2019.	
Translarna - ataluren - EMEA/H/C/002720/II/0056/G, Orphan PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "C.I.13:	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Submission of final results of 8 in vitro genotoxicity studies (not included as post-authorisation measures in the RMP) conducted with four identified organic impurities present in the Translarna (ataluren) drug substance." Opinion adopted on 12.03.2020.	
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." Request for Supplementary Information adopted on 12.12.2019, 14.11.2019.	
Twinrix Adult - hepatitis A (inactivated) and hepatitis B (rDNA) vaccine (adsorbed) - EMEA/H/C/000112/II/0140 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of sections 4.2 and 5.1 of the Twinrix Adult SmPC in order to reflect information on the long-term antibody persistence and immune memory up to 20 years after primary immunisation of adults, based on data from two phase IV long-term follow-up extension studies, HAB-028 EXT Y16-20 (An open, single centre study to evaluate the long-term antibody persistence and immune memory between 16 and 20 years after the primary study HAB-028) and HAB-032 EXT Y16-20 (An open single centre study to evaluate the long-term antibody persistence and immune memory between 16 and 20 years after the primary study HAB-032). In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1 and to make minor editorial changes." Request for Supplementary Information adopted	

on 30.01.2020.	
Twinrix Paediatric - hepatitis A (inactivated) and hepatitis B (rDNA) vaccine (adsorbed) - EMEA/H/C/000129/II/0141 GlaxoSmithkline Biologicals SA, Duplicate, Duplicate of Twinrix Adult, Rapporteur: Bart Van der Schueren, "Update of sections 4.2 and 5.1 of the Twinrix Paediatric SmPC in order to reflect information on the long-term antibody persistence and immune memory up to 15 years after primary immunisation of adolescents, based on data from Phase IV study HAB-084 EXT Y11-15 (An open, long-term follow-up study to evaluate long-term antibody persistence and immune memory between 11 and 15 years after the primary study HAB-084). In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1 and to implement some minor editorial changes." Request for Supplementary Information adopted on 30.01.2020.	
Tygacil - tigecycline - EMEA/H/C/000644/II/0110 Pfizer Europe MA EEIG, Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.4 and 4.8 of the SmPC in order to add a recommendation regarding monitoring of coagulation parameters prior to and during tigecycline treatment and to update the frequency of the existing adverse drug reaction hypofibrinogenaemia from `Not known' to `Rare', based on post-marketing data. The Package Leaflet is updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the PI in line with the Annex to the European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use' (EMA/CHMP/302620/2017 Rev.1) and to bring the PI in line with the latest QRD template version 10.1." Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
Tygacil - tigecycline - EMEA/H/C/000644/II/0111 Pfizer Europe MA EEIG, Rapporteur: Jorge	Request for supplementary information adopted with a specific timetable.

Camarero Jiménez, "Update of section 4.5 of the SmPC in order to add drug interaction information regarding the concomitant use of tigecycline and calcineurin inhibitors, based on pharmacovigilance data." Request for Supplementary Information adopted on 12.03.2020.	
Tyverb - lapatinib - EMEA/H/C/000795/II/0059 Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to update Table 8 based on updated/corrected results from study EGF114299/LAP016A2307, an interventional study with progression free survival rate as primary objective, original report submitted during procedure EMEA/H/C/00795/II/0051." Request for Supplementary Information adopted on 14.11.2019, 26.04.2019.	See agenda 9.1
Xaluprine - mercaptopurine - EMEA/H/C/002022/II/0022, Orphan Nova Laboratories Ireland Limited, Rapporteur: Filip Josephson, "Update of sections 4.4, 4.8 and 4.9 of the SmPC to add further information on hepatic toxicity. The MAH took the opportunity to implement minor editorial changes to the SmPC and PIL." Request for Supplementary Information adopted on 13.02.2020, 21.11.2019, 12.09.2019.	
Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0020/G, Orphan Ipsen Pharma, Rapporteur: Martina Weise, "To update sections 4.5 and 5.2 of the SmPC to update the information on the interaction with Carboxylesterases 2 inhibitors based on final results from the non-clinical study IPS000610; the Package Leaflet is updated accordingly. Furthermore, update of section 5.2 to reflect the results of in vitro study XT175092. Additionally, the final study reports are submitted from studies XT173065, and XT174037, with no subsequent changes to the PI. The MAH took the opportunity to update the PI to the latest QRD template v10.1." Opinion adopted on 19.03.2020. Request for Supplementary Information adopted on 23.01.2020.	Positive Opinion adopted by consensus on 19.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zoely - nomegestrol acetate / estradiol - EMEA/H/C/001213/II/0050	

Theramex Ireland Limited, Rapporteur: Jean-Michel Race, "Update of sections 4.3 and 4.4 of the SmPC in order to add a new contraindication and a new warning regarding meningioma, upon request by PRAC following the assessment of Post-authorisation measure "LEG 014". The Package Leaflet is being updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in the Netherlands and Portugal in the Package Leaflet." Request for Supplementary Information adopted on 12.12.2019, 14.11.2019, 19.09.2019.	
WS1683 **Elebrato Ellipta-EMEA/H/C/004781/ WS1683/0012** **Temybric Ellipta-EMEA/H/C/005254/ WS1683/0001** **Trelegy Ellipta-EMEA/H/C/004363/ WS1683/0010** GlaxoSmithKline Trading Services Limited, Lead Rapporteur: Peter Kiely, "Update of SmPC in order to add information in section 5.1 on survival data from the IMPACT study" Opinion adopted on 10.03.2020. Request for Supplementary Information adopted on 12.12.2019, 17.10.2019.	Negative Opinion adopted by consensus on 10.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1743 **Komboglyze-EMEA/H/C/002059/WS1743/0047** **Onglyza-EMEA/H/C/001039/WS1743/ 0049** **Qtern-EMEA/H/C/004057/WS1743/0026** AstraZeneca AB, Lead Rapporteur: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC in order to add a new warning about Bullous pemphigoid and section 4.8 of the SmPC to include Bullous pemphigoid as a new ADR with a frequency of 'Not known'. The Package Leaflet has been updated accordingly." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1750 **Levitra-EMEA/H/C/000475/WS1750/0066** **Vivanza-EMEA/H/C/000488/WS1750/ 0062** Bayer AG, Lead Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 5.2	Positive Opinion adopted by consensus on 19.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

(Pharmacokinetic properties) of the vardenafil SmPCs and relevant sections of the PLs to expand the information regarding vardenafil interactions with P-glycoprotein (P-gp) as a result of a general review of vardenafil pharmacokinetic properties. Editorial changes proposed by the MAH during the procedure have been accepted." Opinion adopted on 19.03.2020. Request for Supplementary Information adopted on 16.01.2020.	

B.5.3. CHMP-PRAC assessed procedures

Bexsero - meningococcal group B vaccine (recombinant, component, adsorbed) - EMEA/H/C/002333/II/0088 GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.2 and 5.1 of the SmPC in order to reflect the final data of Study V72_38OB listed as category 3 in the RMP; this is an observational effectiveness study of the impact of Bexsero vaccination; the Package Leaflet is updated accordingly. The RMP version 7.3 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to make some rewording in section 5.1 of the SmPC and to bring the PI in line with the latest QRD template version 10.1 and to amend minor typos detected in the European annexes."	
Bortezomib Fresenius Kabi - bortezomib - EMEA/H/C/005074/II/0001/G Fresenius Kabi Deutschland GmbH, Generic, Generic of VELCADE, Rapporteur: Kolbeinn Gudmundsson, PRAC Rapporteur: Amelia Cupelli	
Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0106 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Jean-Michel Dogné, "Update of sections 4.4 and 5.1 of the SmPC based on final results from study HPV-019 listed as a category 3 study in the RMP (in fulfilment of MEA080); this is a safety and immunogenicity study of Cervarix in HIV-positive female subjects aged 15-25 years as compared to HPV-4, which was already	Request for supplementary information adopted with a specific timetable.

submitted in P46-95. In addition, the Marketing authorisation holder (MAH) took the opportunity to reflect an update in section 4.2 of the SmPC to indicate that limited clinical data is now available in 4-6 years old children based on study HPV-073 following assessment in P46-90; this is a safety and immunogenicity study of Cervarix in girls aged 4-6 years, as an alternative to the current adolescent HPV vaccination schedule. The RMP version 21 has also been submitted to reflect the availability of the final results of the HPV-019 and HPV-073 studies, and the use of Cervarix in HIV-infected subjects or subjects with known immune deficiencies has been removed as missing information. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1." Request for Supplementary Information adopted on 12.03.2020.	
Cyramza - ramucirumab - EMEA/H/C/002829/II/0038 Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add posterior reversible encephalopathy syndrome (PRES) and dysphonia as a warning and as undesirable effect, respectively. The Labelling and Package Leaflet are updated accordingly. The RMP version 9.3 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template."	
Desloratadine ratiopharm - desloratadine - EMEA/H/C/002404/II/0023/G ratiopharm GmbH, Generic, Generic of Aerius, Rapporteur: Koenraad Norga, PRAC Rapporteur: Laurence de Fays, "C.I.5.b - Change in the legal status of desloratadine ratiopharm from 'medicinal product subject to medical prescription' to 'medicinal product not subject to medical prescription' in view of the safety profile of desloratadine ratiopharm and the post-marketing experience already available with other medicinal products containing similar long acting histamine antagonists. The RMP version 1.0 has also been submitted. In addition, the	See agenda 9.1

MAH also took the opportunity to bring the PI in line with the latest QRD template (version 10.1), to update the list of local representatives in the package leaflet and to make editorial changes. C.I.6.b - To delete the therapeutic indication in adolescents aged 12 years and older for the relief of symptoms associated with allergic rhinitis and urticaria. Section 4.1 of the SmPC and section 1 of the PL are updated accordingly."	
Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0113 Genzyme Europe BV, PRAC Rapporteur: Liana Gross-Martirosyan, "Submission of the final report from study listed as a category 3 study in the RMP. This is a postauthorisation study (AGALSC08994) on Fabrazyme (agalsidase beta) home infusion educational materials effectiveness evaluation: a survey of healthcare providers and patients / caregivers. The RMP version 2 has also been submitted accordingly and to comply with the Good Pharmacovigilance Practice (GVP) Module V Rev. 2 template and information on study (AGAL02603) and the Fabry Registry/Pregnancy Sub-registry (AGAL 19211)." Request for Supplementary Information adopted on 12.03.2020, 16.01.2020.	Request for supplementary information adopted with a specific timetable.
Fortacin - lidocaine / prilocaine - EMEA/H/C/002693/II/0030 Recordati Ireland Ltd, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, "Change in the legal status of Fortacin from 'medicinal product subject to medical prescription' to 'medicinal product not subject to medical prescription' in view of the safety profile of Fortacin, the post-marketing experience already available with other medicinal products containing amide local anaesthetics and in view of making the product more accessible to the target population. Furthermore, the PI is being brought in line with the latest QRD template (version 10.1). The RMP version 3.1 has also been submitted." Request for Supplementary Information adopted on 12.12.2019.	See agenda 9.1
Jakavi - ruxolitinib - EMEA/H/C/002464/II/0044	Request for supplementary information adopted with a specific timetable.

Novartis Europharm Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Annika Folin, "Update of the SmPC sections 5.1 and 4.8 with the efficacy and safety information to reflect the 5-year follow-up data from the B2301 Week 256 final clinical study report (CSR). The final analyses presented in the CSR are submitted to fulfil the Post-Authorisation Measure, therefore the Annex II.D of the Product Information is updated accordingly. The changes have been reflected in the RMP version 11 submitted with the procedure II/43." Request for Supplementary Information adopted on 12.03.2020, 03.10.2019.	
Kanuma - sebelipase alfa - EMEA/H/C/004004/II/0026/G, Orphan Alexion Europe SAS, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ulla Wändel Liminga, "Grouping consisting of the following variations: -Update of sections 4.2, 4.4, 4.8 and 5.1 of the Summary of Product Characteristics (SmPC) in order to update the clinical information based on the pooled safety and efficacy analysis of already submitted studies (Studies LAL-CL04, LAL-CL03, LAL-CL06, LAL-CL08 and LAL-CL02) and updated population PK analyses in children and adults. The Package Leaflet has been amended accordingly. The ATC code has been added to the SmPC. The RMP version 4 has also been submitted. Annex II is also updated to remove the obligation related to the provision of study LAL-CL08. - Submission of the final report from study LAL-EA01 An open-label study with sebelipase alfa (1 mg/kg every other week for up to 78 weeks or until drug commercialization) in United States (US) patients who did not otherwise qualify for an active sebelipase alfa trial (expanded access protocol)"	See agenda 9.1
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	See agenda 9.1

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." Request for Supplementary Information adopted on 12.12.2019, 19.09.2019.	
NINLARO - ixazomib - EMEA/H/C/003844/II/0019/G, Orphan Takeda Pharma A/S, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Annika Folin, "Group of variations consisting of the: C.I.11.b: Submission of the final report from study NSMM-5001 listed as a Specific Obligation in the Annex II of the Product Information. This is a global, prospective, non-interventional, observational study in multiple myeloma patients. The Annex II and the RMP (submitted version 5) are updated accordingly. C.I.11.z: Submission of an updated RMP version 5 in order to extend the due date of the Post-authorisation efficacy study (PAES) C16010 listed in Annex IID. The MAH also took the opportunity to correct a typographical error in Annex II."	
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." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 16.01.2020, 31.10.2019.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ogivri - trastuzumab -	Positive Opinion adopted by consensus on

EMEA/H/C/004916/II/0009 Mylan S.A.S, Rapporteur: Koenraad Norga, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Submission of the final clinical study report (MYL-Her-3001) (a Multicenter, Double-blind, Randomized, Parallel-group, Phase III Study of the Efficacy and Safety of Hercules Plus Taxane Versus Herceptin Plus Taxane as First Line Therapy in Patients With HER2-Positive Metastatic Breast Cancer) with the final overall survival (OS). The RMP version 3 has also been submitted." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 16.01.2020.	12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0146 GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from a hospital-based surveillance study assessing the impact of Synflorix immunisation program in Kenya on pneumonia, invasive pneumococcal disease (IPD) and replacement disease. This submission is made to fulfil post-authorisation measure MEA 021.8, and propose an update of the Risk Management Plan (RMP) accordingly. Review of the safety concerns listed in the Synflorix RMP in alignment with the recommendations from EU-RMP with GVP module V revision 2 was also carried out, considering the closure of MEA 021.8 and the RMP principle that safety concerns can be removed or reclassified when the safety profile and risks are well-characterised; the MAH revised the Synflorix RMP and removed all well-characterised risks. The RMP version 18 has been approved." Opinion adopted on 12.03.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Talzenna - talazoparib - EMEA/H/C/004674/II/0001 Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations in patients with severe renal impairment and update pharmacokinetic information based on the results from PK study MDV3800-01 (C3441001)	

listed as a category 3 study in the RMP. The RMP version 1.0 has also been submitted. In addition, the MAH took the opportunity to make minor changes through the product information and to bring the PI in line with the latest QRD template version 10.1."	
Tremfya - guselkumab - EMEA/H/C/004271/II/0020 Janssen-Cilag International N.V., Rapporteur: Melinda Sobor, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.4 and 4.8 to include anaphylactic reactions. Additionally the RMP is updated" Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0023 Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jean-Michel Dogné, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and immunogenicity information based on final results from study B1971033 listed as a category 3 study in the RMP (MEA007); this is a duration of immunity study to assess persistence of hSBA response for up to 48 months after completion of vaccination with Trumenba and the immunogenicity, safety, and tolerability of a booster dose of Trumenba; The RMP version 3 has also been submitted, including changes related to this variation, changes agreed during another ongoing variation (II-13) and editorial changes. In addition, the Marketing authorisation holder (MAH) took the opportunity to include editorial changes in Annex II, in the labelling and in the Package Leaflet." Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
Velphoro - iron - EMEA/H/C/002705/II/0021 Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola, "Update of section 5.1 of the SmPC in order to add information related to the results of the VERIFIE study. This was a non-interventional voluntary PASS trial, which aimed to investigate the short	Request for supplementary information adopted with a specific timetable.

and long-term real-life safety, effectiveness, and adherence of Velphoro in patients with hyperphosphataemia undergoing haemodialysis or peritoneal dialysis. It was listed as an additional pharmacovigilance activity (EMEA/H/C/002705/MEA/002), a category 3 study in the RMP. Furthermore, minor editorial wording changes in section 4.2 to provide consistent information between the SmPC and that already existing in the Labelling and PL were introduced. The RMP version 8.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.1." Request for Supplementary Information adopted on 12.03.2020.	
Voncento - human coagulation factor viii / human von willebrand factor - EMEA/H/C/002493/II/0042 CSL Behring GmbH, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Submission of an updated RMP version 7 in order to: - align with the revision of the GVP module V - reflect the completion of the post-marketing study (PMS) in patients with Von Willebrand Disease (VWD) - request a waiver to the post-authorisation safety study (category 3 study) in patients with haemophilia A due to feasibility reasons." Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
Xultophy - insulin degludec / liraglutide - EMEA/H/C/002647/II/0034 Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, "Update of section 4.2 of the SmPC in order to change the wording "transfer from basal insulin" to "transfer from any insulin regimen", and to modify the current recommendation of a starting dose of 16 dose steps to a more flexible wording allowing for individual variation of the starting dose, based on data from study NN9068-4184 (DUAL II Japan: A double-blinded trial comparing the efficacy and safety of insulin degludec/liraglutide and insulin degludec both in combination with metformin in Japanese subjects with type 2 diabetes mellitus inadequately controlled with basal or pre-	

mix/combination insulin therapy and oral anti-diabetic drugs) as well as data from the post-marketing setting. In addition, the MAH took the opportunity to make a minor correction in SmPC section 5.1 and to implement changes in the annexes in accordance with QRD template 10.1. The MAH provided an updated RMP version 9.0 as part of the application." Request for Supplementary Information adopted on 27.02.2020.	
WS1724 **Blitzima-EMEA/H/C/004723/WS1724/0029** **Ritemvia-EMEA/H/C/004725/WS1724/0029** **Truxima-EMEA/H/C/004112/WS1724/0032** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz, Lead PRAC Rapporteur: Hans Christian Siersted, "Submission of the final report from study CT-P10 3.3. This is a category 3 study, a Phase 1/3, randomised, parallel-group, active-controlled, double-blind study to demonstrate equivalence of pharmacokinetics and non-inferiority of efficacy for CT-P10 in comparison with Rituxan. Each Administered in Combination With Cyclophosphamide, Vincristine, and Prednisone (CVP) in Patients With Advanced Follicular Lymphoma. The RMP version 10.0 has also been submitted in order to align the safety concerns with those of MabThera and to incorporate the final results of Study CT-P10 3.3." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.4. PRAC assessed procedures

PRAC Led **Aclasta - zoledronic acid - EMEA/H/C/000595/II/0074/G** Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information regarding acute phase reactions as an outcome of post-authorisation measure (LEG 0037); update of	

section 5.1 further to assessment of 24 month data from paediatric extension study 2337E1 submitted in accordance with article 46. 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 and to bring the PI in line with the latest QRD template version 10.1."	
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 7.2 has also been submitted." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 31.10.2019.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Afstyla - lonoctocog alfa - EMEA/H/C/004075/II/0030** CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sonja Hrabcik, PRAC-CHMP liaison: Andrea Laslop, "C.I.11 b : Submission of an updated RMP version 5.0 as a PDCO commitment (PIP modification request) to stop enrolment in arm 2 Previously Untreated Patient (PUP) of clinical trial CSL627_3001 (remains ongoing). Completion of Arms 1 and 3 (Previously Treated Patient) is also reflected. Updated information on registries/ noninterventional study (NIS) to reflect only those considered additional pharmacovigilance activities, category 3 (addition of registry American Thrombosis and Hemostasis Network [ATHN] 8 removal of registries ATHN 2 and Dutch Hemophilia Registry as well as the AFSTYLA NIS); also to demonstrate how PUP data will be complemented. Clinical trials CSL627_1001 and 3002 removed from Table Part VII-2 as both studies have not been listed in a previous Pharmacovigilance Plan.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Data have been updated to the DLP of 03 July 2019 to be consistent with Periodic Safety Update Report No. 5." Opinion adopted on 12.03.2020.	
PRAC Led **Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0040** Biofrontera Bioscience GmbH, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "To update the RMP for Ameluz to version 11.1 based on the new RMP template (GVP module V, rev.2), as well as the implementation of changes assessed and agreed by PRAC in the recently finalised PSUSA procedure (EMEA/H/C/002204/PSUSA/ 00010006/20180614)." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 13.02.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **BLINCYTO - blinatumomab - EMEA/H/C/003731/II/0033, Orphan** Amgen Europe B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Eva Jirsová, PRAC-CHMP liaison: Ondřej Slanař, "Submission of an updated RMP version 11 in line with the guideline on Good Pharmacovigilance Practices (GVP) Module V on RMP. In accordance with the RMP update, the protocol for Category 1 PASS 20150136 has been updated and the enrolment period for the study has been extended by 1 year. The milestones in the RMP were updated accordingly. In addition, the RMP includes a proposed update to the milestone of the Category 3 PASS 20180138." Request for Supplementary Information adopted on 12.03.2020, 28.11.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Celsentri - maraviroc - EMEA/H/C/000811/II/0061** ViiV Healthcare B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "Submission of the final report from study A4001067 (POEM): An International, Multicenter, Prospective Observational Study of the Safety of Maraviroc Used With Optimized Background Therapy In Treatment-Experienced HIV-1 Infected Patients. Study A4001067	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

(POEM) is a non-interventional PASS (Post-Authorisation Safety Study) listed as a category 3 study in the RMP. The updated EU-RMP (v12.0) is also included in this variation application." Opinion adopted on 12.03.2020.	
PRAC Led **Constella - linaclotide - EMEA/H/C/002490/II/0043** Allergan Pharmaceuticals International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the final report from study "Linaclotide Utilization Study in Selected European Populations" listed as a category 3 study in the RMP. This is a Drug Utilisation Study (DUS) addressing the following safety concerns: - The potential for off-label use and abuse/excessive use - Extent of use in pregnancy and lactation, and male patients - Assess the extent of off-label use and the extent of use in males and in pregnant females" Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 13.02.2020, 28.11.2019.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Flixabi - infliximab - EMEA/H/C/004020/II/0052** Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Update of the RMP to replace the prospective observational cohort study of Flixabi in patients with Crohn's disease (CD) (SB2-G42-CD), with real-world data from PERFUSE, CREDIT and CEDUR studies." Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
PRAC Led **GONAL-f - follitropin alfa - EMEA/H/C/000071/II/0147** Merck Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 2.1 in order to adapt to the RMP template as per Good Pharmacovigilance Practice (GVP) Module	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

V, rev 2, with consequential removal of important identified risks and important potential risks. The missing information on women older than 40 years is changed to women older than 42 years. The requested variation proposed amendments to the Risk Management Plan (RMP)." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 16.01.2020.	
PRAC Led **Iclusig - ponatinib - EMEA/H/C/002695/II/0053, Orphan** Incyte Biosciences Distribution B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Filip Josephson, "Submission of an updated RMP version 20 in order to remove the study AP24534-14-401, a Postmarketing Observational Registry to Evaluate the Incidence of and Risk Factors for Vascular Occlusive Events Associated With Iclusig (Ponatinib) in Routine Clinical Practice in the US (OMNI) from the Pharmacovigilance plan. In addition, in the framework of variation type II/51, it was considered that the distribution of the educational material was not needed anymore. The MAH is therefore also taking the opportunity to amend the RMP to remove reference to these measures." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 28.11.2019.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Instanyl - fentanyl - EMEA/H/C/000959/II/0052** Takeda Pharma A/S, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 19.6 in order to update information relating to educational material." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 28.11.2019.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Jakavi - ruxolitinib - EMEA/H/C/002464/II/0043** Novartis Europharm Limited, Rapporteur: Filip	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Josephson, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Filip Josephson, "Update of the SmPC sections 4.4 and 4.5 to reflect the data submission of the final report from a safety study (INC424AIC01T) of ruxolitinib in myelofibrosis (MF) listed as a category 3 study in the RMP. This is a non-interventional, observational post-authorisation safety study (PASS) intended to provide real-world safety data on patients with MF who were exposed and non-exposed to ruxolitinib and thereby provide insights into disease management and the safety profile of ruxolitinib. The RMP version 11 has also been submitted. The updated RMP v11 reflects the completion of additional pharmacovigilance studies including the above-mentioned PASS (INC424AIC01T, Category 3) as well as the RESPONSE study (INC424B2301, Category 1). This RMP is incorporated in this variation and will be cross-referred in the variation forthcoming submission for the RESPONSE study within a month of this submission. The requested variation amends the Summary of Product Characteristics." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 03.10.2019.	
PRAC Led **Kineret - anakinra - EMEA/H/C/000363/II/0073** Swedish Orphan Biovitrum AB (publ), Rapporteur: Mark Ainsworth, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final report from study (Sobi.ANAKIN-302) listed as a category 3 study in the RMP. This is a non-interventional, post-authorisation safety study to evaluate long-term safety of anakinra (Kineret) in patients with systemic juvenile idiopathic arthritis. The RMP version 5.1 has also been submitted to reflect the completion of the study." Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0079** Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli,	Request for supplementary information adopted with a specific timetable.

PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final report from study ALGMYC07390, Prevalence of immunology testing in patients treated with alglucosidase alfa with significant hypersensitivity/anaphylactic reactions (MEA 053 resulting from variation EMEA/H/C/000636/II/0052) to test the effectiveness of the approved Safety Information Packet (SIP)." Request for Supplementary Information adopted on 12.03.2020.	
PRAC Led **Naglazyme - galsulfase - EMEA/H/C/000640/II/0081** BioMarin International Limited, Rapporteur: Fátima Ventura, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Fátima Ventura, "Submission of an updated RMP version 6.0 in order to update the safety specification plan based on a review of the preclinical, clinical, post-marketing and literature data. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the Naglazyme RMP to the latest EU RMP template." Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Nulojix - belatacept - EMEA/H/C/002098/II/0063/G** Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "Submission of the final report from studies IM103075 and IM103076 listed as category 3 studies in the RMP. Study IM103075 is a prospective cohort study to assess the association between belatacept use and risk of post-transplant lymphoproliferative disorder (PTLD) in renal transplant recipients in the US. Study IM103076 is a prospective patient registry study to estimate the incidence rates of confirmed PTLD, central nervous system (CNS) PTLD and progressive multifocal leukoencephalopathy (PML) in adult renal transplant recipients treated with belatacept in the US. The RMP version 17.2 has also been updated to reflect the completion of both studies and to make some administrative	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

updates." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 16.01.2020.	
PRAC Led **Pergoveris - follitropin alfa / lutropin alfa - EMEA/H/C/000714/II/0066** Merck Europe B.V., Rapporteur: Mark Ainsworth, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Mark Ainsworth, "Submission of an updated RMP version 5.3 (updated to version 6.0) in order to adapt to the RMP template as per Good Pharmacovigilance Practice (GVP) Module V, rev 2, with consequential removal of important identified risks and important potential risks. The requested variation proposed amendments to the Risk Management Plan (RMP)." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Qarziba - dinutuximab beta - EMEA/H/C/003918/II/0015, Orphan** EUSA Pharma (Netherlands) B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "To update the RMP for Qarziba to version 9.0 to remove from the RMP as missing information Drug-drug interaction, Use in adolescents, adults and elderly, Use in patients with an ethnic origin other than Caucasian, Use in patients with hepatic and renal impairment and Potential harm from overdose." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 28.11.2019.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **RoActemra - tocilizumab - EMEA/H/C/000955/II/0094** Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from study WA22480 (ARTIS) listed as a category 3 study in the RMP. This is a phase IV, prospective observational cohort study using Sweden registers to provide long term safety	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

data from the use of tocilizumab in Sweden for RA patients." Opinion adopted on 12.03.2020.	
PRAC Led **Trulicity - dulaglutide - EMEA/H/C/002825/II/0048** Eli Lilly Nederland B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Ilaria Baldelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of the final study report from study B010, investigating the Utilisation of Dulaglutide in European Countries: A Cross-Sectional, Multi-Country and Multi-Source Drug Utilisation Study Using Electronic Health Record Databases. Study B010 is listed as a category 3 study in the RMP (MEA 001). An updated RMP version 5.1 was submitted." Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0021, Orphan** Ipsen Pharma, Rapporteur: Martina Weise, PRAC Rapporteur: Adam Przybylkowski, PRAC-CHMP liaison: Ewa Balkowiec Iskra, "Submission of an updated RMP version 5.0 in order to update to the GVP module V (rev 2). The commitment to revise the RMP was done during variation procedure EMEA/H/C/003937/II/0015." Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.
PRAC Led **WS1711** **Aluvia-EMEA/H/W/000764/WS1711/0112** **Kaletra-EMEA/H/C/000368/WS1711/0181** AbbVie Deutschland GmbH & Co. KG, Lead PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Jean-Michel Race, "To update the RMP for Kaletra and Aluvia (LPV/r) to version 9.0 in order to comply with the current revision 2 of the template. At the same time, the MAH took the opportunity to review the safety information contained in the RMP, removed an important potential risk of drug interaction with telaprevir and boceprevir (HCV protease inhibitors) and missing information regarding use of LPV/r in elderly patients. In addition, the MAH has added information	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

regarding the requirement for a pharmacovigilance (PV) cohort as part of LEG 121 to the RMP." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 28.11.2019.	
PRAC Led **WS1713** **Kivexa-EMEA/H/C/000581/WS1713/0083** **Triumeq-EMEA/H/C/002754/WS1713/0075** **Trizivir-EMEA/H/C/000338/WS1713/0115** **Ziagen-EMEA/H/C/000252/WS1713/0109** ViiV Healthcare B.V., Lead PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Jean-Michel Race, "Submission of updated RMPs (Kivexa, Trizivir, Ziagen version 2.0 and Triumeq version 17.0) in order to remove the additional risk minimisation measure of provision of abacavir hypersensitivity education materials for healthcare professionals. Annex II is updated accordingly. In addition, the MAH took the opportunity to introduce an editorial update in the SmPC of Triumeq." Opinion adopted on 12.03.2020. Request for Supplementary Information adopted on 16.01.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1742** **Ebymect-EMEA/H/C/004162/WS1742/0043** **Edistride-EMEA/H/C/004161/WS1742/0037** **Forxiga-EMEA/H/C/002322/WS1742/0056** **Xigduo-EMEA/H/C/002672/WS1742/0054** AstraZeneca AB, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, "Update of SmPC section 4.4 (Special warning and precaution for use) of Forxiga, Edistride, Xigduo and Ebymect based on the final results of a Post-Authorization Safety Study (listed as a category 3 study in the RMPs): meta-analysis across studies D1690C00018, D1690C00019 and D1693C00001 (DECLARE), for analysis of lower limb amputation and relevant preceding adverse events. These three studies include T2DM patients with established CVD or with	Request for supplementary information adopted with a specific timetable.

CVD risk factors treated with dapagliflozin or placebo in clinical trial settings. The Package Leaflets (PL) are updated accordingly. In addition, the applicant took the opportunity to implement a minor editorial change in section 8 of the Edistride 5 mg SmPC. The updated dapagliflozin RMP version 19 and dapagliflozin/metformin fixed dose combination (FDC) RMP version 12 have also been submitted." Request for Supplementary Information adopted on 12.03.2020.	
PRAC Led **WS1761** **Anoro Ellipta-EMEA/H/C/002751/ WS1761/0029** **Incruse Ellipta-EMEA/H/C/002809/ WS1761/0028** **Laventair Ellipta-EMEA/H/C/003754/ WS1761/0032** **Rolufta Ellipta-EMEA/H/C/004654/ WS1761/0013** GlaxoSmithKline (Ireland) Limited, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Ilaria Baldelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of the final report from study WWE117397 listed as a category 3 study in the RMP. This was a retrospective longitudinal non-interventional observational study of new users of inhaled umeclidinium/vilanterol (UMEC/VI) or new users of inhaled umeclidinium (UMEC) or new users or long-acting bronchodilators (LABD) in the primary care setting. The primary objective of the study was to report the proportion of patients with a possible off-label use and characterize them in new users of UMEC/VI, UMEC, or other LABD. The second objective was to quantify incidence of major cardiovascular and cerebrovascular events, mortality and pneumonia, and rates of exacerbations of COPD during follow-up in new users of UMEC/VI or UMEC. The tertiary objective was in new users of UMEC/VI or UMEC with 12 or more months of follow-up following initiation, to describe treatment patterns and adherence." Request for Supplementary Information adopted on 12.03.2020.	Request for supplementary information adopted with a specific timetable.

B.5.5. CHMP-CAT assessed procedures

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0017/G, Orphan, ATMP

Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang
Opinion adopted on 20.03.2020.
Request for Supplementary Information adopted on 24.01.2020.

Yescarta - axicabtagene ciloleucel - EMEA/H/C/004480/II/0018, Orphan, ATMP

Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus
Opinion adopted on 20.03.2020.

Yescarta - axicabtagene ciloleucel - EMEA/H/C/004480/II/0019, Orphan, ATMP

Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus
Opinion adopted on 20.03.2020.

B.5.6. CHMP-PRAC-CAT assessed procedures

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

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

B.5.7. PRAC assessed ATMP procedures

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

WS1703/G **Advagraf-EMEA/H/C/000712/WS1703/0055/G** **Modigraf-EMEA/H/C/000954/WS1703/0034/G** Astellas Pharma Europe B.V., Lead Rapporteur: Jayne Crowe Request for Supplementary Information adopted on 16.01.2020.	
WS1723 **Advate-EMEA/H/C/000520/WS1723/0103** **ADYNOVI-EMEA/H/C/004195/WS1723/0009** Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 30.01.2020.	
WS1735/G **Comtan-EMEA/H/C/000171/WS1735/0055/G** **Comtess-EMEA/H/C/000170/WS1735/0059/G** **Corbilta-EMEA/H/C/002785/WS1735/0020/G** **Entacapone Orion-EMEA/H/C/002440/WS1735/0018/G** **Levodopa/Carbidopa/Entacapone Orion-EMEA/H/C/002441/WS1735/0029/G** **Stalevo-EMEA/H/C/000511/WS1735/0090/G** Orion Corporation, Lead Rapporteur: Outi Mäki-Ikola Opinion adopted on 12.03.2020.	Positive Opinion adopted by consensus on 12.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1745 **Biktarvy-EMEA/H/C/004449/WS1745/0028** **Descovy-EMEA/H/C/004094/WS1745/0046** **Vemlidy-EMEA/H/C/004169/WS1745/0025** Gilead Sciences Ireland UC, Lead Rapporteur: Bruno Sepodes, "To update section 2 of the Product Information Annexes (PIs) of the medicinal products concerned, to align the pregnancy language between the summary of	

product characteristics (SmPC) and the patient information leaflet (PIL). In addition, the MAH has taken this opportunity to: · Introduce an update to the sodium wording in section 6 of the PIL for Descovy, Biktarvy and Vemlidy. This update is in line with the excipient guidance. · Implement minor linguistic amendments (MLAs) for Descovy to the below languages: CS, ES, FI, MT, NL, NO, PT, RO, SV"	
WS1751/G **Keppra-EMEA/H/C/000277/WS1751/0185/G** UCB Pharma S.A., Lead Rapporteur: Koenraad Norga Request for Supplementary Information adopted on 20.02.2020.	
WS1765 **Halimatoz-EMEA/H/C/004866/WS1765/0018** **Hefiya-EMEA/H/C/004865/WS1765/0018** **Hyrimoz-EMEA/H/C/004320/WS1765/0018** Sandoz GmbH, Lead Rapporteur: Milena Stain, "To update of section 5.1 of the SmPC in line with the reference product to reflect results from the final report from study M11-327: A Multicenter Open-Label Study of the Long-term Safety and Efficacy of the Human Anti-TNF Monoclonal Antibody Adalimumab in Subjects with Non-infectious Intermediate Uveitis, Posterior Uveitis, or Panuveitis; listed as a category 3 study in the RMP of the reference product. Furthermore editorial changes and a brief description of the study design were added to section 5.1 of the SmPC." Opinion adopted on 05.03.2020.	Positive Opinion adopted by consensus on 05.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1768 **Kinzalkomb-EMEA/H/C/000415/WS1768/0111** **MicardisPlus-EMEA/H/C/000413/WS1768/0114** **PritorPlus-EMEA/H/C/000414/WS1768/0121** Boehringer Ingelheim International GmbH, Lead Rapporteur: Daniela Melchiorri, "C.I.z - Update of the SmPC and PL to more accurately describe the shape of the tablets from Oval to Oblong for	Positive Opinion adopted by consensus on 19.03.2020. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

the drug products MicardisPlus, PritorPlus and Kinkalkomb, all strengths; the shape of tablets itself remains unchanged. The requested worksharing procedure proposed amendments to the Summary of Product Characteristics and Package Leaflet." Opinion adopted on 19.03.2020.	
WS1771/G **AZILECT-EMEA/H/C/000574/WS1771/ 0085/G** **Rasagiline ratiopharm-EMEA/H/C/003957/ WS1771/0017/G** Teva B.V., Lead Rapporteur: Bruno Sepodes	
WS1777 **Afinitor-EMEA/H/C/001038/WS1777/ 0065** **Votubia-EMEA/H/C/002311/WS1777/ 0063** Novartis Europharm Limited, Lead Rapporteur: Janet Koenig	

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

Feraccru - ferric maltol - EMEA/H/C/002733/II/0024 Norgine B.V., Rapporteur: Maria Concepcion Prieto Yerro, "To update sections 4.4 and 5.1 of the SmPC in order to update safety and efficacy information based on final results from study ST 10-01-304 this is a phase 3b, randomized, controlled, multicentre study with oral ferric maltol (Feraccru) or intravenous iron (ferric carboxymaltose; FCM), for the treatment of iron deficiency anaemia in subjects with inflammatory bowel disease." Request for Supplementary Information adopted on 13.02.2020. Withdrawal request submitted on 28.02.2020.	The MAH withdrew the procedure on 28.02.2020.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0085 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Update of sections 4.4, and 4.8 of the SmPC in order to amend an existing warning on Other immune-related adverse reactions to include myelitis, and add myelitis to the list of adverse drug reactions (ADRs) with frequency uncommon based on routine pharmacovigilance review process; the Package Leaflet is updated accordingly."	The MAH withdrew the procedure on 12.03.2020.

Withdrawal request submitted on 12.03.2020.

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

hydrocortisone - EMEA/H/C/005105, Orphan
Diurnal Europe BV, replacement therapy for congenital adrenal hyperplasia (CAH) in adolescents aged 12 years and over and adults.

paliperidone - EMEA/H/C/005486
treatment of schizophrenia

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

amikacin - EMEA/H/C/005264, Orphan
Insmed Netherlands B.V., treatment of lung infection as part of combination antibacterial drug regiment in adults
List of Questions adopted on 14.11.2019.

avapritinib - EMEA/H/C/005208, Orphan
Blueprint Medicines (Netherlands) B.V., treatment of gastrointestinal stromal tumours
List of Questions adopted on 14.11.2019.

crizanlizumab - EMEA/H/C/004874, Orphan
Novartis Europharm Limited, Treatment of sickle cell disease
List of Questions adopted on 17.10.2019.

teriparatide - EMEA/H/C/005233
treatment of osteoporosis
List of Questions adopted on 25.07.2019.

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

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

Aripiprazole Accord - aripiprazole -

EMEA/H/C/004021/R/0019
Accord Healthcare S.L.U., Generic, Generic of Abilify, Rapporteur: John Joseph Borg, PRAC Rapporteur: Ana Sofia Diniz Martins

Briviact - brivaracetam - EMEA/H/C/003898/R/0025
UCB Pharma S.A., Rapporteur: Filip Josephson, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Adam Przybylkowski

CIAMBRA - pemetrexed - EMEA/H/C/003788/R/0006
Menarini International Operations Luxembourg S.A., Generic, Generic of Alimta, Rapporteur: Natalja Karpova, PRAC Rapporteur: Ghania Chamouni

Cinacalcet Mylan - cinacalcet - EMEA/H/C/004014/R/0011
Mylan S.A.S, Generic, Generic of Mimpara, Rapporteur: Tomas Radimersky, PRAC Rapporteur: Ulla Wändel Liminga

Ebymect - dapagliflozin / metformin - EMEA/H/C/004162/R/0046
AstraZeneca AB, Rapporteur: Kristina Dunder, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Menno van der Elst

Edistride - dapagliflozin - EMEA/H/C/004161/R/0038
AstraZeneca AB, Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Annika Folin

Genvoya - elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004042/R/0069
Gilead Sciences Ireland UC, Rapporteur: Bruno Sepodes, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ilaria Baldelli

Obizur - susoctocog alfa - EMEA/H/C/002792/R/0033
Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, Co-Rapporteur: Tuomo Lapveteläinen, PRAC Rapporteur: Brigitte Keller-Stanislawski

Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/R/0056
Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald

Praxbind - idarucizumab -
EMEA/H/C/003986/R/0019
Boehringer Ingelheim International GmbH, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Mark Ainsworth, PRAC Rapporteur: Menno van der Elst

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

VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

B.6.6. Type II Variations scope of the Variations: Extension of indication

Doptelet - avatrombopag -
EMEA/H/C/004722/II/0004/G
Dova Pharmaceuticals Ireland Limited, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Eva A. Segovia, "Extension of indication to include the treatment of chronic immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments; consequently, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. Additionally, the SmPC section 5.3 is updated with data from juvenile toxicity studies. Furthermore, an additional pack size of 30 tablets has been introduced with subsequent updates of sections 6.5 and 8 of the SmPC. The Package Leaflet and Labelling are updated in accordance. Version 2.1 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.1."

HyQvia - human normal immunoglobulin -
EMEA/H/C/002491/II/0056
Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension of indication to replace the therapeutic indications of replacement therapy in hypogammablobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia and multiple myeloma and hypogammaglobulinaemia in

patients with HSCT, by the therapeutic indication of replacement therapy in secondary immunodeficiencies (SID) in patients who suffer from severe or recurrent infections, ineffective antimicrobial treatment and either proven specific antibody failure (PSAF) or serum IgG level of <4 g/l. for HyQvia; as a consequence, sections 4.1 and 4.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 10.0 of the RMP has also been submitted."	
Kyprolis - carfilzomib - EMEA/H/C/003790/II/0045, Orphan Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Alexandre Moreau, "Extension of existing indication to include combination of Kyprolis with daratumumab and dexamethasone; 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."	
Orfadin - nitisinone - EMEA/H/C/000555/II/0071 Swedish Orphan Biovitrum International AB, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, "Extension of indication to include treatment of adult patients with alkaptonuria (AKU) for Orfadin; as a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 5.1 and 10 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 5.2 of the RMP has also been submitted accordingly and includes an update in accordance with GVP Module V Revision 2." Request for 1 year of data exclusivity for a new indication (Article 10(5) of Directive 2001/83/EC)	
Saxenda - liraglutide - EMEA/H/C/003780/II/0026 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Menno van der Elst, "Extension of indication to include treatment as an adjunct to a healthy nutrition and physical activity counselling for weight management in adolescent patients from the age of 12 years and above with body weight above 60 kg and obesity (BMI corresponding to ≥30 kg/m2 for adults), based on Study NN8022-4180 that	

evaluated the efficacy of liraglutide 3.0 mg in adolescents aged 12 to less than 18 years with obesity. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are being updated and the Package Leaflet is updated in accordance.
The application relates to paediatric studies submitted according to Article 46 of the paediatric regulation.
The application included an updated RMP version 32.0."

Tecentriq - atezolizumab - EMEA/H/C/004143/II/0039

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Extension of indication to include, in combination with bevacizumab, the treatment of patients with unresectable hepatocellular carcinoma (HCC) who have not received prior systemic therapy, based on the results of the pivotal study YO40245 (IMbrave150) as well as data from Arms A and F of the supportive Phase Ib study GO30140. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the Tecentriq 1200 mg concentrate for solution for infusion SmPC are updated. The Package Leaflet is updated in accordance.
An updated RMP version 13.0 was provided as part of the application."

Zejula - niraparib - EMEA/H/C/004249/II/0019, Orphan

GlaxoSmithKline (Ireland) Limited, Rapporteur: Bjorg Bolstad, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Jan Neuhauser, "Extension of indication to include the maintenance treatment of adult patients with advanced high-grade ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy for Zejula in monotherapy; as a consequence, sections 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The MAH is also taking the opportunity to make minor corrections throughout the PI. The Package Leaflet is updated in accordance. Version 4.0 of the RMP has also been submitted to add the new indication, bring it in line with the RMP template Rev. 2.0.1 and update due

dates for category 3 studies."
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

B.6.7. CHMP assessed procedures scope: Pharmaceutical aspects

Advate - octocog alfa - EMEA/H/C/000520/II/0107
Baxter AG, Rapporteur: Jan Mueller-Berghaus

Cinacalcet Mylan - cinacalcet - EMEA/H/C/004014/II/0009
Mylan S.A.S, Generic, Generic of Mimpara, Rapporteur: Tomas Radimersky

Ilumetri - tildrakizumab - EMEA/H/C/004514/II/0012/G
Almirall S.A, Rapporteur: Jan Mueller-Berghaus

Mekinist - trametinib - EMEA/H/C/002643/II/0038/G
Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik

Nimenrix - Meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0098
Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad

Pelmeg - pegfilgrastim - EMEA/H/C/004700/II/0006/G
Mundipharma Biologics S.L., Rapporteur: Koenraad Norga

POTELIGEO - mogamulizumab - EMEA/H/C/004232/II/0005/G, Orphan
Kyowa Kirin Holdings B.V., Rapporteur: Paula Boudewina van Hennik

Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0185/G
Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder

Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0159
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

XGEVA - denosumab - EMEA/H/C/002173/II/0071/G

Amgen Europe B.V., Rapporteur: Kristina Dunder

WS1786
Hexacima-EMEA/H/C/002702/WS1786/0097
Hexaxim-EMEA/H/W/002495/WS1786/0102
Hexyon-EMEA/H/C/002796/WS1786/0101
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

WS1804/G
HBVAXPRO-EMEA/H/C/000373/WS1804/0068/G
Vaxelis-EMEA/H/C/003982/WS1804/0058/G
MCM Vaccine B.V., Lead Rapporteur: Jan Mueller-Berghaus

B.6.8. CHMP assessed procedures scope: Non-Clinical and Clinical aspects

AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0029
sanofi-aventis groupe, Rapporteur: Martina Weise, "To update section 4.4 of the SmPC to add information on cases of drug-induced liver injury (DILI) observed in the postmarketing setting and section 4.8 of the SmPC to add of the adverse event DILI under the frequency unknown. The package leaflet is updated accordingly."

Bosulif - bosutinib - EMEA/H/C/002373/II/0041
Pfizer Europe MA EEIG, Rapporteur: Janet Koenig, "Update of section 5.2 of the SmPC in order to update the population PK model and the exposure-response model with additional PK and safety data from the recently completed Phase 2 study (B1871048) following a commitment within variation EMEA/H/C/002373/II/0036. In addition, a pooled safety data analysis has been performed to assess the clinical impact of reduced clearance in Asian population. The MAH takes also the opportunity to make editorial changes on the Package Leaflet."

Caelyx pegylated liposomal - doxorubicin - EMEA/H/C/000089/II/0094

Janssen-Cilag International NV, Rapporteur: Ondřej Slanař, "Update of sections 4.2 and 4.8 of the SmPC in line with the SmPC guideline. In addition, the MAH took the opportunity to update the PI in line with the QRD template version 10.1 and with the EDQM standard terms. Furthermore, the list of local representatives in the Package Leaflet is updated."

Darzalex - daratumumab - EMEA/H/C/004077/II/0038, Orphan

Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to:
- add sepsis to the list of adverse drug reactions (ADRs) with frequency common
- add new data on infections and special populations following a review of relevant safety information from the daratumumab clinical program resulting in an updated Company Core Data Sheet (CCDS) based on results from a Phase 3, randomized, controlled study comparing daratumumab in combination with carfilzomib (twice weekly) and dexamethasone (DKd) with carfilzomib (twice weekly) plus dexamethasone (Kd) in subjects with relapsed/refractory multiple myeloma (study 20160275 - CANDOR)

The MAH also proposes the following minor corrections.
- In section 4.8 of the SPC, the ADR frequencies for Neutropenia and Back-pain were corrected.

The Package Leaflet and labelling is updated accordingly"

Dynastat - parecoxib - EMEA/H/C/000381/II/0077

Pfizer Europe MA EEIG, Duplicate, Duplicate of Xapit (SRD), Rapporteur: Jayne Crowe, "SmPC sections 4.3 and 4.4 are updated to include Drug Reaction with Eosinophilia and Systemic Symptoms syndrome (DRESS syndrome)."

Galafold - migalastat - EMEA/H/C/004059/II/0025, Orphan

Amicus Therapeutics Europe Limited, Rapporteur: Johann Lodewijk Hillege, "Update to the Galafold Summary of Product Characteristics (SmPC), section 5.1 Pharmacodynamic Properties to add 1017 new amenable mutations in Table 2: Galafold

(migalastat) amenability table and delete the entire Table 3: Mutations not amenable to Galafold (migalastat). In addition, the MAH took the opportunity to update contact details of the MAH and Belgium local representatives and the Labelling (outer packaging), section 5. Method and Route(s) of administration as well as Package Leaflet, section 3. How to take Galafold in order to improve the instructions for opening and removal of the capsules out of the packaging. Editorial linguistic changes are made in Czech, Dutch, Finnish, Greek, Polish, Icelandic, Italian and Swedish languages."	
LIBTAYO - cemiplimab - EMEA/H/C/004844/II/0007 Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Sinan B. Sarac, Co-Rapporteur: Tuomo Lapveteläinen, "C.I.4, Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning and add new ADRs with frequency uncommon, regarding new safety information in the post marketing setting on the terms "Transplant rejection", "Graft Versus Host Disease (GVHD)" and "Myositis". The MAH took the opportunity to provide minor corrections to the efficacy data in the SmPC from study R2810-ONC-1540 (primary analysis for group 2 and 3 dated 09 Jul 2019), based on errors that were revealed in two patient's data following the completion of the MA. The Package Leaflet is updated accordingly. The MAH also took the opportunity to introduce editorial changes in the PI."	
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0028 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Submission of the final report from study Zoster-060, to fulfil post-authorization measure MEA 011.1, listed as a category 3 study in the RMP for Shingrix. The study was conducted to generate data on long-term immunogenicity in adults 50 years of age and above"	
Signifor - pasireotide - EMEA/H/C/002052/II/0046, Orphan Novartis Europharm Limited, Rapporteur: Kristina Dunder, "Update of sections 4.4 of the SmPC in order to add new warnings on	

cholangitis and ketoacidosis and 4.8 to add diabetic ketoacidosis to the list of adverse drug reactions (ADRs) with frequency not known. The Package Leaflet is updated accordingly."

Stribild - elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil - EMEA/H/C/002574/II/0111/G

Gilead Sciences Ireland UC, Rapporteur: Bruno Sepodes, "Grouped application:

- C.I.4 (Type II): Update of section 4.5 of the SmPC to include data on the drug-drug interaction between Stribild and the thienopyridine anti-platelet drugs clopidogrel and prasugrel, based on a MAH cumulative safety review. The Package Leaflet is updated accordingly.
- C.I.4 (Type II): Update of section 4.5 of the SmPC to include data on the drug-drug interaction between Stribild and medicinal products or oral supplements containing polyvalent cations, based on a MAH cumulative safety review. The Package Leaflet is updated accordingly.
- C.I.3.z (Type IBz): Update of sections 4.5 and 4.8 of the SmPC to implement information related to the interaction with didanosine, and section 4.8 of the SmPC to implement new wording regarding lactic acidosis, in line with the PRAC recommendation from EMEA/H/C/PSUSA/00002892/201903.

In addition, the Marketing Authorisation Holder (MAH) took the opportunity to correct the amount of lactose stated in section 2 of the SmPC, update section 4.5 of the SmPC in line with the clinical study report for Study GS-US-216-0125, update the PI in line with the Annex to the European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use' (EMA/CHMP/302620/2017 Rev.1) regarding sodium content and make minor editorial changes to the PI. Furthermore, the PI is brought in line with the latest QRD template version 10.1."

Vfend - voriconazole - EMEA/H/C/000387/II/0137/G

Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, "Grouping of two type II variations:

-to update of section 4.4 of the SmPC in order

to add a new warning on adrenal events, along with editorial changes to the paragraph and the abbreviation of severe cutaneous adverse reactions (SCARs),
-to update section 4.5. of the SmPC in order to add drug-drug interaction information with naloxegol, ivacaftor and corticosteroids following PRAC request during the assessment of PSUR 18 (for corticosteroids) and the French National Agency for the Safety of Medicines and Health Products (ANSM) update of the French "Medical Interaction Thesaurus" (May 2018), where voriconazole is classified as a strong CYP3A4 inhibitor.
In addition the MAH has taken the opportunity to update the information in the SmPC in line with the EU excipient guidance from October 2017 (SANTE-2017-11668) for sodium and cyclodextrin, to introduce a correction to the amount of sodium per vial for the IV presentations in Sections 2. QUALITATIVE AND QUANTITATIVE COMPOSITION and 4.4 Special warnings and precautions for use of the SmPC. The Package Leaflet is updated accordingly.
Following a recent discussion with EMA/EDQM; the MAH is also updating Annex IIIA Outer carton text for both iv presentations 16. INFORMATION IN BRAILLE to include: "Justification for not including Braille accepted."
In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1."

WS1779
Thymanax-EMEA/H/C/000916/WS1779/0044
Valdoxan-EMEA/H/C/000915/WS1779/0046

Les Laboratoires Servier, Lead Rapporteur: Bjorg Bolstad, "Update of section 4.8 of the SmPC to add 'Blood creatine phosphokinase increased', 'Myalgia' and 'Muscle spasms' with a frequency uncommon and 'Muscle Fatigue' with a frequency rare following routine pharmacovigilance review. The Package Leaflet section 4 is updated accordingly.
In addition, the Work Share Applicant takes the opportunity to bring the Product Information of Valdoxan and Thymanax in line with the latest QRD template version 10.1."

WS1798

Lyrica-EMEA/H/C/000546/WS1798/0104 Pregabalin Pfizer-EMEA/H/C/003880/ WS1798/0033

Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, "Update section 4.8 and section 5.1 SmPC to reflect data from study A0081106 "A 12-Month Open-Label Study to Evaluate the Safety and Tolerability of Pregabalin as Adjunctive Therapy in Pediatric Subjects 1 Month to 16 Years of Age With Partial Onset Seizures and Pediatric and Adult Subjects 5 to 65 Years of Age With Primary Generalized Tonic-Clonic Seizures""

B.6.9. CHMP-PRAC assessed procedures

Bavencio - avelumab - EMEA/H/C/004338/II/0015

Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Hans Christian Siersted, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to change posology recommendations, amend an existing warning and add new ADRs with frequency uncommon regarding myasthenia gravis and myasthenic syndrome. The update results from an update of the Company Core Data Sheet (CCDS) based on the review of cases of myasthenia gravis/myasthenic syndrome. The Package Leaflet is updated accordingly. The RMP version 2.2 has also been submitted with the proposal to reclassify "Other immune-related events (myasthenic syndrome)" from an important potential risk to an important identified risk of "Other immune-related events (myasthenia gravis/myasthenic syndrome)""

Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0087

UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to introduce a change in posology for axial spondyloarthritis (axSpA) and to update the safety and efficacy information based on the results of the study AS0005 (C-OPTIMISE) listed as a category 3 study in the RMP; this is a multicentre, open-label (part A) followed by a randomised, double-blind, parallel-group, placebo-controlled study (part B) to evaluate maintenance of remission in subjects with active

axSpA receiving either certolizumab pegol 200mg q2w or 200mg q4w as compared to placebo. The package leaflet is updated accordingly. The RMP version 17.0 has also been submitted to reflect the completion of study AS0005 and update to list of safety concerns. In addition, the interim study reports AS0006 and AS0007 have been submitted to include additional pooled safety data in the SmPC. Study AS0006 is a phase 3, multicenter, randomised, placebo-controlled, double-blind study to evaluate efficacy and safety of certolizumab pegol in subjects with active aSpA without x-ray evidence of ankylosing spondylitis and objective signs of inflammation. Study AS0007 is a multicenter, open-label study to assess the effects of certolizumab pegol on the reduction of anterior uveitis flares in aSpA subjects with a history of anterior uveitis (C-view)."	
Firmagon - degarelix - EMEA/H/C/000986/II/0037 Ferring Pharmaceuticals A/S, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "C.I.11.b update of Annex II to revise risk minimisation measures based on previous and a newly submitted study. As a consequence, the RMP is updated accordingly. The MAH took the occasion to transfer to GVP V revision 2 of the RMP, to align the PI to QRD template v.10.1 and propose combination of different strengths."	
Kyntheum - brodalumab - EMEA/H/C/003959/II/0014 LEO Pharma A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia, "Update of sections 4.4 and 4.8 of the SmPC and relevant sections of the PL to reflect a signal of anaphylactic reaction detected in the post marketing setting. Minor updates have also been included throughout the product information."	
NexoBrid - concentrate of proteolytic enzymes enriched in bromelain - EMEA/H/C/002246/II/0047, Orphan MediWound Germany GmbH, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, "Submission of the final report from study	

MW2013-06-01, listed as a category 3 study in the RMP. This is an international, observational retrospective, data-collection study assessing efficacy of applied risk-minimisation measures in burn patients treated with NexoBrid. The RMP version 7.0 has also been submitted. In addition, the MAH took the opportunity to revise the RMP in line with the new RMP template (GVP Rev. 2) and to change the due date for the following category 3 studies: MW2013-06-01 and MW2010-03-02 (DETECT)"

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

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

Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0009/G

Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "C.I.4, C.I.3, C.I.6 (non-EoI) Update of section 5.2 of the SmPC in order to update pharmacokinetic information based on results from study CSR 19-514 (PK Comparability) and CSR 16-508 (Japanese Ethnicity Study) listed as a specific obligation in the Annex II. Annex II was proposed to be updated accordingly. The RMP version 2.1 has also been submitted."

ProQuad - measles, mumps, rubella and varicella vaccine (live) - EMEA/H/C/000622/II/0139

MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Further to the MAH evaluation of new significant Pharmacovigilance data, the

SmPC is updated to further characterize the risk of secondary transmission. This SmPC update is accompanied by RMP version 7.1, with consequential proposed RMP revisions: the important potential risk of "potential secondary transmission of Oka/Merck varicella vaccine virus strain in susceptible highrisk individuals leading to severe clinical consequences" is renamed to "secondary transmission of Oka/Merck varicella vaccine virus strain in susceptible individuals leading to disseminated disease" and is reclassified to important identified risk. In addition, information pertaining to the important identified risk of "Disseminated Disease Caused by Oka/Merck Varicella Vaccine Virus Strain" was updated for accuracy and clarity and to align with the RMP for another MMRV vaccines owned by the MAH, including the post-marketing search strategy used to inform frequency. The Package Leaflet is updated accordingly. The MAH takes the opportunity to: - Implement the following guidelines: -Excipients in the labelling and package leaflet of medicinal products for human use -Guideline on quality aspects included in the product information for vaccines for human use (18-Oct-2018). Notably, section 6.5 of the SmPC is updated with information on the glass type for the immediate container. Consequently, Annex A has been updated with the same information - Implement QRD v10.1 taking into account the 'Compilation of QRD decisions on stylistic matters in product information' (EMA/25090/2002 rev.19) - Align some wordings across other MMRV vaccines owned by the MAH, in particular section 6.6 'Special precautions for disposal and other handling'."	
Resolor - prucalopride - EMEA/H/C/001012/II/0051 Shire Pharmaceuticals Ireland Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.4 'Special warnings and precautions for use' of the Summary of Product Characteristics (SmPC) with text relating to suicidal ideation and behaviour and to add 'suicidal ideation and behaviour' to the list of safety concerns as an	

important potential risk in the EU Risk Management Plan (RMP vs 16.0) based on post-marketing reports.
The package leaflet is proposed to be updated accordingly.
The MAH has also taken to opportunity to make editorial changes to RMP and SmPC."

SCENESSE - afamelanotide - EMEA/H/C/002548/II/0033, Orphan
Clinuvel Europe Limited, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, "Update of section 4.8 of the SmPC to revise the frequencies of adverse drug reactions (ADRs) based on safety reports and to add new ADRS based on post-marketing spontaneous reports as requested during Scenesse Renewal procedure (EMEA/H/C/002548/R/0026); the Package Leaflet is updated accordingly. The RMP version 9.0 (in line with rev 2 of the template) has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes in section 2 of the SmPC and Annex IIIA."

WS1664
Keppra-EMEA/H/C/000277/WS1664/0187
UCB Pharma S.A., Lead Rapporteur: Koenraad Norga, Lead PRAC Rapporteur: Laurence de Fays, "Update of section 4.2 of the SmPC to recommend the same dosing for monotherapy and adjunctive therapy based on data from modelling and simulation project.
The Package Leaflet is updated accordingly.
The RMP version 9.0 has also been submitted.
The MAH took the opportunity to move Braille to another box section and to review and adapt the German PI according to the current QRD template."

B.6.10. PRAC assessed procedures

PRAC Led
Duavive - estrogens conjugated / bazedoxifene - EMEA/H/C/002314/II/0024
Pfizer Europe MA EEIG, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Update of the Risk Management Plan (RMP) to V3.0, to include amended study milestones and to revise the

RMP document format in line with latest Good Pharmacovigilance Practices Guidance Module V, revision 2 guidelines, as requested during the assessment of the renewal."

PRAC Led

Moventig - naloxegol - EMEA/H/C/002810/II/0029/G

Kyowa Kirin Holdings B.V., Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ronan Grimes, PRAC-CHMP liaison: Peter Kiely, "Submission of an updated RMP version 6 in order to update the list of safety concerns"

PRAC Led

Replagal - agalsidase alfa - EMEA/H/C/000369/II/0106

Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of section 4.8 of the Summary of Product Characteristics (SmPC) in order to update the list of adverse drug reactions (ADRs) information based on the final results from study HGT-REP-081 " a Multicenter Open-label Treatment Protocol to Observe the Safety of Replagal (agalsidase alfa) Enzyme Replacement Therapy in Canadian Patients with Fabry Disease". In addition, the MAH took the opportunity to introduce editorial and QRD changes in sections throughout the Product Information according to the QRD templates and current guidelines, including new warnings related to sodium excipient and traceability of biological medicinal products. The Package Leaflet is updated accordingly."

PRAC Led

Tybost - cobicistat - EMEA/H/C/002572/II/0054

Gilead Sciences Ireland UC, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "Update of sections 4.4 and 4.5 of the SmPC in order to add a new contraindication regarding drug-drug interactions between cobicistat-containing products and thienopyridines. The proposed addition is based on a cumulative safety review conducted by MAH and related to the Pharmacovigilance Risk Assessment Committee recommendation dated June 2019 with regards to the interaction of clopidogrel

with boosted antiviral HIV therapy leading to insufficient inhibition of platelet aggregation. In addition, the MAH took also the opportunity to amend of the amount of sunset yellow FCF aluminium lake (E110) per tablet in section 2 of the SmPC following the suggestion done by EMA Labelling group during the renewal application (EMEA/H/C/002572/R/0041). Moreover, the sodium excipient wording is added in accordance with the "Excipients in the labelling and package leaflet of medicinal products for human use"(SANTE-2017-11668). Finally, some minor linguistic amendments are also implemented. The Package Leaflet is updated accordingly."

PRAC Led
Xadago - safinamide -
EMEA/H/C/002396/II/0035
Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "C.I.13 - Results of a DUS and changes to RMP."

B.6.11. CHMP-CAT assessed procedures

Spherox - spheroids of human autologous matrix-associated chondrocytes -
EMEA/H/C/002736/II/0015, ATMP
CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder, , "Update of section 4.8 and 5.1 of the SmPC following the 48-month follow up data for trial cod 16 HS 13, a study assessing the long-term efficacy and safety of Spherox."

B.6.12. CHMP-PRAC-CAT assessed procedures

B.6.13. PRAC assessed ATMP procedures

B.6.14. Unclassified procedures and worksharing procedures of type I variations

WS1781/G
Infanrix hexa-EMEA/H/C/000296/
WS1781/0272/G
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1788/G
Ambirix-EMEA/H/C/000426/WS1788/

0106/G
Cervarix-EMEA/H/C/000721/WS1788/
0108/G
Infanrix hexa-EMEA/H/C/000296/
WS1788/0273/G
Twinrix Adult-EMEA/H/C/000112/
WS1788/0141/G
Twinrix Paediatric-EMEA/H/C/000129/
WS1788/0142/G
GlaxoSmithkline Biologicals SA, Lead
Rapporteur: Bart Van der Schueren

B.7. DOCUMENTS TABLED IN MMD AFTER THE CHMP PLENARY

B.7.1. Yearly Line listing for Type I and II variations

B.7.2. Monthly Line listing for Type I variations

B.7.3. Opinion on Marketing Authorisation transfer (MMD only)

B.7.4. Notifications in accordance with Article 61(3) of Council Directive 2001/83/EC (MMD only)

B.7.5. Request for supplementary information relating to Notification of Type I variation (MMD only)

B.7.6. Notifications of Type I Variations (MMD only)

C. Annex C - Post-Authorisation Measures (PAMs), (Line listing of Post authorisation measures with a description of the PAM. Procedures starting in that given month with assessment timetabled)

D. Annex D - Post-Authorisation Measures (PAMs), (Details on PAMs including description and conclusion, for adoption by CHMP in that given month, or finalised ones with PRAC recommendation and no adoption by CHMP needed)

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES

Information related to plasma master files cannot be released at the present time as these contain commercially confidential information.

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

E.2. Timetables – starting & ongoing procedures: For information

PMF timetables starting and ongoing procedures	Tabled in MMD and sent by post mail (folder E).

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

F.1. Parallel Distribution - Pursuant to Article 9 of Council Regulation (EC) No. 2743/98 of 14 December 1998, as amended

F.2. Request for scientific opinion on justification of exceptional circumstance and for imperative grounds of public health

G. ANNEX G

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

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

G.2. PRIME

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

G.2.1. List of procedures concluding at 23-26 March 2020 CHMP plenary:

G.2.2. List of procedures starting in March 2020 for April 2020 CHMP adoption of outcomes

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