11 October 2021
EMA/CHMP/573222/2021
Human Medicines Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 11-14 October 2021

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

11 October 2021, 09:00 – 19:30, virtual meeting/ room 1C

12 October 2021, 08:30 – 19:30, virtual meeting/ room 1C

13 October 2021, 08:30 – 19:30, virtual meeting/ room 1C

14 October 2021, 08:30 – 15:00, virtual meeting/ room 1C

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 11-14 October 2021. See October 2021 CHMP minutes (to be published post November 2021 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 11-14 October 2021

1.3. Adoption of the minutes

CHMP minutes for 13-16 September 2021.

Minutes from PReparatory and Organisational Matters (PROM) meeting held on 04 October 2021.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. bevacizumab - EMEA/H/C/005433

indicated in adults for the treatment of neovascular macular degeneration associated with aging and diabetes

Scope: Oral explanation

Action: Oral explanation to be held on 12 October 2021 at 14:00

List of Outstanding Issues adopted on 20.05.2021. List of Questions adopted on 17.09.2020.

2.1.2. avacopan - Orphan - EMEA/H/C/005523

Vifor Fresenius Medical Care Renal Pharma France; Treatment of granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA)

Scope: Oral explanation

Action: Oral explanation to be held on 12 October 2021 at 16:00

List of Outstanding Issues adopted on 22.07.2021. List of Questions adopted on 25.02.2021.

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

No items

2.4. Referral procedure oral explanations

2.4.1. Lidocain/ Prilocain IDETEC – lidocaine, prilocaine - EMEA/H/A-29(4)/1506

International Drug Development France

Referral Rapporteur: Kristine Moll Harboe, Co-Rapporteur: Paula Boudewina van Hennik

Scope: Oral explanation

Action: Oral explanation to be held on 12 October 2021 at 11:00

Summary: Decentralised Procedure number: DK/H/3106/001/DC, notification by the Danish Agency notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC. The objecting MS is of the opinion that therapeutic equivalence has not been demonstrated between the test and the reference product.

List of questions adopted on 25.03.2021.

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. pegcetacoplan - Orphan - EMEA/H/C/005553

Swedish Orphan Biovitrum AB (publ); paroxysmal nocturnal haemoglobinuria (PNH)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 24.06.2021. List of Questions adopted on 28.01.2021.

3.1.2. abrocitinib - EMEA/H/C/005452

Indicated for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy.

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 16.09.2021, 24.06.2021. List of Questions adopted

on 28.01.2021.

3.1.3. amivantamab - EMEA/H/C/005454

for treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating epidermal growth factor receptor (EGFR) Exon 20 insertion mutations, after failure of platinum-based chemotherapy.

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 16.09.2021. List of Questions adopted on 20.05.2021.

3.1.4. sitagliptin fumarate - EMEA/H/C/005741

treatment of type 2 diabetes mellitus

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 22.07.2021. List of Questions adopted on 25.03.2021.

3.1.5. sacituzumab govitecan - EMEA/H/C/005182

treatment of unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 14.09.2021. List of Questions adopted on 22.06.2021.

3.1.6. pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/005477

immunisation for the prevention of invasive disease and pneumonia caused by Streptococcus pneumoniae

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 16.09.2021. List of Questions adopted on 22.04.2021.

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

3.2.1. lisocabtagene maraleucel / lisocabtagene maraleucel - Orphan - ATMP - EMEA/H/C/004731

Bristol-Myers Squibb Pharma EEIG; treatment of large B-cell lymphoma, diffuse large B-cell lymphoma (DLBCL), primary mediastinal large B-cell lymphoma (PMBCL) and follicular lymphoma grade 3B (FL3B)

Scope: List of outstanding issues

Action: For information

List of Outstanding Issues adopted on 16.04.2021. List of Questions adopted on 06.11.2020.

3.2.2. gefapixant - EMEA/H/C/005476

treatment of refractory or unexplained chronic cough

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 24.06.2021.

3.2.3. gefapixant - EMEA/H/C/005884

treatment of refractory or unexplained chronic cough

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 24.06.2021.

3.2.4. metformin hydrochloride / sitagliptin hydrochloride monohydrate - EMEA/H/C/005678

treatment of type 2 diabetes mellitus

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 25.03.2021.

3.2.5. voxelotor - Orphan - EMEA/H/C/004869

Global Blood Therapeutics Netherlands; Indicated for the treatment of haemolytic anaemia in adults and paediatric patients 12 years of age and older with sickle cell disease (SCD).

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.05.2021.

3.2.6. anifrolumab - EMEA/H/C/004975

indicated as an add-on therapy for the treatment of adult patients with moderate to severe systemic lupus erythematosus (SLE), despite standard therapy

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 22.07.2021. List of Questions adopted on 25.02.2021.

3.2.7. sapropterin - EMEA/H/C/005646

treatment of hyperphenylalaninemia (HPA)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.05.2021.

3.2.8. semaglutide - EMEA/H/C/005422

treatment for weight loss and weight maintenance

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.05.2021.

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

3.3.1. copanlisib - Orphan - EMEA/H/C/004334

Bayer AG; treatment of adult patients with relapsed marginal zone lymphoma

Scope: List of questions

Action: For adoption

3.3.2. dimethyl fumarate - EMEA/H/C/005956

treatment of multiple sclerosis

Scope: List of questions

Action: For adoption

3.3.3. dimethyl fumarate - EMEA/H/C/005955

treatment of multiple sclerosis

Scope: List of questions

Action: For adoption

3.3.4. maribavir - Orphan - EMEA/H/C/005787

Shire Pharmaceuticals Ireland Limited; treatment of cytomegalovirus (CMV) infection

Scope: List of questions

Action: For adoption

3.3.5. tezepelumab - EMEA/H/C/005588

add-on maintenance treatment in adults and adolescents 12 years and older with severe asthma

Scope: List of questions

Action: For adoption

3.3.6. faricimab - EMEA/H/C/005642

treatment of neovascular (wet) age-related macular degeneration (nAMD) and visual impairment due to diabetic macular oedema (DME)

Scope: List of questions

Action: For adoption

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

3.4.1. betaine anhydrous - EMEA/H/C/005637

treatment of homocystinuria

Scope: Letter from the applicant dated 30 September 2021 requesting an extension to the clock stop to respond to the list of questions adopted in July 2021.

Action: For adoption

List of Questions adopted on 22.04.2021.

3.4.2. ganirelix - EMEA/H/C/005641

Prevention of premature luteinising hormone (LH) surges in women undergoing controlled ovarian hyperstimulation (COH) for assisted reproduction techniques (ART).

Scope: Letter from the applicant dated 22 September 2021 requesting an extension to the clock stop to respond to the list of questions adopted in July 2021.

Action: For adoption

List of Questions adopted on 22.07.2021

3.4.3. hepatitis B surface antigen - EMEA/H/C/005466

indicated for the prevention of infection caused by all known subtypes of the hepatitis B virus in adults.

Scope: Letter from the applicant dated 07 October 2021 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in September 2021.

Action: For adoption

List of Outstanding Issues adopted on 16.09.2021. List of Questions adopted on 22.04.2021.

3.4.4. lonafarnib - Orphan - EMEA/H/C/005271

EigerBio Europe Limited; treatment of Hutchinson-Gilford Progeria Syndrome and Progeroid Laminopathies

Scope: Letter from the applicant dated 04 October 2021 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in September 2021.

Action: For adoption

List of Outstanding Issues adopted on 16.09.2021, 25.02.2021. List of Questions adopted on 23.07.2020.

3.4.5. arimoclomol - Orphan - EMEA/H/C/005203

Orphazyme A/S; treatment of Niemann-Pick disease type C (NPC)

Scope: Letter from the applicant dated 23 September 2021 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in September 2021.

Action: For adoption

List of Outstanding Issues adopted on 16.09.2021. List of Questions adopted on 25.03.2021.

3.4.6. bevacizumab - EMEA/H/C/005574

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: Letter from the applicant dated 28 September 2021 requesting an extension to the clock stop to respond to the list of questions adopted in April 2021.

Action: For adoption

List of Questions adopted on 22.04.2021

3.4.7. enfortumab vedotin - EMEA/H/C/005392

Accelerated assessment

treatment of locally advanced (LA) or metastatic urothelial cancer (mUC)

Scope: Letter from the applicant dated 27 September 2021 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in September 2021.

Action: For adoption

List of Outstanding Issues adopted on 14.09.2021. List of Questions adopted on 22.06.2021.

3.4.8. sugammadex - EMEA/H/C/005760

Reversal of neuromuscular blockade induced by rocuronium or vecuronium.

Scope: Letter by the applicant dated 30 September 2021 requesting an extension to the clock stop to respond to list of questions adopted in July 2021.

Action: For adoption

List of Questions adopted on 22.07.2021.

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

3.5.1. Flynpovi - eflornithine / sulindac - Orphan - EMEA/H/C/005043

Cancer Prevention Pharma (Ireland) Limited; treatment of adult patients with familial adenomatous polyposis (FAP)

Scope: Opinion

Action: For adoption

Fixed combination application (Article 10b of Directive No 2001/83/EC)

Opinion adopted on 24.06.2021. List of Outstanding Issues adopted on 25.03.2021. List of Questions adopted on 15.10.2020.

3.5.2. Nexviadyme - avalglucosidase alfa - Orphan - EMEA/H/C/005501

Genzyme Europe BV; for long-term enzyme replacement therapy for the treatment of patients with Pompe disease.

Scope: List of experts for the Ad-hoc expert group (AHEG) meeting, List of questions to the AHEG

Action: For adoption

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

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

4.1.1. Comirnaty - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/X/0044/G

BionTech Manufacturing GmbH

Rapporteur: Filip Josephson

Scope: Extension application to add a new pharmaceutical form (dispersion for injection) with a new strength (0.1 mg/ml).
C.I.z - To update sections 6.4, 6.5 and 6.6 of the SmPC, section 5, 6 and information for healthcare professionals of the PL, section 1 of the Carton Box Label as well as section 1 and 5 of the Vial Label to ensure the correct handling by providing dose verification information about strength, age range, colour information of the flip-off plastic cap and greyscale images.
C.I.z - To update section 4.2 of the SmPC to ensure the correct handling in accordance to interchangeability of the medicinal product.
C.I.z - To update section 8 of Carton Box Label to clarify expiry date "EXP" by adding storage temperature "(at -90°C to -60°C)" to ensure the correct handling of the medicinal product.
A.3 - To change the name of the active substance from COVID-19 mRNA Vaccine (nucleoside modified) to Tozinameran.
The marketing authorisation holder has taken the opportunity to implement minor editorial changes.

Action: For adoption

4.1.2. Nitisinone MDK - nitisinone - EMEA/H/C/004281/X/0007

MendeliKABS Europe Limited

Rapporteur: Alar Irs, PRAC Rapporteur: Ilaria Baldelli

Scope: "Extension application to add a new strength of 20 mg (hard capsule)."

Action: For adoption

List of Outstanding Issues adopted on 25.02.2021. List of Questions adopted on 17.09.2020.

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. Ferriprox - deferiprone - EMEA/H/C/000236/X/0145

Chiesi Farmaceutici S.p.A.

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant

Scope: "Extension application to introduce a new pharmaceutical form (gastro-resistant tablets). The RMP (version 14.0) is updated in accordance."

Action: For adoption

List of Outstanding Issues adopted on 24.06.2021, 25.02.2021. List of Questions adopted on 17.09.2020.

4.2.2. Kaftrio - ivacaftor / tezacaftor / elexacaftor - Orphan - EMEA/H/C/005269/X/0008/G

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber

Scope: "Extension application to introduce new strengths of 37.5 mg/ 25 mg/ 50 mg film-coated tablets. Grouped with a type II variation (C.I.6.a) to include paediatric use (6 to 11 years)."

Action: For adoption

List of Questions adopted on 22.07.2021.

4.2.3. Ozempic - semaglutide - EMEA/H/C/004174/X/0021

Novo Nordisk A/S

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Annika Folin

Scope: "Extension application to add a new strength of 2 mg solution for injection."

Action: For adoption

List of Questions adopted on 20.05.2021.

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. Biktarvy - bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449/X/0040/G

Gilead Sciences Ireland UC

Rapporteur: Jean-Michel Race, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Extension application to introduce a new strength 30/120/15 mg. The extension application is grouped with a type II variation (C.I.6.a) to include paediatric indication: use in patients 2 years of age and older and weighing at least 14 kg. Sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC and the Package Leaflet are updated to support the extended indication. The RMP (version 3.1) is updated in accordance."

Action: For adoption

4.3.2. Lyumjev - insulin lispro - EMEA/H/C/005037/X/0010

Eli Lilly Nederland B.V.

Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Annika Folin

Scope: Quality variation "The RMP is updated (version 11.1) accordingly."

Action: For adoption

4.3.3. Sogroya - somapacitan - Orphan - EMEA/H/C/005030/X/0001/G

Novo Nordisk A/S

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber

Scope: "Extension application to add a new strength of 5 mg/1.5 mL (3.3 mg/mL) grouped with a Type II Quality variation and a Type IA variation. The RMP was updated (version 2.0) accordingly.
Type II variation (B.II.b.1.c)
Type IA variation (B.II.d.1.a."

Action: For adoption

4.3.4. Trydonis - beclometasone dipropionate / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004702/X/0015

Chiesi Farmaceutici S.p.A.

Rapporteur: Janet Koenig, PRAC Rapporteur: Jan Neuhauser

Scope: "Extension application to add a new pharmaceutical form (inhalation powder) associated with new strength (88µg / 5µg / 9µg). The RMP (version 7.1) is updated in accordance."

Action: For adoption

4.3.5. Zejula - niraparib - Orphan - EMEA/H/C/004249/X/0029

GlaxoSmithKline (Ireland) Limited

Rapporteur: Ingrid Wang, PRAC Rapporteur: Jan Neuhauser

Scope: "Extension application to introduce a new pharmaceutical form (100 mg film-coated tablet). The RMP (version 5.1) is updated in accordance."

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. Cosentyx - secukinumab - EMEA/H/C/003729/II/0079

Novartis Europharm Limited

Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Eva A. Segovia

Scope: "C.I.6 (Extension of indication)
Extension of indication to include treatment of Juvenile Idiopathic Arthritis (Enthesitis-Related Arthritis and Juvenile Psoriatic Arthritis) in patients 2 years and older whose disease has responded inadequately to, or who cannot tolerate, conventional therapy for Cosentyx; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 10.0 of the RMP has also been submitted."

Action: For adoption

5.1.2. Entyvio - vedolizumab - EMEA/H/C/002782/II/0061

Takeda Pharma A/S

Rapporteur: Armando Genazzani, PRAC Rapporteur: Adam Przybylkowski

Scope: "To add a new therapeutic indication "treatment of adult patients with pouchitis, who have undergone proctocolectomy and ileal pouch anal anastomosis for ulcerative colitis, and have had an inadequate response with, lost response to, or were intolerant to antibiotic therapy" for Entyvio 300 mg (powder for concentrate for solution for infusion), based on final results from study Vedolizumab-4004 (ERNEST). This was an interventional, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of Entyvio (intravenous) in the treatment of chronic pouchitis.
As a consequence, sections 4.1, 4.2, 4.5, 5.1 and 5.2 of the SmPC for Entyvio 300 mg are updated. The Package Leaflet are updated in accordance. Version 7.0 of the RMP is also submitted." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

5.1.3. Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0129

CSL Behring GmbH

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication for Hizentra in order to align the wording for the already approved Secondary immunodeficiency (SID) indications in the Hizentra SmPC with the wording of the Guideline on core SmPC for human normal immunoglobulin for intravenous administration (EMA/CHMP/BPWP/94038/ 2007 Rev 5; CHMP, 2018).
As a consequence, sections 4.1 and 4.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.6 of the RMP 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."

Action: For adoption

Request for Supplementary Information adopted on 22.07.2021.

5.1.4. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/II/0096

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Maria del Pilar Rayon

Scope: "Extension of indication for Kalydeco tablets in combination regiment with Kaftrio to include the treatment of adults, adolescents and children aged 6 years and older with cystic fibrosis who are homozygous for the F508del mutation in the CFTR gene or heterozygous for F508del and have a minimal function (MF) mutation in the CFTR gene. This application is based on the results of study VX18-445-106, a phase 3, open-label, multicentre study in subjects 6 through 11 years of age, with F/MF and F/F genotypes. As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC are updated. The Packaged Leaflet is updated in accordance. Version 12.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 22.07.2021.

5.1.5. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0104

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication for Keytruda to include in combination with lenvatinib first line treatment of adults with advanced renal cell carcinoma (RCC); as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 32.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 16.10.2021, 24.06.2021.

5.1.6. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0105

Merck Sharp & Dohme B.V.

Rapporteur: Armando Genazzani, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include pembrolizumab in combination with lenvatinib for the treatment of advanced endometrial carcinoma in adults who have disease progression following prior systemic therapy in any setting and who are not candidates for curative surgery or radiation; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 33.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021, 24.06.2021.

5.1.7. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0108

Merck Sharp & Dohme B.V.

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

Scope: "C.I.6.a
Update of sections 4.1, 4.2 and 5.1 of the SmPC in order to extend the existing therapeutic indications for Keytruda to include the adjuvant treatment in monotherapy of adults with renal cell carcinoma (RCC) at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions. The Package Leaflet are updated accordingly. The RMP version 35.1 has also been submitted"

Action: For adoption

5.1.8. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0109

Merck Sharp & Dohme B.V.

Rapporteur: Armando Genazzani, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication for Keytruda as monotherapy in the treatment of unresectable or metastatic MSI-H or dMMR colorectal, endometrial, gastric, small intestine, biliary, or pancreatic cancer in adults who have received prior therapy. The proposed indication is based on the results from the KEYNOTE-164 (KN164) and KEYNOTE-158 (KN158) trials. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. An updated version of the RMP (Version 34.1) has been submitted."

Action: For adoption

5.1.9. Kineret - anakinra - EMEA/H/C/000363/II/0086

Swedish Orphan Biovitrum AB (publ)

Rapporteur: Kirstine Moll Harboe, Co-Rapporteur: Fátima Ventura, PRAC Rapporteur: Anette Kirstine Stark

Scope: "C.I.6 - Extension of indication to include treatment of coronavirus disease 2019 (COVID-19) in adult patients with pneumonia who are at risk of developing severe respiratory failure for Kineret; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 5.6 of the RMP has also been submitted."

Action: For adoption

5.1.10. Kisplyx - lenvatinib - EMEA/H/C/004224/II/0045

Eisai GmbH

Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: David Olsen

Scope: "Extension of indication for Kisplyx to include in combination with pembrolizumab first line treatment of adults with advanced renal cell carcinoma (RCC); as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 13 of the RMP has also been submitted. In addition, the Marketing authorisation holder took the opportunity to update the list of local representatives in the Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 16.10.2021, 24.06.2021.

5.1.11. Lenvima - lenvatinib - EMEA/H/C/003727/II/0042

Eisai GmbH

Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Annika Folin

Scope: "Extension of indication to include lenvatinib in combination with pembrolizumab for the treatment of adult patients with advanced endometrial carcinoma (EC) who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 14.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to make minor editorial

changes to the SmPC and update the list of local representatives in the Package Leaflet in line with the latest QRD template version 10.2.", 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 16.09.2021, 24.06.2021.

5.1.12. Lonquex - lipegfilgrastim - EMEA/H/C/002556/II/0058/G

Teva B.V.

Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kirsti Villikka

Scope: "Extension of indication to include treatment of the paediatric population for Lonquex and introduction of an age appropriate presentation in vials; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 12.0 of the RMP 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. Furthermore, the PI is brought in line with the latest QRD template version 10.1."

Action: For adoption

Request for Supplementary Information adopted on 12.11.2020.

5.1.13. Olumiant - baricitinib - EMEA/H/C/004085/II/0028

Eli Lilly Nederland B.V.

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Christophe Focke, PRAC Rapporteur: Adam Przybylkowski

Scope: "C.I.6 - Extension of indication to include treatment of coronavirus disease 2019 (COVID 19) in hospitalised adult and paediatric patients aged 10 years and older who require low-flow oxygen or non-invasive ventilation/high flow oxygen for Olumiant; as a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Annex II and the Package Leaflet are updated in accordance. Version 11.1 of the RMP 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 22.07.2021.

5.1.14. Repatha - evolocumab - EMEA/H/C/003766/II/0049/G

Amgen Europe B.V.

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Kimmo Jaakkola

Scope: "C.I.6 (EoI)
Extension of indication to include one new paediatric indication in paediatric patients aged

10 years and over with heterozygous familial hypercholesterolaemia as an adjunct to diet, alone or in combination with other lipid-lowering therapy, to reduce LDL-C based on results of study 20120123 (HAUSER-RCT). It is a randomized, multicenter, placebo-controlled, double blind, parallel group, 24-week trial in 158 paediatric patients aged 10 to > 18 years with heterozygous familial hypercholesterolaemia. As a consequence, sections 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet are updated in accordance. Version 7.0 of the RMP has also been submitted.
C.I.6 (EoI)
Extension of indications to modify the existing indication for treatment of adults and paediatric patients aged 10 years and over with homozygous familial hypercholesterolaemia in combination with other lipid-lowering therapies based on interim results from study 20120124 (HAUSER-OLE). It was an open label, single arm, multicenter, 80-week trial to evaluate the safety, tolerability and efficacy of Repatha for LDL-C reduction in paediatric patients from aged ≥ 10 to < 18 years of age with homozygous familial hypercholesterolaemia. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated accordingly."

Action: For adoption

Request for Supplementary Information adopted on 24.06.2021.

5.1.15. RoActemra - tocilizumab - EMEA/H/C/000955/II/0101

Roche Registration GmbH

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "C.I.6 - Extension of indication to include the treatment of coronavirus disease 2019 in hospitalised adults who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation for RoActemra; as a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.8, 5.1 and 5.2 of the SmPC for RoActemra 20 mg/mL concentrate for solution for infusion are updated. The Package Leaflet is updated in accordance. Version 27 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.2 rev. 1."

Action: For adoption

5.1.16. Senshio - ospemifene - EMEA/H/C/002780/II/0041

Shionogi B.V.

Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Kirsti Villikka

Scope: "Extension of indication by deletion of information on specific subset of patients for Senshio. This is supported by the submission of the final study report of the imposed non-interventional post-authorisation safety study. As mentioned in Annex IID, this is an observational retrospective cohort study of ospemifene to assess the incidence of venous thromboembolism and other safety concerns as agreed in the Risk Management Plan (RMP), in vulvar and vaginal atrophy (VVA) patients treated with ospemifene compared to 1) patients newly prescribed SERMs for oestrogen-deficiency conditions or breast cancer prevention, and 2) the incidence in untreated VVA patients. As a consequence, sections 4.1 and 4.4 of the SmPC are updated. The Package Leaflet and Annex IID are updated in

accordance. Version 2 of the RMP has also been submitted. In addition, the Marketing authorisation holder took the opportunity to update the list of local representatives in the Package Leaflet."

Action: For adoption

5.1.17. Skyrizi - risankizumab - EMEA/H/C/004759/II/0014

AbbVie Deutschland GmbH & Co. KG

Rapporteur: Peter Kiely, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Extension of indication for the treatment of active psoriatic arthritis in adults. Consequently, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 to the SmPC have been updated. The Package leaflet is updated accordingly. Additionally, Annex II is also updated."

Action: For adoption

Request for Supplementary Information adopted on 22.07.2021.

5.1.18. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0064

Roche Registration GmbH

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

Scope: "C.I.6 (Extension of indication)
Extension of indication to include adjuvant treatment of non-small cell lung cancer (NSCLC) following resection and platinum-based chemotherapy for adult patients whose tumours have PD-L1 expression on ≥ 1% of tumour cells (TC) for Tecentriq as monotherapy based on the results from the pivotal phase III Study GO29527 (IMpower010); as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of both the Tecentriq 840 mg concentrate for solution for infusion SmPC and the Tecentriq 1,200 mg concentrate for solution for infusion SmPC are updated. Minor editorial changes have been made throughout the SmPC. The Package Leaflets are updated in accordance. Version 21.0 of the RMP has also been submitted."

Action: For adoption

5.1.19. Verzenios - abemaciclib - EMEA/H/C/004302/II/0013

Eli Lilly Nederland B.V.

Rapporteur: Filip Josephson, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of indication to include Verzenios in combination with endocrine therapy for adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive early breast cancer at high risk of recurrence; as a consequence, section 4.1, 4.2, 4.4, 4.6, 4.8, 5.1 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP 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 24.06.2021, 25.02.2021.

5.1.20. Xeljanz - tofacitinib - EMEA/H/C/004214/II/0035

Pfizer Europe MA EEIG

Rapporteur: Armando Genazzani, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Extension of indication to include treatment of adult patients with active ankylosing spondylitis (AS) who have responded inadequately to conventional therapy for Xeljanz film-coated tablets; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 17.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 20.05.2021.

5.1.21. Zeposia - ozanimod - EMEA/H/C/004835/II/0002/G

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Bruno Sepodes, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Maria del Pilar Rayon

Scope: "C.I.6 (Extension of indication)
Extension of indication to include the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent for Zeposia; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.2 and 5.1 of the SmPC and Annex IID are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement editorial changes throughout the product information.
C.I.4
Update of sections 4.4 and 4.5 of the SmPC in order to update the current SmPC description about PK interaction with BCRP inhibitors based on the study report from a drug interaction study with cyclosporine l(RPC-1063-CP-001)."

Action: For adoption

Request for Supplementary Information adopted on 22.07.2021, 25.03.2021.

5.1.22. Zerbaxa - ceftolozane / tazobactam - EMEA/H/C/003772/II/0036

Merck Sharp & Dohme B.V.

Rapporteur: Ingrid Wang, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension of indication to include treatment of paediatric patients aged birth to less than 18 years for Zerbaxa, based on final results from studies MK-7625A-034 (A Phase 2, Randomized, Active Comparator-Controlled, Double-Blind Clinical Trial to Study the Safety and Efficacy of Ceftolozane/Tazobactam Versus Meropenem in Paediatric Subjects with

Complicated Urinary Tract Infection, Including Pyelonephritis) and MK-7625A-035 (A Phase 2, Randomized, Active Comparator-Controlled, Double-Blind Clinical Trial to Study the Safety and Efficacy of Ceftolozane/Tazobactam Plus Metronidazole Versus Meropenem in Paediatric Subjects with Complicated Intra-Abdominal Infection).
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. Version 3.1 of the RMP 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."

Action: For adoption

5.1.23. WS1952
Edistride - dapagliflozin - EMEA/H/C/004161/WS1952/0042
Forxiga - dapagliflozin - EMEA/H/C/002322/WS1952/0060

AstraZeneca AB

Lead Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: "Extension of indication for Forxiga / Edistride to include treatment of children aged 10 years and adolescents with T2DM based on the results from studies MB10209/D1690C000016 and MB102-138/D1690C00017; these are paediatric studies submitted according to Article 46 of the Paediatric Regulation. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 21 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 22.04.2021.

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. Xalkori - crizotinib - EMEA/H/C/002489/II/0072

Pfizer Europe MA EEIG

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant

Scope: "Extension of indication to include treatment of paediatric patients (age ≥ 6 to < 18 years) with relapsed or refractory systemic anaplastic lymphoma kinase (ALK)-positive anaplastic large cell lymphoma (ALCL) and with unresectable, recurrent, or refractory ALK-positive inflammatory myofibroblastic tumour (IMT) for XALKORI based on the results from Studies ADVL0912 and A8081013; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 8.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the ATC code for crizotinib. Moreover, the MAH took the opportunity to implement a minor change in the list of local representatives in the Package Leaflet."

Scope: Letter from the applicant dated 28 September 2021 requesting an extension to the clock stop to respond to the request for supplementary information adopted in September

2021.

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021.

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. fosdenopterin - H0005378

Treatment of molybdenum cofactor deficiency type A
Treatment of patients with molybdenum cofactor deficiency (MoCD) Type A

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

Action: For adoption

8.1.2. spesolimab - H0005874

Treatment of flares in adult patients with generalized pustular psoriasis (GPP)

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. Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0026

AstraZeneca AB

Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné

Scope: "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to include updated efficacy and safety information based on primary analysis from study D8110C00001 listed as a specific obligation in Annex II; this is a phase III randomised, double-blind, placebo-controlled, multicenter study in adults to determine the safety, efficacy and immunogenicity of Vaxzevria; the Package Leaflet and Annex II are updated accordingly. The updated RMP Version 3 Succession 2 has also been submitted."

Update on the status of this application

Action: For information

Request for Supplementary Information adopted on 16.09.2021, 22.07.2021

9.1.2. Pramipexole Accord - pramipexole - EMEA/H/C/002291

Accord Healthcare S.L.U.; treatment of idiopathic Parkinson's disease and treatment of idiopathic Restless Legs Syndrome

Rapporteur: Ingrid Wang

Scope: Withdrawal of marketing authorisation

Action: For information

Generic application (Article 10(1) of Directive No 2001/83/EC)

9.1.3. Equidacent – bevacizumab – EMEA/H/C/005181

Centus Biotherapeutics; 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.

Rapporteur: Ingrid Wang, Co-Rapporteur: Outi Mäki-Ikola

Scope: Withdrawal of marketing authorisation

Action: For information

Similar biological application (Article 10(4) of Directive No 2001/83/EC)

9.1.4. Klisyri - tirbanibulin - EMEA/H/C/005183/ANX/001

Rapporteur: Peter Kiely, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Michal Radik

CHMP Request for PRAC advice on PASS protocol assessment

The CHMP is requesting PRAC advice for the protocol assessment of study M-14789-41, a phase 4, multi-centre, randomised, investigator-blinded, active controlled, parallel-group study, requested by CHMP to further investigate the risk of progression of actinic keratosis to squamous cell carcinoma in adult patients with non-hyperkeratotic, non-hypertrophic actinic keratosis treated with tirbanibulin.

Action: For adoption

9.1.5. Impact of tocilizumab potential shortages on CAR-T cell-based ATMPs use in EU – regulatory options and recommendations

Scope: Scientific and regulatory considerations regarding the treatment of cytokine release syndrome following CAR-T cell administration.

Action: For discussion

9.1.6. Leganto – Rotigotine – EMA/H/C/002380

UCB Pharma S.A.

Rapporteur: Bruno Sepodes, Co-Rapporteur: Johann Lodewijk Hillege

Scope: Notification letter of MA received on 05.10.2021 informing of a marketing cessation in DE in Q2/Q3 2022 for commercial reasons

Action: For information

9.1.7. Invokana - canagliflozin - EMEA/H/C/002649/II/0055

Janssen-Cilag International NV

Rapporteur: Martina Weise

Scope: Update to sections 4.2 and 5.1 of the Invokana SmPC to amend posology information concerning the treatment of patients with eGFR between ⩾30 and <45 mL/min/1.73 m2, whether or not albuminuria is present; the update is based on further analysis of previously submitted CANVAS data (studies DIA3008 and DIA4003). The Applicant has also taken the opportunity to make minor editorial changes to section 4.5.

Action: For adoption

Request for Supplementary Information adopted on 22.04.2021, 28.01.2021.

9.1.8. Xeljanz - tofacitinib - EMEA/H/C/004214/X/0030/G

Pfizer Europe MA EEIG

Rapporteur: Armando Genazzani, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "This is an extension application to add a new strength (22 mg prolonged-release tablet) grouped with a type II variation C.I.4: Update of sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of Xeljanz 11 mg prolonged-release tablets SmPC to include the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent; as an alternative to the immediate release film-coated tablets; section 4.2 of Xeljanz film-coated tablets is also updated to include switching with the prolonged-release tablet in the treatment of UC. The Package Leaflet is updated accordingly. The RMP version 15.1 has also been submitted."

Letter from the MAH dated 05.10.2021 informing of the withdrawal of the extension application

Action: For information

List of Outstanding Issues adopted on 16.09.2021. List of Questions adopted on 25.02.2021.

9.1.9. Nulojix - belatacept - EMEA/H/C/002098/II/0065/G

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Filip Josephson

Scope: Quality variation

Action: For discussion

Request for Supplementary Information adopted on 25.03.2021, 12.11.2020, 12.03.2020.

9.1.10. Visudyne - verteporfin – EMEA/H/C/000305

CHEPLAPHARM Arzneimittel GmbH

Rapporteur: Alexandre Moreau, Co-Rapporteur: Kirstine Moll Harboe

Scope: Adoption of a DHPC

Action: For adoption

10. Referral procedures

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

No items

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

No items

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

No items

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

10.4.1. Nazolam – midazolam - EMEA/H/A-29(4)/1511

MAH: Tiofarma B.V

Rapporteur: TBC, Co-Rapporteur: TBC

Scope: Appointment of Rapporteurs, List of Questions, Timetable

Action: For adoption

Decentralised procedure number: NL/H/5089/001-003/DC, notification by the Agency of the Netherlands dated 24 September 2021 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. STRESAM and generics – etifoxine (hydrochloride) - EMEA/H/A-31/1509

Various

Referral Rapporteur: John Joseph Borg, Co-Rapporteur: Simona Badoi (collaboration with Bulgaria)

Scope: list of outstanding issues/ opinion

Action: For adoption

Summary: ANSM has triggered a referral under Article 31 of Directive 2011/83/EC to review the B/R balance of etifoxine containing products, in light of the new results from the AMETIS study.

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

October 2021 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

No items

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. Election of new CHMP vice-chair

Bruno Sepodes has served as vice-chair of the CHMP since 19 October 2018 and his first 3-year mandate will shortly come to an end.

The election of a new vice-chairperson will take place at the end of the October 2021 CHMP plenary meeting as previously communicated to the Committee.

Candidates for the position of CHMP vice-chair are now invited to indicate their interest in standing for this position. Although candidates can express their interest until the start of the October 2021 CHMP meeting, we would appreciate receiving nominations **by Wednesday, 06 October 2021** EOB to facilitate preparation of the meeting.

Any questions regarding the election can be addressed to EMA.

Candidature(s) received

14.1.2. Structured guidance on reflection of use of extrapolation - development of an assessor's guidance template

This document reflects on the published reflection paper on the use of extrapolation of efficacy and safety data in the development of medicines, with a focus on paediatrics.

Action: For discussion

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for October 2021

Action: For adoption

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

14.3.1. Biologics Working Party (BWP)

Chair: Sol Ruiz/TBC

Election of a new BWP vice-chair. Nanna Aaby Kruse (DK) has resigned from her position as BWP vice-chair following the September 2021 meeting.

Candidature(s) received

Action: For adoption

Reports from BWP October 2021 meeting to CHMP for adoption:

- 22 reports on products in scientific advice and protocol assistance
- 9 reports on products in pre-authorisation procedures
- 2reports on products in post-authorisation procedures
- 0 reports on products in plasma master file

Action: For adoption

14.3.2. Safety Working Party (SWP)

Chairs: Jan Willem Van der Laan/Susanne Brendler-Schwaab

Election of a new SWP chair. Jan Willem Van der Laan's second term will expire on 18 October 2021.

Candidature(s) received

Action: For adoption

14.3.3. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 16-17 September 2021.

Action: For adoption

14.3.4. Scientific Advice Working Party (SAWP)

Chair: Anja Schiel

Report from the SAWP meeting held on 27-30 September 2021. 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

14.7.1. Supplementary Urgency Procedures for Regulatory Assessment (SUPRA)

Update on the progress of SUPRA initiative which is currently part of the CHMP work plan 2021. Feedback from Workshop which took place on 22 September 2021.

Action: For information

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Update on COVID-19

Action: For information

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)*

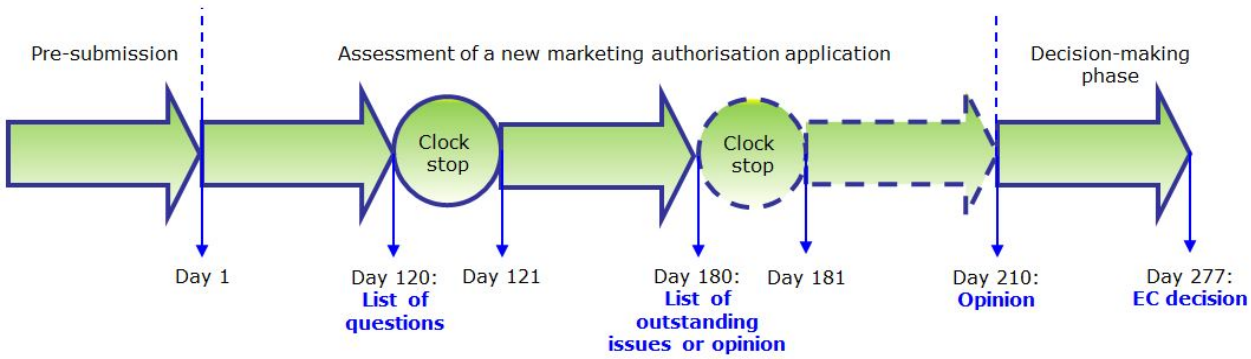
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

11 October 2021
EMA/CHMP/572819/2021

Annex to 11-14 October 2021 CHMP Agenda

Pre-submission and post-authorisations issues

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A. PRE-SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for October 2021: **For adoption**

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

Final Outcome of Rapporteurship allocation for October 2021: **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

Chenodeoxycholic acid Leadiant - chenodeoxycholic acid - EMEA/H/C/004061/S/0017, Orphan
Leadiant GmbH, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Adam Przybylkowski
Request for Supplementary Information adopted on 22.07.2021.

MVABEA - ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005343/S/0006
Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jean-Michel Dogné

Qarziba - dinutuximab beta - EMEA/H/C/003918/S/0028, Orphan
EUSA Pharma (Netherlands) B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski

ZABDENO - ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005337/S/0005
Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur:

Jean-Michel Dogné

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Roteas - edoxaban -
EMEA/H/C/004339/R/0021
Berlin Chemie AG, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Tiphaine Vaillant

B.2.2. Renewals of Marketing Authorisations for unlimited validity

AMGEVITA - adalimumab -
EMEA/H/C/004212/R/0029
Amgen Europe B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Ulla Wändel Liminga

Chenodeoxycholic acid Leadiant - chenodeoxycholic acid -
EMEA/H/C/004061/R/0018, Orphan
Leadiant GmbH, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Adam Przybylkowski

Rolufta Ellipta - umeclidinium -
EMEA/H/C/004654/R/0019
GlaxoSmithKline Trading Services Limited, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Ilaria Baldelli
Request for Supplementary Information adopted on 16.09.2021.

Vemlidy - tenofovir alafenamide -
EMEA/H/C/004169/R/0035
Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Ilaria Baldelli
Request for Supplementary Information adopted on 22.07.2021.

Xeljanz - tofacitinib -
EMEA/H/C/004214/R/0040
Pfizer Europe MA EEIG, Rapporteur: Armando Genazzani, Co-Rapporteur: Johann Lodewijk

Hillege, PRAC Rapporteur: Liana Gross-Martirosyan

B.2.3. Renewals of Conditional Marketing Authorisations

COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/R/0046
BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 16.09.2021.

CRYSVITA - burosumab - EMEA/H/C/004275/R/0026, Orphan
Kyowa Kirin Holdings B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Brigitte Keller-Stanislawski

Holoclar - ex vivo expanded autologous human corneal epithelial cells containing stem cells - EMEA/H/C/002450/R/0039, Orphan, ATMP
Holostem Terapie Avanzate s.r.l., Rapporteur: Egbert Flory, CHMP Coordinator: Jan Mueller-Berghaus, PRAC Rapporteur: Rhea Fitzgerald

Polivy - polatuzumab vedotin - EMEA/H/C/004870/R/0008, Orphan
Roche Registration GmbH, Rapporteur: Alexandre Moreau, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Annika Folin
Request for Supplementary Information adopted on 16.09.2021.

RETSEVMO - selpercatinib - EMEA/H/C/005375/R/0008
Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst

Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/R/0037
AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 27-30 September 2021 PRAC:

Signal of erythema multiforme

Comirnaty - COVID-19 mRNA vaccine (nucleoside-modified)
Rapporteur: Filip Josephson, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Menno van der Elst
PRAC recommendation on a variation
Action: For adoption

Signal of erythema multiforme

Spikevax - COVID-19 mRNA vaccine (nucleoside-modified)
Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Hans Christian Siersted
PRAC recommendation on a variation
Action: For adoption

Signal of immune thrombocytopenia

Vaxzevria - COVID-19 Vaccine (ChAdOx1-S [recombinant])
Rapporteur: Sol Ruiz, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jean-Michel Dogné
PRAC recommendation on a variation, DHPC, Communication plan – adopted via written procedure on 1 October 2021
Action: For information

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its September 2021 meeting:

EMEA/H/C/PSUSA/00000918/202103
(dabigatran)
CAPS:
Pradaxa (EMEA/H/C/000829) (dabigatran etexilate), Boehringer Ingelheim International GmbH, Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Anette Kirstine Stark, "18/03/2020 To: 18/03/2021"

EMEA/H/C/PSUSA/00000998/202103
(dexmedetomidine)
CAPS:
Dexdor (EMEA/H/C/002268)
(dexmedetomidine), Orion Corporation,
Rapporteur: Filip Josephson
NAPS:
NAPs - EU
PRAC Rapporteur: Ulla Wändel Liminga,
"16/03/2020 To: 15/03/2021"

EMEA/H/C/PSUSA/00002182/202101
(estradiol / nomegestrol acetate)
CAPS:
Zoely (EMEA/H/C/001213) (nomegestrol
acetate / estradiol), Theramex Ireland Limited,
Rapporteur: Jean-Michel Race
NAPS:
NAPs - EU
PRAC Rapporteur: Tiphaine Vaillant,
"26/01/2018 To: 26/01/2021"

EMEA/H/C/PSUSA/00002435/202102
(pirfenidone)
CAPS:
Esbriet (EMEA/H/C/002154) (pirfenidone),
Roche Registration GmbH, Rapporteur: Peter
Kiely, PRAC Rapporteur: Rhea Fitzgerald,
"27/02/2020 To: 27/02/2021"

EMEA/H/C/PSUSA/00010120/202102
(nalmefene)
CAPS:
Selincro (EMEA/H/C/002583) (nalmefene), H.
Lundbeck A/S, Rapporteur: Janet Koenig,
PRAC Rapporteur: Martin Huber, "24/02/2018
To: 24/02/2021"

EMEA/H/C/PSUSA/00010127/202102
(pomalidomide)
CAPS:
Imnovid (EMEA/H/C/002682)
(pomalidomide), Bristol-Myers Squibb Pharma
EEIG, Rapporteur: Blanca Garcia-Ochoa, PRAC
Rapporteur: Eva A. Segovia, "07/02/2019 To:
07/02/2021"

EMEA/H/C/PSUSA/00010413/202103 (guanfacine) CAPS: **Intuniv** (EMEA/H/C/003759) (guanfacine), Takeda Pharmaceuticals International AG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Maria del Pilar Rayon, "18/03/2020 To: 17/03/2021"	
EMEA/H/C/PSUSA/00010758/202103 (fremanezumab) CAPS: **AJOVY** (EMEA/H/C/004833) (fremanezumab), TEVA GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Kirsti Villikka, "13/09/2020 To: 13/03/2021"	
EMEA/H/C/PSUSA/00010823/202102 (upadacitinib) CAPS: **RINVOQ** (EMEA/H/C/004760) (upadacitinib), AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce, "15/08/2020 To: 15/02/2021"	
EMEA/H/C/PSUSA/00010851/202103 (isatuximab) CAPS: **SARCLISA** (EMEA/H/C/004977) (isatuximab), sanofi-aventis groupe, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Eva A. Segovia, "01/09/2020 To: 01/03/2021"	
EMEA/H/C/PSUSA/00010900/202103 (cabotegravir) CAPS: **Vocabria** (EMEA/H/C/004976) (cabotegravir), ViiV Healthcare B.V., Rapporteur: Jean-Michel Race, PRAC Rapporteur: Martin Huber, "18/03/2020 To: 17/03/2021"	

B.4. EPARs / WPARs

Artesunate Amivas - artesunate - EMEA/H/C/005550, Orphan Amivas Ireland Ltd, treatment of malaria, 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.
Brukinsa - zanubrutinib - EMEA/H/C/004978, Orphan BeiGene Ireland Ltd, treatment of	For information only. Comments can be sent to the PL in case necessary.

Waldenström's macroglobulinaemia (WM), New active substance (Article 8(3) of Directive No 2001/83/EC)	
GAVRETO - pralsetinib - EMEA/H/C/005413 Roche Registration GmbH, treatment of non-small cell lung cancer (NSCLC), 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.
Hukyndra - adalimumab - EMEA/H/C/005548 STADA Arzneimittel AG, treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn's disease, paediatric Crohn's disease, ulcerative colitis, uveitis, paediatric uveitis, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Libmyris - adalimumab - EMEA/H/C/005947 STADA Arzneimittel AG, treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn's disease, paediatric Crohn's disease, ulcerative colitis, uveitis, paediatric uveitis, Duplicate, Duplicate of Hukyndra, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
QINLOCK - ripretinib - EMEA/H/C/005614, Orphan Deciphera Pharmaceuticals (Netherlands) B.V., Treatment of patients with advanced gastrointestinal stromal tumour (GIST), 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.
Raylumis - tanezumab - EMEA/H/C/005189 Pfizer Europe MA EEIG, treatment of moderate to severe chronic pain associated with osteoarthritis (OA) in adult patients for whom treatment with non-steroidal anti-inflammatory drugs (NSAIDs) and/or an opioid is ineffective, not tolerated or inappropriate, New active substance (Article 8(3) of Directive No	For information only. Comments can be sent to the PL in case necessary.

2001/83/EC)	
Rivaroxaban Mylan - rivaroxaban - EMEA/H/C/005600 Mylan Ireland Limited, Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors. Treatment of deep vein thrombosis and pulmonary embolism and prevention of recurrent DVT and PE in adults. Prevention of venous thromboembolism in adult patients undergoing elective hip or knee replacement surgery. Generic, Generic of Xarelto, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Sugammadex Mylan - sugammadex - EMEA/H/C/005403 Mylan Ireland Limited, treatment of neuromuscular blockade induced by rocuronium or vecuronium, Generic, Generic of Bridion, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Vumerity - diroximel fumarate - EMEA/H/C/005437 Biogen Netherlands B.V., treatment of relapsing remitting multiple sclerosis, Known active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0049/G Biofrontera Bioscience GmbH, Rapporteur: Janet Koenig	
Bavencio - avelumab - EMEA/H/C/004338/II/0028 Merck Europe B.V., Rapporteur: Filip Josephson	
Buvidal - buprenorphine - EMEA/H/C/004651/II/0015/G Camurus AB, Rapporteur: Peter Kiely Opinion adopted on 23.09.2021.	Positive Opinion adopted by consensus on 23.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Cerezyme - imiglucerase - EMEA/H/C/000157/II/0123/G Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege	
Cinacalcet Mylan - cinacalcet - EMEA/H/C/004014/II/0016 Mylan S.A.S, Generic, Generic of Mimpara, Rapporteur: Tomas Radimersky Request for Supplementary Information adopted on 23.09.2021.	Request for supplementary information adopted with a specific timetable.
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0054/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Grouped Variation: · Type II C.I.11.b, To update Annex II to implement changes and provision of data to fulfil specific obligations SO2f, SO4 and SO5."	
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0056/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "C.I.11.b, (Type II)- To submit additional data to complete characterisation of the active substance and finished product, which are a condition to the Marketing Authorisation (Special Obligation SO1) C.I.11.b, (Type II)- To submit additional data to enhance the control strategy, including the active substance and finished product specifications, which are a condition to the Marketing Authorisation (Special Obligation SO2)"	
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0071 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 06.10.2021.	Positive Opinion adopted by consensus on 06.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0072/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0073/G	

BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
Drovelis - drospirenone / estetrol - EMEA/H/C/005336/II/0003 Chemical Works of Gedeon Richter Plc. (Gedeon Richter Plc.), Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 23.09.2021.	Request for supplementary information adopted with a specific timetable.
Drovelis - drospirenone / estetrol - EMEA/H/C/005336/II/0004/G Chemical Works of Gedeon Richter Plc. (Gedeon Richter Plc.), Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 23.09.2021.	Request for supplementary information adopted with a specific timetable.
Dupixent - dupilumab - EMEA/H/C/004390/II/0050/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus	
Epidyolex - cannabidiol - EMEA/H/C/004675/II/0014/G, Orphan GW Pharma (International) B.V., Rapporteur: Kirstine Moll Harboe Request for Supplementary Information adopted on 02.09.2021.	
HEPLISAV B - hepatitis B surface antigen - EMEA/H/C/005063/II/0010 Dynavax GmbH, Rapporteur: Filip Josephson	
Herceptin - trastuzumab - EMEA/H/C/000278/II/0174/G Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus	
Jivi - damoctocog alfa pegol - EMEA/H/C/004054/II/0019/G Bayer AG, Rapporteur: Kirstine Moll Harboe	
Kaftrio - ivacaftor / tezacaftor / elexacaftor - EMEA/H/C/005269/II/0011/G, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 08.07.2021.	
Kevzara - sarilumab - EMEA/H/C/004254/II/0028/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus	

Lydisilka - drospirenone / estetrol - EMEA/H/C/005382/II/0003 Estetra SRL, Duplicate, Duplicate of Drovelis, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 23.09.2021.	Request for supplementary information adopted with a specific timetable.
Lydisilka - drospirenone / estetrol - EMEA/H/C/005382/II/0004/G Estetra SRL, Duplicate, Duplicate of Drovelis, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 23.09.2021.	Request for supplementary information adopted with a specific timetable.
Neulasta - pegfilgrastim - EMEA/H/C/000420/II/0117 Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege	
Nimenrix - Meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0111/G Pfizer Europe MA EEIG, Rapporteur: Ingrid Wang Opinion adopted on 30.09.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Nulojix - belatacept - EMEA/H/C/002098/II/0065/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson Request for Supplementary Information adopted on 25.03.2021, 12.11.2020, 12.03.2020.	See 9.1
Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0020/G Alexion Europe SAS, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 08.07.2021.	
Onpattro - patisiran - EMEA/H/C/004699/II/0021/G, Orphan Alnylam Netherlands B.V., Rapporteur: Kristina Dunder	
Puregon - follitropin beta - EMEA/H/C/000086/II/0122 Organon N.V., Rapporteur: Peter Kiely Opinion adopted on 30.09.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Reagila - cariprazine - EMEA/H/C/002770/II/0020/G Gedeon Richter Plc., Rapporteur: Kristina Dunder	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 30.09.2021.	
Reagila - cariprazine - EMEA/H/C/002770/II/0022 Gedeon Richter Plc., Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 30.09.2021.	Request for supplementary information adopted with a specific timetable.
Remicade - infliximab - EMEA/H/C/000240/II/0229 Janssen Biologics B.V., Rapporteur: Kristina Dunder	
Retacrit - epoetin zeta - EMEA/H/C/000872/II/0105 Pfizer Europe MA EEIG, Rapporteur: Martina Weise Opinion adopted on 23.09.2021.	Positive Opinion adopted by consensus on 23.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
RINVOQ - upadacitinib - EMEA/H/C/004760/II/0011 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder Opinion adopted on 23.09.2021.	Positive Opinion adopted by consensus on 23.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Silapo - epoetin zeta - EMEA/H/C/000760/II/0065 STADA Arzneimittel AG, Rapporteur: Martina Weise Opinion adopted on 23.09.2021.	Positive Opinion adopted by consensus on 23.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Skyrizi - risankizumab - EMEA/H/C/004759/II/0017/G AbbVie Deutschland GmbH & Co. KG, Rapporteur: Peter Kiely Request for Supplementary Information adopted on 23.09.2021.	Request for supplementary information adopted with a specific timetable.
Skyrizi - risankizumab - EMEA/H/C/004759/II/0018 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Peter Kiely	
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0035 Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 05.10.2021. Request for Supplementary Information adopted on 27.09.2021.	Positive Opinion adopted by consensus on 05.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

TAKHZYRO - lanadelumab - EMEA/H/C/004806/II/0021/G, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 24.06.2021.	
Taltz - ixekizumab - EMEA/H/C/003943/II/0045/G Eli Lilly and Co (Ireland) Limited, Rapporteur: Kristina Dunder	
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0030/G AstraZeneca AB, Rapporteur: Sol Ruiz Request for Supplementary Information adopted on 30.09.2021, 02.09.2021.	Request for supplementary information adopted with a specific timetable.
Vazkepa - icosapent ethyl - EMEA/H/C/005398/II/0003 Amarin Pharmaceuticals Ireland Limited, Rapporteur: Martina Weise Request for Supplementary Information adopted on 02.09.2021.	
VEYVONDI - vonicog alfa - EMEA/H/C/004454/II/0017 Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 23.09.2021. Request for Supplementary Information adopted on 22.07.2021.	Positive Opinion adopted by consensus on 23.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
VITRAKVI - larotrectinib - EMEA/H/C/004919/II/0017 Bayer AG, Rapporteur: Filip Josephson Request for Supplementary Information adopted on 30.09.2021.	Request for supplementary information adopted with a specific timetable.
WS2044 **Herceptin-EMEA/H/C/000278/WS2044/0171** **MabThera-EMEA/H/C/000165/WS2044/0184** Roche Registration GmbH, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 23.09.2021. Request for Supplementary Information adopted on 24.06.2021.	Positive Opinion adopted by consensus on 23.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2146 **Nuwiq-EMEA/H/C/002813/WS2146/0046** **Vihuma-EMEA/H/C/004459/WS2146/**	

0028
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus

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

Alunbrig - brigatinib / brigatinib - EMEA/H/C/004248/II/0033/G
Takeda Pharma A/S, Rapporteur: Sinan B. Sarac, "Update of section 4.5 of the SmPC in order to add drug-drug interaction information about the effect of brigatinib on the pharmacokinetics of a sensitive cytochrome P450 3A substrate (midazolam) in patients with ALK-positive or ROS1-positive solid tumours based on a clinical study report (Study 1001). Update of section 4.2 of the SmPC in order to clarify the existing renal impairment dosage adjustment recommendation based on results of previously submitted studies (clinical study AP26113-15-108, study 108). Update of section 4.2 of the SmPC in order to clarify the existing hepatic impairment dosage adjustment recommendation based on results of previously submitted studies (clinical study AP26113-15-107, study 107). Update of section 4.4 and 4.5 of the SmPC in order to update drug-drug interaction information regarding concomitant treatment with moderate CYP3A inhibitors or inducers based on results of previously submitted studies (physiologically-based pharmacokinetic (PBPK) report and PBPK report addendum). Update of section 5.1 of the SmPC in order to amend the ATC code;
the Package Leaflet is updated accordingly.
In addition, the MAH took the opportunity to implement a statement regarding the sodium content of Alunbrig in section 4.4 of the SmPC and Package Leaflet. The MAH also took the opportunity to bring the Product Information in line with the latest QRD template (version 10.2 rev.1) and to update the list of local representatives in the Package Leaflet.
Moreover, the MAH took the opportunity to introduce minor editorial changes in the PI in different languages."
Request for Supplementary Information adopted on 22.07.2021.

Alunbrig - brigatinib / brigatinib - EMEA/H/C/004248/II/0034

Takeda Pharma A/S, Rapporteur: Sinan B. Sarac, "Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on photosensitivity based on a report of cumulative evidence for an association between exposure to brigatinib and subsequent development of photosensitivity reaction; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make a minor editorial change in section 4.8 of the SmPC."
Request for Supplementary Information adopted on 22.07.2021.

Beovu - brolucizumab - EMEA/H/C/004913/II/0006

Novartis Europharm Limited, Rapporteur: Alexandre Moreau, "C.I.4 - Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data"
Request for Supplementary Information adopted on 25.02.2021.

Bexsero - meningococcal group B vaccine (recombinant, component, adsorbed) - EMEA/H/C/002333/II/0105

GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to add lymphadenopathy to the list of adverse drug reactions. The Package Leaflet section 4 is updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2 rev1 (including addition of the "sodium-free" statement in the SmPC section 4.4) and update the list of local representatives."

Braftovi - encorafenib - EMEA/H/C/004580/II/0020

Pierre Fabre Medicament, Rapporteur: Janet Koenig, "Update of sections 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information with rosuvastatin and bupropion based on final results from Arm 2 of study ARRAY-818-103. This is a Phase 1, three-arm, open-label drug-drug interaction study in patients with BRAF V600-mutant unresectable or metastatic melanoma or other BRAF V600-E and/or K-mutant advanced solid tumours."

Brilique - ticagrelor - EMEA/H/C/001241/II/0054 AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning and new adverse drug reactions on bradyarrhythmia and AV blocks based on a review of all currently available information, including clinical trial data, post- marketing reports, and plausible mechanism."	
Calquence - acalabrutinib - EMEA/H/C/005299/II/0006 AstraZeneca AB, Rapporteur: Filip Josephson, "Submission of updated report from study 1000-171974-6 in order to provide additional long-term stability data for the metabolite of acalabrutinib ACP-5862." Opinion adopted on 30.09.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Calquence - acalabrutinib - EMEA/H/C/005299/II/0007 AstraZeneca AB, Rapporteur: Filip Josephson, "Submission of the final report from ACE-HV-114, an open-label, fixed sequence study in healthy subjects to assess the pharmacokinetics of acalabrutinib and its active metabolite, ACP-5862, when administered alone and in combination with moderate CYP3A4 inhibitors fluconazole or isavuconazole." Opinion adopted on 30.09.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0062 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Update of sections 4.2 and 4.4 of the SmPC in order to introduce a third dose of Comirnaty for individuals 12 years of age and older who are severely immunocompromised, based on published literature data; the Package Leaflet is updated accordingly." Opinion adopted on 04.10.2021.	Positive Opinion adopted by consensus on 04.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0067 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to introduce a booster dose (third dose) of Comirnaty for individuals 18 years of age and older, based on	Positive Opinion adopted by consensus on 04.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

interim safety and immunogenicity data from the interventional study C4591001, " A Phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals". The package leaflet is updated accordingly."
Opinion adopted on 04.10.2021.

Darzalex - daratumumab - EMEA/H/C/004077/II/0050, Orphan
Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, "C.I.4
Update of section 4.8 of the SmPC in order to add hypogammaglobulinemia to the list of adverse drug reactions (ADRs) with frequency common, based on new information and previously reviewed pooled safety data from Part 2 of Phase 3 Clinical Study 54767414MMY3006 comparing daratumumab versus observation as maintenance in patients with newly diagnosed Multiple Myeloma who are post-ASCT transplant. The Package Leaflet is updated accordingly."
Request for Supplementary Information adopted on 02.09.2021.

Darzalex - daratumumab - EMEA/H/C/004077/II/0051/G, Orphan
Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, "C.I.4
Update of section 5.1 of the SmPC in order to update PFS and OS data based on interim results from study MMY3006 (CCO 27/8/2020); this is a Phase 3, randomized, open-label, parallel-group, active-control, multicenter study of daratumumab combined with VTd for NDMM patients eligible for ASCT. This fulfils a post-approval commitment of procedure EMEA/H/C/004077//II/0030 to provide updated Part 1 PFS and OS data, with censoring the patients randomized to daratumumab in Part 2 of this study.
C.I.4
Update of section 5.1 of the SmPC of DARZALEX SC formulation to provide the mature OS data based on final results from study MMY3012 (CCO 04/11/2020); this is a Phase 3, multicenter, randomized, open-label, active-controlled study to demonstrate that the

efficacy and PK for daratumumab SC are not inferior to those for daratumumab IV in subjects with RRMM submitted for the approval of the SC formulation in procedure EMEA/H/C/004077//II/0032" Request for Supplementary Information adopted on 02.09.2021.	
Darzalex - daratumumab - EMEA/H/C/004077/II/0053, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, "C.I.4 Update of section 5.1 of the SmPC in order to update PFS and OS (CCO 19/2/2021) data based on interim results from study MMY3008; This is a Phase 3, randomized, open-label, active controlled, parallel-group, multicenter study in adults with newly diagnosed MM not eligible for ASCT comparing DRd vs Rd. The Marketing authorisation holder (MAH) took the opportunity to make minor formatting and linguistic changes in the PI." Request for Supplementary Information adopted on 02.09.2021.	
Drovelis - drospirenone / estetrol - EMEA/H/C/005336/II/0002 Chemical Works of Gedeon Richter Plc. (Gedeon Richter Plc.), Rapporteur: Kristina Dunder, "Update of section 5.3 of the SmPC following a revision of the Environmental Risk Assessment (ERA) in order to include the E4 PECsw based on a refined Fpen of 0.0044. In addition, the MAH has taken the opportunity to implement minor editorial changes in the SmPC, Labelling and Package Leaflet." Opinion adopted on 30.09.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Dupixent - dupilumab - EMEA/H/C/004390/II/0046 sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Kimmo Jaakkola, "Update of section 4.8 of the SmPC to introduce a new ADR (facial rash) with uncommon frequency. The package leaflet will be updated accordingly." Opinion adopted on 30.09.2021. Request for Supplementary Information adopted on 08.07.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Entyvio - vedolizumab - EMEA/H/C/002782/II/0059/G	

Takeda Pharma A/S, Rapporteur: Armando Genazzani, "C.I.4
Update of section 4.6 of the SmPC in order to implement information on lactation based on study Vedolizumab-4001 (An Open-Label, Multicenter and Open Enrollment Model, Postmarketing, Milk-Only Lactation Study to Assess Concentration of Vedolizumab in Breast Milk of Lactating Women With Active Ulcerative Colitis or Crohn's Disease Who Are Receiving Vedolizumab Therapeutically). The study aimed to determine the PK parameters of vedolizumab in breast milk and to estimate mean daily infant dosage over the dosing interval through breast milk, and percentage of maternal dose consumed in breast milk by the infants.
C.I.4
Update of section 5.2 of the SmPC in order to adjust the values for clearance and serum half-life of vedolizumab IV and SC in subjects with ulcerative colitis and Crohn's disease. The updated pop PK dataset consists of pooled data across 4 phase 3 studies (C13006, C13007, MLN0002SC-3027, MLN0002SC-3031) and 1 open-label extension study (MLN0002SC-3030).
In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, to correct minor typographical errors and to bring the PI in line with the latest QRD template version 10.2 rev. 1."
Request for Supplementary Information adopted on 02.09.2021, 10.06.2021.

Erleada - apalutamide - EMEA/H/C/004452/II/0015

Janssen-Cilag International N.V., Rapporteur: Blanca Garcia-Ochoa, "An updated OS analysis was conducted at the time of final study analysis when 405 deaths were observed with a median follow-up of 44 months. Results from this updated analysis were consistent with those from the pre specified interim analysis. The improvement in OS was demonstrated even though 39% of patients in the placebo arm crossed over to receive Erleada, with a median treatment of 15 months on Erleada crossover. Consistent improvement in OS was observed across patient subgroups including high- or low-volume disease, metastasis stage at diagnosis (M0 or M1), and Gleason score at diagnosis (≤7 vs. >7)."

Request for Supplementary Information adopted on 02.09.2021, 08.07.2021.	
Erleada - apalutamide - EMEA/H/C/004452/II/0016 Janssen-Cilag International N.V., Rapporteur: Blanca Garcia-Ochoa, "Update of section 4.8 of the SmPC in order to add Stevens-Johnson Syndrome (SJS) to the list of adverse drug reactions (ADRs) with frequency not known. Cases of SJS were observed in post-marketing data. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 02.09.2021.	
PRAC Led **Fasenra - benralizumab - EMEA/H/C/004433/II/0036** AstraZeneca AB, Rapporteur: Fátima Ventura, PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Ingrid Wang, "Update of RMP to remove long-term use of benralizumab, serious hypersensibility, loss/reduction of long-term efficacy due to persistent neutralising anti-drug antibodies as safety concerns and to change categorisation of helminth infection from important identified risk to important potential risk. RMP version 4.1 is accepted." Opinion adopted on 30.09.2021. Request for Supplementary Information adopted on 08.07.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Iclusig - ponatinib - EMEA/H/C/002695/II/0061, Orphan Incyte Biosciences Distribution B.V., Rapporteur: Filip Josephson, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC based on results from the OPTIC study (AP24534-14-203) listed as a specific obligation in the Annex II. This is a randomised, open-label, Phase 2 trial of ponatinib in patients with chronic myeloid leukaemia to characterise the efficacy and safety of ponatinib over a range of doses; the Package Leaflet is updated accordingly."	
Invokana - canagliflozin - EMEA/H/C/002649/II/0055 Janssen-Cilag International NV, Rapporteur: Martina Weise, "Update to sections 4.2 and 5.1 of the INVOKANA SmPC to amend posology information concerning the treatment of	See 9.1

patients with eGFR between ≥30 and <45 mL/min/1.73 m2, whether or not albuminuria is present; the update is based on further analysis of previously submitted CANVAS data (studies DIA3008 and DIA4003). The Applicant has also taken the opportunity to make minor editorial changes to section 4.5." Request for Supplementary Information adopted on 22.04.2021, 28.01.2021.	
Ivemend - fosaprepitant - EMEA/H/C/000743/II/0045 Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC with the final results from study P045; a non-randomised, single-group, multi-site, open-label study to evaluate the safety and tolerability of consecutive 3-day intravenous fosaprepitant in paediatric participants scheduled to receive a moderately or highly emetogenic chemotherapy agent/regimen or a chemotherapy agent/regimen not previously tolerated due to vomiting. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and correct the date of the latest renewal in section 9 of the SmPC." Opinion adopted on 23.09.2021.	Positive Opinion adopted by consensus on 23.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Lydisilka - drospirenone / estetrol - EMEA/H/C/005382/II/0002 Estetra SRL, Duplicate, Duplicate of Drovelis, Rapporteur: Kristina Dunder, "Update of section 5.3 of the SmPC following a revision of the Environmental Risk Assessment (ERA) in order to include the E4 PECsw based on a refined Fpen of 0.0044. In addition, the MAH has taken the opportunity to implement minor editorial changes in the SmPC, the Labelling and Package Leaflet." Opinion adopted on 30.09.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Mayzent - siponimod - EMEA/H/C/004712/II/0011/G Novartis Europharm Limited, Rapporteur: Kirstine Moll Harboe, "- Update of sections 4.4 and 4.5 of the SmPC to add information in case of administration of non-live attenuated vaccines, based on the vaccination study A2130. - Update of section 4.5 of the SmPC to clarify the CYP2C9/CYP3A4 inhibitors/inducers information.	Request for supplementary information adopted with a specific timetable.

- Update of section 5.2 to add information regarding CYP2C9 genotypes less frequent alleles." Request for Supplementary Information adopted on 23.09.2021.	
Mektovi - binimetinib - EMEA/H/C/004579/II/0015 Pierre Fabre Medicament, Rapporteur: Janet Koenig, "Submission of the final results from Arm 2 of study ARRAY-818-103. This is a Phase 1, three-arm, open-label drug-drug interaction study in patients with BRAF V600-mutant unresectable or metastatic melanoma or other BRAF V600-E and/or K-mutant advanced solid tumours."	
Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0050 Orexigen Therapeutics Ireland Limited, Rapporteur: Kirstine Moll Harboe, "Submission of the final report of study 20077697; a Toxicity Study of Bupropion and Naltrexone by Twice Daily Oral (Gavage) in Juvenile Mice." Request for Supplementary Information adopted on 30.09.2021.	Request for supplementary information adopted with a specific timetable.
Noxafil - posaconazole - EMEA/H/C/000610/II/0067 Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau, "Update of sections 4.4 and 4.5 of the SmPC in order to add drug-drug interaction information between posaconazole and venetoclax. The Package leaflet is updated accordingly." Request for Supplementary Information adopted on 30.09.2021.	Request for supplementary information adopted with a specific timetable.
Nuceiva - botulinum toxin type A - EMEA/H/C/004587/II/0017 Evolus Pharma Limited, Rapporteur: Peter Kiely, "Submission of the final reports of the non-interventional immunogenicity analysis (RMP cat 3 study)." Request for Supplementary Information adopted on 23.09.2021.	Request for supplementary information adopted with a specific timetable.
Pergoveris - follitropin alfa / lutropin alfa - EMEA/H/C/000714/II/0075 Merck Europe B.V., Rapporteur: Kirstine Moll Harboe, "Update of sections 4.1, 4.2, 4.4, 5.1, 5.2 and 6.6 of the SmPC in order to revise the	

definition of severe LH and FSH deficiency and to clarify the treatment target and the pharmacokinetic and pharmacodynamic properties of the two gonatropins included in the medicinal product, as well as disposal precautions, based on current medical guidelines, clinical practice and literature; the Package Leaflet and Labelling are updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1 and to align with the guideline on the Excipients in the labelling and package leaflet of the medicinal products for human use." Request for Supplementary Information adopted on 02.09.2021.	
Phesgo - pertuzumab / trastuzumab - EMEA/H/C/005386/II/0007 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of the immunogenicity information in section 4.8 of the SmPC based on the analysis of the Federica study (Phase III clinical trial in patients with HER2 overexpressing early breast cancer)." Opinion adopted on 23.09.2021.	Positive Opinion adopted by consensus on 23.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
ProQuad - measles, mumps, rubella and varicella vaccine (live) - EMEA/H/C/000622/II/0151/G MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC to remove adverse events with no biological plausible cause in response to an EMA comment received during procedure EMEA/H/C/000622/WS1392. In addition, the MAH proposed amendments to other aspects of SmPC section 4.8 to minimise redundancies and update outdated terms to the current version of the Medical Dictionary for Regulatory Activities (MedDRA). The Package Leaflet is updated accordingly. Update of section 4.9 of the SmPC to revise the information on overdose following review of MAH`s safety database search for ProQuad. In addition, the MAH took the opportunity to update the contact details for the local representatives in the Package Leaflet." Opinion adopted on 30.09.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Revestive - teduglutide - EMEA/H/C/002345/II/0053, Orphan	

Shire Pharmaceuticals Ireland Limited, Rapporteur: Kirstine Moll Harboe, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update the Product information with results from two studies included in the paediatric investigation plan (PIP). Study SHP633-1 was performed to evaluate the safety, efficacy/pharmacodynamics (PD), and pharmacokinetics (PK) of teduglutide in infants 4 to 12 months gestational age with SBS and who are dependent on parenteral support. The second study is a paediatric population PK model including data from study SHP633-301. The Package Leaflet was updated accordingly. In addition, the MAH took the opportunity to make editorial changes to section 4.5 of the SmPC." Request for Supplementary Information adopted on 24.06.2021.	
SIRTURO - bedaquiline - EMEA/H/C/002614/II/0043, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC to include reference on the use of bedaquiline as specified in the product information of other medicines used for the treatment of pulmonary tuberculosis (TB) caused by multidrug-resistant Mycobacterium tuberculosis (MDR-TB), based on recent information regarding EU approval of pretomanid, as part of a combination regimen with bedaquiline and linezolid. In addition, the MAH took the opportunity to include an editorial correction in section 5.1 of the SmPC and to update the contact details for the local representative for UK in the package leaflet, in line with QRD version 10.2." Request for Supplementary Information adopted on 22.07.2021, 24.06.2021.	
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0031 Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2 and 4.4 of the SmPC in order to introduce a third dose of Spikevax in the primary vaccination schedule for individuals 12 years of age and older who are severely immunocompromised, based on published literature data; the Package	Positive Opinion adopted by consensus on 04.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Leaflet is updated accordingly. The MAH took the opportunity to make minor administrative and editorial corrections throughout the product information." Opinion adopted on 04.10.2021.	
Talzenna - talazoparib - EMEA/H/C/004674/II/0010/G Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, "Update of section 4.4 of the SmPC in order to update the frequency of myelodysplastic syndrome/acute myeloid syndrome (MDS/AML) based on a cumulative safety review; Update of section 5.1 of the SmPC with the revised ATC code. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and make minor corrections in the SmPC and PL." Request for Supplementary Information adopted on 30.09.2021.	Request for supplementary information adopted with a specific timetable.
Tivicay - dolutegravir - EMEA/H/C/002753/II/0073/G ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of section 5.1 of the Tivicay SmPC in order to add new information on efficacy and safety based on data from studies 204861 (GEMINI-1) and 205543 (GEMINI-2). These are Phase III, identical, ongoing, randomized, double-blind, parallel group studies, to provide longer term efficacy and safety data on the use of dolutegravir (DTG) for the treatment of HIV-1 infection. The Package Leaflet is updated accordingly. The grouping includes a Type IA variation to update the ATC code for both Film Coated and Dispersible Tablets. In addition, the MAH took the opportunity to include an editorial correction to the list of excipients in the SmPC and Package Leaflet and to update the list of local representatives in the Package Leaflet." Opinion adopted on 23.09.2021.	Positive Opinion adopted by consensus on 23.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Toviaz - fesoterodine - EMEA/H/C/000723/II/0063 Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro, "C.I.3 Update of sections 4.2, 5.1 and 5.2 of the SmPC with the results from study A0221047, to evaluate the safety and efficacy of fesoterodine	

in subjects aged 6 to 17 years with neurogenic detrusor overactivity. The change was suggested in the outcome of the EMEA/H/C/000723/P46/030.1. 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."	
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0031 AstraZeneca AB, Rapporteur: Sol Ruiz, "Submission of the final study report for MS1222-0002 "In Vitro Assay to Determine Release of Spike Protein From Transduced Cells" to fulfil the imposed study as reflected in Annex II of the product information and the RMP. As a result, Annex II of the product information is being updated to remove this study. The MAH is taking the opportunity to provide two additional studies linked to support the investigation on the platelet activation: the final study report for MS1222-0001 "Computational Prediction of Spike Protein Interaction with Platelet Factor 4 (PF4)" which is the first report requested within the required studies for "in vitro interaction of AZD1222 or spike protein with PF4 and/or platelets" as reflected in the RMP; and the study report for 520447 "Investigative Vaccine Study in the Mouse" to evaluate spike protein levels and haematology parameters." Request for Supplementary Information adopted on 23.09.2021.	Request for supplementary information adopted with a specific timetable.
Veklury - remdesivir - EMEA/H/C/005622/II/0025/G Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, "Update of sections 4.4, 4.5 and 5.1 of the SmPC with nonclinical results following final study reports addressing the activity of remdesivir in additional cell lines and chloroquine/ hydroxychloroquine antagonism (fulfilment of 3 components of the Specific Obligation SOB 012 from EMEA/H/C/005622/R/0015). In addition, the Marketing authorisation holder (MAH) took the opportunity to submit the interim results of the non-clinical studies related to the	

characterisation of clinical isolates and/or recombinant viruses with P323L, A97V, and A547V substitutions."	
Vemlidy - tenofovir alafenamide - EMEA/H/C/004169/II/0032 Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, "Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to add new information on efficacy and safety based on final results from study GS-US-320-4035. This was a phase 2, open-label study to evaluate the safety and efficacy of switching to tenofovir alafenamide from tenofovir disoproxil fumarate and/or other oral antiviral treatment in virologically suppressed chronic hepatitis B subjects with renal and/or hepatic impairment." Opinion adopted on 30.09.2021. Request for Supplementary Information adopted on 10.06.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Venclyxto - venetoclax - EMEA/H/C/004106/II/0035 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Submission of the final report from study M12-175 listed as a category 3 study in the RMP. This is a Phase 1 study evaluating the safety and pharmacokinetics of venetoclax in subjects with relapsed or refractory Chronic Lymphocytic Leukaemia and Non-Hodgkin's Lymphoma." Opinion adopted on 30.09.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Venclyxto - venetoclax - EMEA/H/C/004106/II/0036 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Submission of the final report from study M13-982 listed as a category 3 study in the RMP. This is a phase 2 open-label study of the efficacy of ABT-199 in subjects with relapsed or refractory Chronic Lymphocytic Leukaemia Harboring the 17p Deletion." Opinion adopted on 30.09.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vocabria - cabotegravir - EMEA/H/C/004976/II/0007 ViiV Healthcare B.V., Rapporteur: Jean-Michel Race, "Update of section 4.8 of the SmPC in order to update the adverse reactions section, adding information regarding events of pyrexia	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

have a close temporal association with injections. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to include minor typographical updates." Opinion adopted on 30.09.2021.	
Votrient - pazopanib - EMEA/H/C/001141/II/0068 Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to add skin ulcer to the list of adverse drug reactions (ADRs) with frequency of "uncommon" and to update the frequency of the ADR aneurysm from "not known" to "rare". Further editorial changes and a simplification in the presentation of the frequencies of ADRs in section 4.8 are being proposed. The Package Leaflet is updated accordingly."	
Xyrem - sodium oxybate - EMEA/H/C/000593/II/0093 UCB Pharma S.A., Rapporteur: Bruno Sepodes, "Update of section 4.9 of the SmPC in order to add a new warning on acidosis and its management following the assessment of the signal 'metabolic acidosis' triggered by routine literature review. In addition, the MAH took the opportunity to implement a minor editorial change in section 4.8 of the SmPC, to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.2." Opinion adopted on 23.09.2021.	Positive Opinion adopted by consensus on 23.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zeffix - lamivudine - EMEA/H/C/000242/II/0082 GlaxoSmithKline (Ireland) Limited, Duplicate, Duplicate of Epivir, Rapporteur: Jean-Michel Race, "Update of section 5.2 of the SmPC in order to update pharmacokinetic information based on results from bioavailability studies (204993 and 204994) with lamivudine-containing products." Opinion adopted on 23.09.2021.	Positive Opinion adopted by consensus on 23.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zeffix - lamivudine - EMEA/H/C/000242/II/0083 GlaxoSmithKline (Ireland) Limited, Duplicate, Duplicate of Epivir, Rapporteur: Jean-Michel Race, "Update of sections 4.9 of the SmPC in order to update the Overdosage of the GDS for	Positive Opinion adopted by consensus on 23.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

lamivudine-human immunodeficiency virus (HIV) information based on the safety database. The section 3 of the package Leaflet is updated accordingly." Opinion adopted on 23.09.2021.	
WS1874/G **Advagraf-EMEA/H/C/000712/WS1874/0058/G** **Modigraf-EMEA/H/C/000954/WS1874/0036/G** Astellas Pharma Europe B.V., Lead Rapporteur: Jayne Crowe, "C.I.4 Update of sections 4.4 and 4.5 of the SmPC on the drug-drug interaction with CYP3A4 based on a comprehensive review of available data. Section 4.5 of the SmPC is also updated to include impact of direct acting antiviral therapy. C.I.z Update of section 4.8 of the SmPC to add posterior reversible encephalopathy syndrome as an adverse reaction. The MAH took also the opportunity to change the SOC for febrile neutropenia from General disorders and administration site conditions to Blood and lymphatic system disorders in section 4.8 of the SmPC and to update the instruction for handling of the product in section 6.6 of the SmPC. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 24.06.2021, 25.02.2021, 17.09.2020.	
WS2048 **Kalydeco-EMEA/H/C/002494/WS2048/0101** **Symkevi-EMEA/H/C/004682/WS2048/0030** Vertex Pharmaceuticals (Ireland) Limited, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Rhea Fitzgerald, "Update of the Product information to provide the final clinical study report (CSR) Part A of Study VX17- 661-116 (A Phase 3, Open-label, Rollover Study to Evaluate the Safety and Efficacy of Long-term Treatment With Tezacaftor in Combination With Ivacaftor in Subjects With Cystic Fibrosis Aged 6 Years and Older, Homozygous or Heterozygous for the F508del-CFTR Mutation). Consequently, the SmPC sections 4.2, 4.5, 4.8 and 5.1 and the package leaflet are updated	

accordingly. The RMP is also updated." Request for Supplementary Information adopted on 24.06.2021.	
WS2085 **Kaftrio-EMEA/H/C/005269/WS2085/0014** **Kalydeco-EMEA/H/C/002494/WS2085/0099** Vertex Pharmaceuticals (Ireland) Limited, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Martin Huber, "Update of SmPC sections 4.4 and 4.8 following cases of liver failure in the post- marketing setting. The PL is updated accordingly. The RMP version 3.1 is submitted for Kaftrio." Request for Supplementary Information adopted on 16.09.2021, 24.06.2021.	

B.5.3. CHMP-PRAC assessed procedures

ADCETRIS - brentuximab vedotin - EMEA/H/C/002455/II/0093, Orphan Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC based on results from study C25004, an open-label study in order to assess the safety and tolerability of brentuximab vedotin when combined with multiagent chemotherapy regimen for first-line treatment of advanced-stage Hodgkin lymphoma in paediatric patients. The RMP version 16 has also been submitted." Request for Supplementary Information adopted on 30.09.2021.	Request for supplementary information adopted with a specific timetable.
Adenuric - febuxostat - EMEA/H/C/000777/II/0061 Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop, PRAC Rapporteur: Jan Neuhauser, "C.I.4 - Update of sections 4.4, 4.8 and 5.1 of the SmPC based on the final results from study FAST (Febuxostat versus Allopurinol Streamlined Trial) listed as a category 3 study in the RMP; this is an interventional study investigating the cardiovascular safety of febuxostat in comparison with allopurinol in patients with chronic symptomatic hyperuricaemia. The Package Leaflet is updated accordingly. The RMP	

version 8.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to update the warning relevant to the content of sodium according to the Annex to the European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use'." Request for Supplementary Information adopted on 24.06.2021.	
Alunbrig - brigatinib / brigatinib - EMEA/H/C/004248/II/0037 Takeda Pharma A/S, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of section 5.1 of the SmPC in order to update efficacy information based on final results from study AP26113-13-301 listed as a PAES in the Annex II; this is a randomised, open-label, multicentre phase III study comparing brigatinib versus crizotinib in patients with advanced ALK-positive NSCLC who have not previously received ALK-directed therapy; The RMP version 5.4 has also been submitted." Request for Supplementary Information adopted on 30.09.2021.	Request for supplementary information adopted with a specific timetable.
COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0018 Janssen-Cilag International N.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of an updated RMP version 2.2 in order to include the following: • To include thrombocytopenia as an important potential risk following the outcome of the signal of Embolic and Thrombotic events (SDA 018.1, EPITT number 19689) and the opinion of procedure EMEA/H/C/005737/II/0006/G • To propose studies aimed at further characterisation of Thrombosis with Thrombocytopenia syndrome (TTS) and thrombocytopenia, following the outcome of the signal of Embolic and Thrombotic events (SDA 018.1, EPITT number 19689) • To include Guillain-Barré syndrome as an important identified risk and update the RMP	Request for supplementary information adopted with a specific timetable.

accordingly (EMEA/H/C/005737/II/0012). In addition, the MAH took the opportunity to update in the EU-RMP the submission milestone dates for VAC31518COV4001 and VAC31518COV4002 studies." Request for Supplementary Information adopted on 30.09.2021.	
Galafold - migalastat - EMEA/H/C/004059/II/0034, Orphan Amicus Therapeutics Europe Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ulla Wändel Liminga, "To update sections 4.8, 5.1 and 5.2 of the SmPC based on final results from study AT1001-020 listed as category 3 in the RMP. Study AT1001-020-is a Phase 3b, 2-stage, open-label, uncontrolled, multicenter study to evaluate the safety, pharmacokinetic, pharmacodynamic and efficacy of migalastat treatment in paediatric subjects 12 to < 18 years of age and weighing ≥ 45 kg with Fabry disease and with amenable GLA variants. The updated RMP version 7.0 has also been submitted. The final results of study AT1001-020, which is involving paediatric patients are submitted in fulfilment of Article 46 of Regulation 1901/2006, as amended. In addition, the MAH took the opportunity to introduce some minor editorial changes to the SmPC and Package Leaflet and bring the PI in line with the latest QRD template v. 10.2." Request for Supplementary Information adopted on 30.09.2021.	Request for supplementary information adopted with a specific timetable.
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0068, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of section 4.4 of the SmPC in order to add baseline monitoring in addition to the current warnings for periodic monitoring of cardiac failure and cardiac arrhythmias in patients receiving ibrutinib. The Package Leaflet is updated accordingly. The RMP version 18.1 has also been submitted." Request for Supplementary Information adopted on 30.09.2021.	Request for supplementary information adopted with a specific timetable.
TOOKAD - padeliporfin - EMEA/H/C/004182/II/0015 STEBA Biotech S.A, Rapporteur: Bruno Sepodes,	Request for supplementary information adopted with a specific timetable.

PRAC Rapporteur: Maia Uusküla, "C.I.11.b - Submission of the Clinical Study Report for Category 1 study: Post-authorisation efficacy study (PAES): CLIN1001 PCM301FU5, A European Randomised Phase 3 Study to Assess the Efficacy and Safety of TOOKAD Soluble for Localised Prostate Cancer compared to Active Surveillance. The Annex 2 has been updated to remove reference to this study." Request for Supplementary Information adopted on 30.09.2021.	
Tremfya - guselkumab - EMEA/H/C/004271/II/0028 Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.8 and 5.1 of the SmPC in order to revise the safety and efficacy profile in the EU product information based on 5 years data from the final study reports of pivotal psoriasis studies PSO3001 and PSO3002 listed as additional PV activities (category 3 studies) in the RMP; these are randomized, double-blind, multicenter, placebo- and active comparator-controlled studies through 48 weeks of treatment. In the long-term extension part of these studies subjects received open-label guselkumab q8w, starting at week 52 in PSO3001 and at week 76 in PSO3002, with the last dose at week 252 and the last safety follow-up visit at week 264. The RMP version 8.1 is accepted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet." Opinion adopted on 30.09.2021. Request for Supplementary Information adopted on 02.09.2021, 10.06.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Trogarzo - ibalizumab - EMEA/H/C/004961/II/0015 Theratechnologies Europe Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: David Olsen, "Submission of an updated RMP version 2.0 in order to reflect the new timelines of the PROMISE study and to align the information included in the RMP with the latest PSUR. As the PROMISE study is a condition of the Trogarzo marketing authorisation, the delayed start date results in a change to Annex II of the marketing authorisation. The date for providing the final study report is changing ."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 30.09.2021.	
Ultomiris - ravulizumab - EMEA/H/C/004954/II/0016 Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Kimmo Jaakkola, "to update section 4.4 Special warnings and precautions for use and section 4.8 Undesirable effects of the SmPC, with consequential updates to sections 2 and 4 of the Patient Information Leaflet regarding anaphylactic reaction, hypersensitivity, and infusion-related reactions." Opinion adopted on 30.09.2021. Request for Supplementary Information adopted on 08.07.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0026 AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to include updated efficacy and safety information based on primary analysis from study D8110C00001 listed as a specific obligation in Annex II; this is a phase III randomised, double-blind, placebo-controlled, multicenter study in adults to determine the safety, efficacy and immunogenicity of Vaxzevria; the Package Leaflet and Annex II are updated accordingly. The updated RMP Version 3 Succession 2 has also been submitted." Request for Supplementary Information adopted on 16.09.2021, 22.07.2021.	See 9.1
WS2127 Effentora-EMEA/H/C/000833/WS2127/ 0058 Teva B.V., Lead Rapporteur: Janet Koenig, Lead PRAC Rapporteur: Martin Huber, "To bring the RMP in line with the GVP version 2 and to update the list of safety concerns in line with the recommendation from PSUSA/00001369/201704. In addition, the outcome of PSUSA/00001369/202004 is endorsed by the MAH and the list of key messages in educational materials to include greater emphasis on explaining off-label use and its potential to lead to serious risks such as misuse, abuse and dependence are implemented. Other elements were added to	

promote the safe and effective use of fentanyl rapid-onset products.”	

B.5.4. PRAC assessed procedures

PRAC Led **AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0038** sanofi-aventis groupe, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, “Submission of the final PASS OBS12753 study report listed as a category 3 study in the RMP. This is a prospective cohort study of long-term safety of teriflunomide in multiple sclerosis patients in Europe. The updated RMP v 7.1 is proposed.” Request for Supplementary Information adopted on 30.09.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Beovu - brolucizumab - EMEA/H/C/004913/II/0008** Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, “Update of section 4.8 of the SmPC in order to include the description of intraocular inflammation, based on final results from a non-interventional retrospective real-world evidence study conducted in patients with neovascular (wet) age-related macular degeneration (nAMD) to better understand the incidence of adverse events/safety signal after initiating treatment with brolucizumab for up to 6 months.” Request for Supplementary Information adopted on 10.06.2021.	
PRAC Led **COMIRNATY - |COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0059** BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of an updated RMP for COMIRNATY version 2.3 in order to add myocarditis/pericarditis as an important identified risk as per PRAC outcome EMEA/H/C/005735/SDA/032, dated 08. July	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

2021 (EPITT: 19712)]. This includes update of the risk minimisation measures related to myocarditis/pericarditis. The MAH is taking the opportunity to update the RMP in line with exposure data at DLP 18 June 2021, the information on planned/ongoing safety studies (protocols C4591011 [US], C4591012 [US], and C4591021 [EU]) and inclusion of two new non-interventional US PASS: C4591009 and Pediatric Heart Network." Opinion adopted on 30.09.2021.	
PRAC Led **COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0020** Janssen-Cilag International N.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, " Update of sections 4.4 and 4.8 of the SmPC to add a new warning on immune thrombocytopenia (ITP), and to add dizziness and ITP to the list of adverse drug reactions with frequencies uncommon and not known, respectively; based on the PRAC request from the post-authorisation measure MEA/014.3 (4th Monthly Summary Safety Report covering the month of June 2021). The package leaflet is updated accordingly. A DHPC and communication plan was adopted." Opinion adopted on 30.09.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Fotivda - tivozanib - EMEA/H/C/004131/II/0018** EUSA Pharma (Netherlands) B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Rugile Pilviniene, PRAC-CHMP liaison: Romaldas Mačiulaitis, "Submission of an updated RMP version 4.0 in order to include data from the phase III Study TIVO-3, a randomised, controlled, multi-centre, open-label study to compare tivozanib with sorafenib in subjects with advanced Renal Cell Carcinoma. Additional updates to the RMP include new information from clinical studies and post-marketing exposure." Opinion adopted on 30.09.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Inflectra - infliximab -**	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP

EMEA/H/C/002778/II/0100/G Pfizer Europe MA EEIG, Duplicate, Duplicate of Remsima, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of the final CSRs for CT-P13 registry studies in Inflammatory Bowel Disease (IBD), Ankylosing Spondylitis (AS) and Rheumatoid Arthritis (RA) initiated with the objective of assessing long-term safety in these indications: • Final report for CT-P13 4.3 (EU and Korean IBD Registry; one study for Remsima and one study for Inflectra) • Final report for CT-P13 4.4 (EU and Korean AS Registry; one study for Remsima and one study for Inflectra) • Final report for BSRBR-RA Registry (one study equally applicable to Remsima and Inflectra) • Final report for RABBIT Registry (one study equally applicable to Remsima and Inflectra)" Opinion adopted on 30.09.2021.	Members were in agreement with the CHMP recommendation.
PRAC Led **Mavenclad - cladribine - EMEA/H/C/004230/II/0015** Merck Europe B.V., Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, PRAC-CHMP liaison: Bruno Sepodes, "Submission of an updated RMP version 1.5.2 in order to bring it in line with the RMP template Rev. 2.0.1. In addition, the MAH took the opportunity to include long-term safety data from the completed PREMIERE registry: a prospective observational long-term safety registry of multiple sclerosis patients who have participated in cladribine clinical studies; and to remove it from the pharmacovigilance plan. Furthermore, the status of the post-approval safety studies MS 700568-0002: a long term, prospective, observational cohort study evaluating the safety profile in patients with highly active relapsing multiple sclerosis newly started on oral cladribine (CLARION); and MS 700568-0004: pregnancy outcomes in women exposed to oral cladribine: a multi-country cohort database study (CLEAR) are updated. Finally, the RMP is updated in line with the conclusions of the PSUSA procedure (PSUSA/00010634/201907)." Opinion adopted on 30.09.2021. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 10.06.2021, 06.05.2021, 14.01.2021.	
PRAC Led **Nivestim - filgrastim - EMEA/H/C/001142/II/0063** Pfizer Europe MA EEIG, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of an updated RMP version 10.1 in order to update the RMP in accordance with GVP Module V and the Guidance on the format of the RMP in the EU - in integrated format (Rev. 2.0.1) and to propose deletion of selected safety concerns listed as important identified risk, important potential risk and missing information." Opinion adopted on 30.09.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **OCALIVA - obeticholic acid - EMEA/H/C/004093/II/0026, Orphan** Intercept Pharma International Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of the RMP to version 1.3 (dated of 11 June 2021) in order to update the format in accordance with template to EMA/164014/2018 Rev.2.0.1 and to add Specific Obligation clinical studies 747-302 and 747-401 to part IV. Plans for post-authorisation efficacy studies of the RMP. This change has been agreed by the CHMP in the outcome Ocaliva 2020 Annual Renewal (EMEA/H/C/004093/R/0023). Other changes also include an update to the exposure data from clinical studies and addition of data on post-marketing experience up to the DLP (26 May 2020) and addition of some specific relevant SmPC wording in the risk minimisation measures." Opinion adopted on 30.09.2021. Request for Supplementary Information adopted on 06.05.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Otezla - apremilast - EMEA/H/C/003746/II/0038** Amgen Europe B.V., Rapporteur: Peter Kiely, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "C.I.13 - Submission of the final study report (CSR) from PsOBest Registry, listed as a category 3 study in the RMP. This is an observational study to	Request for supplementary information adopted with a specific timetable.

assess the long-term safety and effectiveness of apremilast in routine clinical practice in Germany. The RMP version 14.0 has also been submitted." Request for Supplementary Information adopted on 30.09.2021.	
PRAC Led **Otezla - apremilast - EMEA/H/C/003746/II/0039** Amgen Europe B.V., Rapporteur: Peter Kiely, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "C.I.13- Submission of the final study report (CSR) from UK Clinical Practice Research Database (CPRD), listed as a category 3 study in the RMP. This is an observational study to assess the long-term data of apremilast in patients with psoriasis and psoriatic arthritis. The RMP version 14.0 has also been submitted." Request for Supplementary Information adopted on 30.09.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0126/G** Boehringer Ingelheim International GmbH, Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Kirstine Moll Harboe, "C.I.13: Submission of the final report from drug utilisation study, 1160.129, GLORIA AF. This is a three-phase, international, multicenter, prospective, observational registry program in patients with newly diagnosed non-valvular atrial fibrillation (NV AF) at risk for stroke. The objective of the registry program is to investigate patient characteristics influencing the choice of antithrombotic treatment for the prevention of stroke in NV AF patients globally and to collect data from clinical practice settings on important outcome events of antithrombotic treatments for the prevention of stroke. C.I.13: Submission of the final report from drug utilisation study, 1160.136, EU GLORIA AF listed as a category 3 study in the RMP. This is a three-phase, international, multicenter, prospective, observational registry program in patients with newly diagnosed non-valvular atrial fibrillation (NV AF) at risk for stroke. The objective of the registry program is to	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

investigate patient characteristics influencing the choice of antithrombotic treatment for the prevention of stroke in NV AF patients from participating countries in EU/EEA Member States and to collect data from clinical practice settings on important outcome events of antithrombotic treatments for the prevention of stroke. The RMP version 39 has also been submitted." Opinion adopted on 30.09.2021. Request for Supplementary Information adopted on 10.06.2021.	
PRAC Led **Remsima - infliximab - EMEA/H/C/002576/II/0103/G** Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of the final CSRs for CT-P13 registry studies in IBD, AS and RA initiated with the objective of assessing long-term safety in these indications: • Final report for CT-P13 4.3 (EU and Korean IBD Registry) • Final report for CT-P13 4.4 (EU and Korean AS Registry) • Final report for BSRBR-RA Registry • Final report for RABBIT Registry" Opinion adopted on 30.09.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Suliqua - insulin glargine / lixisenatide - EMEA/H/C/004243/II/0024** sanofi-aventis groupe, Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final Clinical Study Report of the category 3 PASS INSLIC08571, a 'Survey to evaluate the knowledge and understanding of the key safety messages in the healthcare professional guide and the patient guide'. The provision of the final survey results addresses post-authorisation measure (PAM) MEA 002. The updated RMP version 6.0 has also been submitted." Request for Supplementary Information adopted on 30.09.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Truvada - emtricitabine / tenofovir disoproxil - EMEA/H/C/000594/II/0173** Gilead Sciences Ireland UC, Rapporteur: Bruno	Request for supplementary information adopted with a specific timetable.

Sepodes, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "Removal of the additional risk minimisation measures (aRMMs) for the PrEP indication risks, from the Truvada EU RMP and Annex II of the Truvada PI. With this variation, version 17.2 of the RMP (dated 1st July 2021) is submitted." Request for Supplementary Information adopted on 30.09.2021.	
PRAC Led **WS1970** **Eucreas-EMEA/H/C/000807/WS1970/0081** **Galvus-EMEA/H/C/000771/WS1970/0067** **Icandra-EMEA/H/C/001050/WS1970/0084** **Jalra-EMEA/H/C/001048/WS1970/0069** **Xiliarx-EMEA/H/C/001051/WS1970/0067** **Zomarist-EMEA/H/C/001049/WS1970/0083** Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP (version 15.0) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' and aligned with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00003113/201802) adopted in October 2018. Annex II.D of the product information is updated to remove the statement around submission of an RMP update every 3 years." Opinion adopted on 30.09.2021. Request for Supplementary Information adopted on 06.05.2021, 14.01.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS2050/G** **Corlentor-EMEA/H/C/000598/WS2050/0056/G** **Procoralan-EMEA/H/C/000597/WS2050/0055/G** Les Laboratoires Servier, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "To update the RMP for Procoralan and Corlentor following the assessment for the same changes approved for Ivabradine Anpharm EMEA/H/C/4187/R/014.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

In addition, the PI also has been updated following EMA QRD review following the same assessment. The MAH has finally also introduced changes related to QRD 10.2 in section 6 of the PL."
Opinion adopted on 30.09.2021.

PRAC Led
WS2078
Lixiana-EMEA/H/C/002629/WS2078/0034
Roteas-EMEA/H/C/004339/WS2078/0020
Daiichi Sankyo Europe GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "C.I.13: Submission of the final report from study ETNA-VTE-EUROPE (DSE-EDO-05-14-EU), listed as a category 3 study in the RMP. This is a Non-Interventional Study on Edoxaban Treatment in Routine Clinical Practice in Patients with Venous Thromboembolism in Europe. The RMP version 12.0 has also been submitted."

B.5.5. CHMP-CAT assessed procedures

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0046, ATMP
Amgen Europe B.V., Rapporteur: Heli Suila, CHMP Coordinator: Johanna Lähteenvuo, "Submission of the final report from study 20110265 listed as an obligation in the Annex II of the Product Information. This is a Phase 1b/3, multicenter, trial of talimogene laherparepvec in combination with pembrolizumab for treatment of unresectable stage IIIB to IVM1c melanoma. The Annex II is updated accordingly."

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0040, Orphan, ATMP
Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Johanna Lähteenvuo

Libmeldy - atidarsagene autotemcel - EMEA/H/C/005321/II/0004, Orphan, ATMP
Orchard Therapeutics (Netherlands) BV, Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege

Tecartus - autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - EMEA/H/C/005102/II/0012, Orphan, ATMP

Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

Zolgensma - onasemnogene abeparvovec - EMEA/H/C/004750/II/0015, Orphan, ATMP

Novartis Gene Therapies EU Limited, Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege, "Updates to sections 4.4, 4.8 and 5.1 of the SmPC to reflect the final study results AVXS-101-CL-302; a Post-authorisation efficacy study intended to confirm the efficacy and
safety and tolerability of a single dose of Zolgensma in patients younger than 6 months of age with SMA Type 1 with One or Two SMN2 Copies. The package leaflet has been updated accordingly and annex II has been updated to reflect completion of this Specific Obligation." Request for Supplementary Information adopted on 16.07.2021.

Zolgensma - onasemnogene abeparvovec - EMEA/H/C/004750/II/0017/G, Orphan, ATMP

Novartis Gene Therapies EU Limited, Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

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

WS2088/G
Brimica Genuair-EMEA/H/C/003969/
WS2088/0033/G
Duaklir Genuair-EMEA/H/C/003745/

WS2088/0033/G AstraZeneca AB, Lead Rapporteur: Ewa Balkowiec Iskra	
WS2099 **HyQvia-EMEA/H/C/002491/WS2099/0073** **Kiovig-EMEA/H/C/000628/WS2099/0111** Takeda Manufacturing Austria AG, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 02.09.2021.	
WS2103 **Enurev Breezhaler-EMEA/H/C/002691/WS2103/0038** **Seebri Breezhaler-EMEA/H/C/002430/WS2103/0038** **Tovanor Breezhaler-EMEA/H/C/002690/WS2103/0042** **Ultibro Breezhaler-EMEA/H/C/002679/WS2103/0040** **Ulunar Breezhaler-EMEA/H/C/003875/WS2103/0041** **Xoterna Breezhaler-EMEA/H/C/003755/WS2103/0044** Novartis Europharm Limited, Lead Rapporteur: Kirstine Moll Harboe, Opinion adopted on 30.09.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2105/G **Corbilta-EMEA/H/C/002785/WS2105/0025/G** **Levodopa/Carbidopa/Entacapone Orion-EMEA/H/C/002441/WS2105/0033/G** **Stalevo-EMEA/H/C/000511/WS2105/0095/G** Orion Corporation, Lead Rapporteur: Outi Mäki-Ikola	
WS2122 **Aprovel-EMEA/H/C/000141/WS2122/0185** **CoAprovel-EMEA/H/C/000222/WS2122/0204** **Karvea-EMEA/H/C/000142/WS2122/0187** **Karvezide-EMEA/H/C/000221/WS2122/0204** sanofi-aventis groupe, Lead Rapporteur: Maria Concepcion Prieto Yerro Opinion adopted on 23.09.2021.	Positive Opinion adopted by consensus on 23.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2144 **Abseamed-EMEA/H/C/000727/WS2144/**	

0095 **Binocrit-EMEA/H/C/000725/WS2144/0094** **Epoetin alfa Hexal-EMEA/H/C/000726/WS2144/0094** Sandoz GmbH, Lead Rapporteur: Alexandre Moreau	
WS2152 **Aflunov-EMEA/H/C/002094/WS2152/0072** **Foclivia-EMEA/H/C/001208/WS2152/0069** Seqirus S.r.l, Lead Rapporteur: Armando Genazzani	
WS2157 **Epclusa-EMEA/H/C/004210/WS2157/0062** **Harvoni-EMEA/H/C/003850/WS2157/0102** **Sovaldi-EMEA/H/C/002798/WS2157/0076** **Vosevi-EMEA/H/C/004350/WS2157/0049** Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, "To update the due date for the hepatocellular carcinoma (HCC) recurrence post authorisation safety study (PASS) in Annex II of the PI." Opinion adopted on 30.09.2021.	Positive Opinion adopted by consensus on 30.09.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

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

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

vutrisiran - EMEA/H/C/005852, Orphan Alnylam Netherlands B.V., treatment of hereditary transthyretin-mediated amyloidosis
mavacamten - EMEA/H/C/005457 treatment of symptomatic obstructive hypertrophic cardiomyopathy
dimethyl fumarate - EMEA/H/C/005963

treatment of multiple sclerosis
pegfilgrastim - EMEA/H/C/005810 Treatment of neutropenia
maralixibat - EMEA/H/C/005857 Treatment of cholestatic liver disease in patients with Alagille syndrome (ALGS) 1 year of age and older
relatlimab / nivolumab - EMEA/H/C/005481 indicated for the first-line treatment of advanced (unresectable or metastatic) melanoma in adults and adolescents (12 years and older and weighing at least 40 kg).
regdanvimab - EMEA/H/C/005854 Treatment of Covid-19
efbemalenograstim alfa - EMEA/H/C/005828 Reduction in the duration of neutropenia and the incidence of febrile neutropenia.
teriflunomide - EMEA/H/C/005962 treatment of multiple sclerosis (MS)

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

RINVOQ - upadacitinib - EMEA/H/C/004760/X/0012/G AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce, "Extension application to add a strength (45 mg) of the prolonged-release tablets, grouped with a type II variation (C.I.6.a) to include the treatment of adults with moderately to severely active ulcerative colitis who had an inadequate response, lost response or were intolerant to either conventional therapy or a Biologic agent; as a consequence sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. The RMP (version 6.0) has also been submitted."	
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/X/0044/G	See 4.1

BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Extension application to add a new pharmaceutical form (dispersion for injection) with a new strength (0.1 mg/ml). C.I.z - To update sections 6.4, 6.5 and 6.6 of the SmPC, section 5, 6 and information for healthcare professionals of the PL, section 1 of the Carton Box Label as well as section 1 and 5 of the Vial Label to ensure the correct handling by providing dose verification information about strength, age range, colour information of the flip-off plastic cap and greyscale images. C.I.z - To update sections 4.2 of the SmPC ensure the correct handling in accordance to interchangeability of the medicinal product. C.I.z - To update section 8 of Carton Box Label to clarify expiry date "EXP" by adding storage temperature "(at -90°C to -60°C)" to ensure the correct handling of the medicinal product. A.3 - To change the name of the active substance from COVID-19 mRNA Vaccine (nucleoside modified) to Tozinameran. The marketing authorisation holder has taken the opportunity to implement minor editorial changes.	

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

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

Brineura - cerliponase alfa - EMEA/H/C/004065/S/0035, Orphan BioMarin International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga
Increlex - mecasermin - EMEA/H/C/000704/S/0070 Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka
Lojuxta - lomitapide - EMEA/H/C/002578/S/0048 Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst
Strensiq - asfotase alfa -

EMEA/H/C/003794/S/0056, Orphan
Alexion Europe SAS, Rapporteur: Armando Genazzani, PRAC Rapporteur: Rhea Fitzgerald

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

Axumin - fluciclovine (18F) - EMEA/H/C/004197/R/0027
Blue Earth Diagnostics Ireland Limited, Rapporteur: Janet Koenig, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Rugile Pilviniene

BESPONSA - inotuzumab ozogamicin - EMEA/H/C/004119/R/0023, Orphan
Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, Co-Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Brigitte Keller-Stanislawski

Febuxostat Mylan - febuxostat - EMEA/H/C/004374/R/0011
Mylan S.A.S, Generic, Generic of Adenuric, Rapporteur: Elita Poplavska, PRAC Rapporteur: Jan Neuhauser

Ivabradine Accord - ivabradine - EMEA/H/C/004241/R/0010
Accord Healthcare S.L.U., Generic, Generic of Procoralan, Rapporteur: Eleftheria Nikolaidi, PRAC Rapporteur: Menno van der Elst

Kalydeco - ivacaftor - EMEA/H/C/002494/R/0106, Orphan
Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Maria del Pilar Rayon

Kevzara - sarilumab - EMEA/H/C/004254/R/0029
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Eva A. Segovia

Rixathon - rituximab - EMEA/H/C/003903/R/0053
Sandoz GmbH, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Anette Kirstine Stark

Riximyo - rituximab -
EMEA/H/C/004729/R/0054
Sandoz GmbH, Duplicate, Duplicate of Rixathon, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Anette Kirstine Stark

Spherox - spheroids of human autologous matrix-associated chondrocytes -
EMEA/H/C/002736/R/0024, ATMP
CO.DON AG, Rapporteur: Lisbeth Barkholt, Co-Rapporteur: Heli Suila, PRAC Rapporteur: Brigitte Keller-Stanislawski

Trimbow - beclometasone / formoterol / glycopyrronium bromide -
EMEA/H/C/004257/R/0025
Chiesi Farmaceutici S.p.A., Rapporteur: Janet Koenig, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Jan Neuhauser

Trumenba - meningococcal group B vaccine (recombinant, adsorbed) -
EMEA/H/C/004051/R/0036
Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Jean-Michel Dogné

Veltassa - patiromer -
EMEA/H/C/004180/R/0028
Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Jayne Crowe, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Kirsti Villikka

Zykadia - ceritinib -
EMEA/H/C/003819/R/0042
Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Ingrid Wang, PRAC Rapporteur: Annika Folin

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

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

EXPAREL liposomal - bupivacaine -
EMEA/H/C/004586/II/0005
Pacira Ireland Limited, Rapporteur: Elita Poplavska, Co-Rapporteur: Margareta Bego, PRAC Rapporteur: Rhea Fitzgerald, "Extension

of indication to include children over 6 years old.”	
Jardiance - empagliflozin - EMEA/H/C/002677/II/0060 Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia, “Extension of indication to add the treatment of patients with Heart Failure with preserved ejection fraction based on the results from the clinical study 1245.110 EMPEROR-preserved. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC and sections 1 and 4 of the PIL are updated accordingly. Further, the MAH applied for an additional year of market protection. The updated RMP v 16.0 has also been submitted. In addition, the statement 'sodium free' was re-located from section 2 of the SmPC to section 4.4. to comply with EMA'S QRD guidance and minor linguistic changes to the national translations are included in this submission” Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)	
Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0044, Orphan, ATMP Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Extension of indication to include treatment of adult patients with follicular lymphoma (FL) after two or more lines of therapy who are refractory, or relapsed during or within 6 months after completion of anti-CD20 antibody maintenance, or relapsed after autologous haematopoietic stem cell transplantation (HSCT) for Kymriah. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and corresponding sections in the Package Leaflet are updated accordingly. The RMP has been updated to version 4.0 to align with the indication extension. Lastly, the minor editorial corrections are made throughout the SmPC and package leaflet to align with the current QRD template version 10.2. ” Request for 1 year of market protection for a new indication (Article 14(11) of Regulation	

(EC) 726/2004)	
Olumiant - baricitinib - EMEA/H/C/004085/II/0029/G Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski, "Grouping of the following variations: C.I.6 - Extension of indication to include treatment of severe alopecia areata in adult patients for Olumiant; as a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 12.1 of the RMP has also been submitted. C.I.11.z - Update of RMP (version 12.1) to change the category 3 study PASS I4V-MC-B011 end of data collection for the Atopic Dermatitis cohort and the subsequent final study report milestone ." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)	
Xeljanz - tofacitinib - EMEA/H/C/004214/II/0039 Pfizer Europe MA EEIG, Rapporteur: Armando Genazzani, PRAC Rapporteur: Liana Gross-Martirosyan, "Extension of indication to include treatment of active ankylosing spondylitis for Xeljanz prolonged release; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 18.1 of the RMP has also been submitted."	

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0069/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0071 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	See B.5.1

COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0072/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	See B.5.1
COMIRNATY - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0073/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	See B.5.1
Erelzi - etanercept - EMEA/H/C/004192/II/0038/G Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege	
Fendrix - hepatitis B (rDNA) vaccine (adjuvanted, adsorbed) - EMEA/H/C/000550/II/0076/G GlaxoSmithKline Biologicals, Rapporteur: Christophe Focke	
Imfinzi - durvalumab - EMEA/H/C/004771/II/0036 AstraZeneca AB, Rapporteur: Sinan B. Sarac	
Kirsty - insulin aspart - EMEA/H/C/004965/II/0003/G Mylan IRE Healthcare Limited, Rapporteur: Kirstine Moll Harboe	
Myocet liposomal - doxorubicin hydrochloride - EMEA/H/C/000297/II/0066 Teva B.V., Rapporteur: Filip Josephson	
Natpar - parathyroid hormone - EMEA/H/C/003861/II/0033/G, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Karin Janssen van Doorn	
Nimenrix - Meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0112 Pfizer Europe MA EEIG, Rapporteur: Ingrid Wang	
Palynziq - pegvaliase - EMEA/H/C/004744/II/0024, Orphan BioMarin International Limited, Rapporteur: Johann Lodewijk Hillege	
Revestive - teduglutide - EMEA/H/C/002345/II/0055, Orphan	

Shire Pharmaceuticals Ireland Limited, Rapporteur: Kirstine Moll Harboe

Spectrila - asparaginase - EMEA/H/C/002661/II/0026
medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Andrea Laslop

Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0166/G
GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder

Trogarzo - ibalizumab - EMEA/H/C/004961/II/0016/G
Theratechnologies Europe Limited, Rapporteur: Johann Lodewijk Hillege

YUFLYMA - adalimumab - EMEA/H/C/005188/II/0009/G
Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola

Zutectra - human hepatitis B immunoglobulin - EMEA/H/C/001089/II/0050
Biotest Pharma GmbH, Rapporteur: Jan Mueller-Berghaus

WS2119/G
M-M-RVAXPRO-EMEA/H/C/000604/ WS2119/0110/G
ProQuad-EMEA/H/C/000622/WS2119/ 0152/G
MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus

WS2132
Infanrix hexa-EMEA/H/C/000296/ WS2132/0305
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke

WS2138/G
Hexacima-EMEA/H/C/002702/WS2138/ 0120/G
Hexyon-EMEA/H/C/002796/WS2138/ 0124/G
Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus

WS2142

M-M-RVAXPRO-EMEA/H/C/000604/ WS2142/0111
ProQuad-EMEA/H/C/000622/WS2142/ 0153
MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus

WS2165/G
Blitzima-EMEA/H/C/004723/WS2165/ 0048/G
Truxima-EMEA/H/C/004112/WS2165/ 0052/G
Celltrion Healthcare Hungary Kft., Duplicate, Duplicate of Truxima, Lead Rapporteur: Sol Ruiz

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

Edarbi - azilsartan medoxomil - EMEA/H/C/002293/II/0030/G
Takeda Pharma A/S, Rapporteur: Johann Lodewijk Hillege, "Group of variations:
· Type II C.I.4. - Update of SmPC sections 4.2, 4.8 and 5.1 with paediatric clinical data from study AR14.001 (PIP study 8) following the outcome of procedure EMEA/H/C/002293/P46/012.
· Type II C.I.4. - Update of SmPC section 5.2 with paediatric clinical data from study TAK-491_109 (PIP study 7) following the outcome of procedure EMEA/H/C/002293/P46/011.
· Type II C.I.4. - Update of SmPC section 5.3 with data from juvenile animal toxicity studies.
· Type II C.I.4. - Update of SmPC section 4.5 with drug-drug interaction information from clinical pharmacology studies TAK-491-013 and TAK-563-004.
Furthermore, the MAH is taking the opportunity to update the PI in line with the latest QRD template version 10.2, update the local representatives for Ireland, Slovenia and United Kingdom in the Package Leaflet (PL) and update minor editorial/typographical to Product information."

Evrysdi - risdiplam - EMEA/H/C/005145/II/0003, Orphan
Roche Registration GmbH, Rapporteur: Bruno Sepodes, "Update of section 4.8 of the SmPC to add undesirable effects based on post-marketing experience. The Package Leaflet (PL)

is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of local representatives in the PL."	
Ganfort - bimatoprost / timolol - EMEA/H/C/000668/II/0038 Allergan Pharmaceuticals Ireland, Rapporteur: Kirstine Moll Harboe, "C.I.4 Update of section 4.8 of the SmPC in order to add periorbital and lid changes associated with periorbital fat atrophy and skin tightness to the list of adverse drug reactions (ADRs) with frequency uncommon."	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0114 Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, "Update of section 5.1 of the SmPC in order to update efficacy information based on final results from study KEYNOTE-087 listed as an imposed PAES in the Annex II; this is a multicenter, single-arm, multi-cohort, non-randomized Phase 2 study of IV pembrolizumab in participants with relapsed or refractory classical Hodgkin lymphoma (cHL)."	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0115 Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, "Update of section 5.1 of the SmPC in order to update efficacy information based on final results from study KEYNOTE-426 listed as imposed PAES in the Annex II; this is a Phase III Randomized, Open-label Study to Evaluate Efficacy and Safety of Pembrolizumab (MK-3475) in combination with Axitinib versus Sunitinib Monotherapy as a First-line Treatment for Locally Advanced or Metastatic Renal Cell Carcinoma (mRCC)."	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0116 Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, "Update of section 5.1 of the SmPC in order to update efficacy information based on final results from study KEYNOTE-177 listed as PAES in Annex II of the Product Information; this is a 2-arm, multicenter, international, randomized, open-	

label, Phase 3 study evaluating the efficacy and safety of pembrolizumab monotherapy versus globally-accepted SOC therapies for Colorectal carcinoma (CRC) in participants with locally confirmed Deficient mismatch repair (dMMR) or Microsatellite instability-high (MSI-H) unresectable or metastatic CRC who have not received prior chemotherapy for their disease."

Kovaltry - octocog alfa - EMEA/H/C/003825/II/0038

Bayer AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of the SmPC sections 4.8 and 5.1 to include data from the LEOPOLD Kids Part B (previously submitted as Art 46; an addendum on biomarker data is included in this submission) and extension study results included as part of this submission. In addition, an editorial revision in section 4.2 and a clarification in section 6.5 of the SmPC are proposed. Section 4 of the Package is updated accordingly. A correction of a typo in the Greek product information is also included. The Risk Management Plan for Kovaltry is updated using Revision 2.0.1 of the template format."

Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0030

Roche Registration GmbH, Rapporteur: Kirstine Moll Harboe, "to include new clinical efficacy data in section 5.1 of the SmPC to reflect on the newly available post hoc pooled analyses results related to the time-to-walking aid data performed on clinical studies WA21092 (OPERA I) and WA21093 (OPERA II) in the RMS population."

Oxlumo - lumasiran - EMEA/H/C/005040/II/0007, Orphan

Alnylam Netherlands B.V., Rapporteur: Martina Weise, "Update of section 5.3 of the SmPC in order to update the non-clinical information based on the final results from the 26-week GLP carcinogenicity study of lumasiran by subcutaneous injection in TgRasH2 mice, as agreed as part of protocol assistance (EMEA/H/SA/4014/2/2019/PA/PR/I). In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet."

Tecentriq - atezolizumab - EMEA/H/C/004143/II/0067

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to include the new ADR of rhinorrhoea identified in the IMpassion031 study and reviewed in the context of a drug safety report. The package leaflet is proposed to be updated accordingly.
Additional amendments are proposed to the footnotes of ADRs in the SmPC, the removal of the term 'lung infection', the inclusion of the term 'orthostatic hypertension' and the inclusion of a new footnote listing the terms covered for the ADR of psoriasis."

Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0090

MCM Vaccine B.V., Rapporteur: Christophe Focke, "Update of section 4.8 of the Summary of Product Characteristics (SmPC) in order to add Convulsions with or without fever with frequency Not known to the list of post-marketing adverse events. The package leaflet (PL) is updated accordingly."

Veklury - remdesivir - EMEA/H/C/005622/II/0026/G

Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, "Grouped variation updating sections 5.2 and 5.3 of the SmPC in order to add additional pharmacokinetic (PK) data coming non clinical and clinical studies to fulfil two Post-Authorisation Measures for Veklury: Recommendation (REC) number 4 (non-clinical data to further characterise a previously unidentified metabolite, M27); and REC number 7 (to submit data from additional analysis of the circulating species of remdesivir from the human mass-balance study, GS-US-399-4231). Both were agreed during the initial conditional marketing application (EMEA/H/C/005622)."

VITRAKVI - larotrectinib - EMEA/H/C/004919/II/0021

Bayer AG, Rapporteur: Filip Josephson, Co-Rapporteur: Alexandre Moreau, "Update of section 5.2 of the SmPC in order to reflect the outcome of an updated analysis of the

population pharmacokinetic (PopPk) model based on additional PK sampling in patients aged 1 month to 6 years from study LOXO-TRK-15003 (SCOUT) imposed as a specific obligation (SOB). The MAH is also proposing to delete this SOB from Annex II. The MAH took the opportunity of this variation to introduce corrections to section 4.8 of the SmPC and to Annex II."	
WS2145 **DuoPlavin-EMEA/H/C/001143/WS2145/0059** **Iscover-EMEA/H/C/000175/WS2145/0145** **Plavix-EMEA/H/C/000174/WS2145/0143** sanofi-aventis groupe, Lead Rapporteur: Bruno Sepodes, "Update of section 4.5 of the SmPC to add the drug-drug interaction between clopidogrel and rosuvastatin based on a review of the available data including literature and the MAH safety database. The package leaflet is updated accordingly."	
WS2154 **CONTROLOC Control-EMEA/H/C/001097/WS2154/0038** **PANTOLOC Control-EMEA/H/C/001100/WS2154/0043** **PANTOZOL Control-EMEA/H/C/001013/WS2154/0040** **SOMAC Control-EMEA/H/C/001098/WS2154/0039** Takeda GmbH, Lead Rapporteur: Romaldas Mačiulaitis, "C.1.4 - Update of section 4.8 of the SmPC to update the existing term "Interstitial nephritis" to "Tubulointerstitial nephritis (TIN)" in line with the updated Company Core Data Sheet. In addition, section 4.4 of the SmPC for centralised authorised products is updated with the Excipient warning for Sodium as per EMA guideline EMA/CHMP/302620/2017/EN Rev. 1. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the PL and to bring the PI in line with the last QRD template (version 10.1). This procedure also includes NAPs as listed in Annex B."	

B.6.10. CHMP-PRAC assessed procedures

Erleada - apalutamide - EMEA/H/C/004452/II/0017

Janssen-Cilag International N.V., Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Tiphaine Vaillant, "Update of section 5.3 of the SmPC in order to update non-clinical information based on final results from study TOX11338 listed as PAM (EMEA/H/C/004452/MEA/006); this is a 2-year carcinogenicity study of JNJ-56021927-AAA by oral gavage in rats; The RMP version 4.1 has also been submitted. In addition, the MAH has taken this opportunity to include general information in the RMP regarding study TITAN (PCR3002)."

Imraldi - adalimumab - EMEA/H/C/004279/II/0048/G

Samsung Bioepis NL B.V., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Ulla Wändel Liminga

Tecentriq - atezolizumab - EMEA/H/C/004143/II/0066

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "C.I.13: Submission of the final report from study WO29635 to fulfil a category 3 study activity (MEA/FSR 007). This is A Phase IB/II study of the safety and pharmacology of
Atezolizumab administered with or without Bacille Calmette-Guérin in patients with High Risk Non-Muscle-Invasive Bladder Cancer. The RMP version 22.0 has also been submitted. The RMP has additionally been amended to revise the due date for the submission of the final CSR for study MO39171 (TAIL)."

Tresiba - insulin degludec - EMEA/H/C/002498/II/0054

Novo Nordisk A/S, Rapporteur: Kristina Dunder, Co-Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Annika Folin, "Update of sections 4.6 and 5.1 of the Summary of product characteristics in order to include new clinical data from the pregnancy trial EXPECT conducted for Tresiba.
The Package Leaflet is updated in accordance.
The RMP version 9.0 is also submitted."

Uptravi - selexipag - EMEA/H/C/003774/II/0034

Janssen-Cilag International N.V., Rapporteur: Martina Weise, PRAC Rapporteur: Tiphaine Vaillant, "Update of section 4.8 of the SmPC to add 'dyspepsia' as a new ADR with frequency 'common', and to include further information on the frequency of 'dyspepsia' and 'anaemia' specific to initial 2-step triple combination therapy, based on the Studies AC-065A308 (TRITON) and AC-065A404 (TRACE). AC-065A308 (TRITON) study was a randomized, double-blind, placebo-controlled, parallel-group, Phase 3b, efficacy and safety study comparing triple oral combination therapy (selexipag, macitentan, tadalafil) with double oral combination therapy (placebo, macitentan, tadalafil) in newly diagnosed, treatment-naïve participants with PAH. The AC-065A404 (TRACE) study was a randomized, double-blind, placebo-controlled, parallel-group, exploratory Phase 4 study in participants with PAH to assess the effect of selexipag on daily life physical activity and participant's self-reported symptoms and their impacts. The package leaflet is updated accordingly. A revised RMP version 9.2 was provided as part of the application."

B.6.11. PRAC assessed procedures

PRAC Led

Adasuve - loxapine - EMEA/H/C/002400/II/0033

Ferrer Internacional s.a., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update safety information on Bronchospasm based on final results from study AMDC-204-401 EU PASS (assessed in procedure EMEA/H/C/0002400/II/0032): Post-authorisation Observational Study to Evaluate the Safety of ADASUVE (Staccato loxapine for inhalation) in Agitated Persons in Routine Clinical Care, a category 3 study in the RMP; the Package Leaflet and Labelling are updated accordingly. In addition, the MAH took the opportunity to update the list of local

representatives in the Package Leaflet."

PRAC Led

Evenity - romosozumab - EMEA/H/C/004465/II/0010

UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 2.0 in order to remove the important identified risk of "immunogenicity", based on the Good Pharmacovigilance Practices (GVP) guidelines, EMA guidance on immunogenicity assessment, and the available non-clinical, clinical and post-marketing data. In addition, following the Pharmacovigilance Risk Assessment Committee (PRAC) recommendation (EMA/PRAC/265359/2021) dated 06 May 2021, the MAH is taking this opportunity to add "cardiac arrythmia" as an important potential risk of romosozumab, update the protocol for the ongoing post authorization safety study (PASS) OP0004 to include cardiac arrhythmias as specific events to monitor, and include a targeted follow-up questionnaire related to cardiac arrhythmias in the RMP Part VII Annex 4.
The MAH is also taking this opportunity to introduce minor changes in the PASS protocols of three studies OP0004, OP0005 and OP0006."

PRAC Led

Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0023

Seqirus Netherlands B.V., Rapporteur: Sol Ruiz, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of section 4.6 of the SmPC in order to update information on Pregnancy Registry 130_110B, listed as a category 3 study in the RMP. The PL is updated accordingly. The RMP version 3.1 has also been submitted in order to update information related to the pregnancy study, clinical and post-marketing exposure."

PRAC Led

Latuda - lurasidone - EMEA/H/C/002713/II/0036

Aziende Chimiche Riunite Angelini Francesco A.C.R.A.F. S.p.A., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "Update of

section 4.8 of the SmPC to amend the frequency of ADRs in adults and to add 'syncope' (frequency uncommon) and 'cerebrovascular accident' (frequency rare) following the assessment of the procedure EMEA/H/C/PSUSA/00010114/202010. The Package Leaflet is updated accordingly. Minor adjustments of the PTs based on the MedDRA definitions were implemented and the ADR 'blood creatine phosphokinase increased' was moved to the SOC Investigations. In addition, the marketing authorisation holder has taken the opportunity to combine all the dosages in a single version of the SmPC, to update the list of local representatives in the PL and to bring the PI in line with the latest QRD template version 10.2 Rev. 1."	
PRAC Led **Prolia - denosumab - EMEA/H/C/001120/II/0091/G** Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "- C.I.11.b: Submission of an updated RMP version 28.0 in order to remove osteonecrosis outside the jaw (OOJ) including external auditory canal (OEAC) as an important potential risk. - C.I.11.b: Submission of an updated RMP version 28.0 in order to remove immunogenicity following a significant change to the manufacturing process as missing information. - C.I.11.b: Submission of an update RMP version 28.0 in order to introduce changes to the category 3 PASS-retrospective cohort database study (study 20190038) for the potential increased risk of cardiovascular and cerebrovascular events among women with PMO and men with osteoporosis by adding the study objectives. In addition, the MAH took the opportunity to update the RMP in order to provide the date for the provision of the final study report for study 20190038 and to include the post-marketing exposure data from the last submitted PSUR/PBRER (#13)."	
PRAC Led **Prolia - denosumab - EMEA/H/C/001120/II/0092** Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga,	

PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from study 20190038 "Incidence of Cardiovascular and Cerebrovascular Events Among Postmenopausal Women and Men With Osteoporosis Who Initiated Treatment With Denosumab or Zoledronic Acid - a Retrospective Cohort Study". This is an observational PASS listed as category 3 study in the RMP."

PRAC Led

TRISENOX - arsenic trioxide - EMEA/H/C/000388/II/0076

Teva B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "Update of section 4.6 of the SmPC in order to update information on pregnancy and contraception in male patients following the decision and discussion made for EMEA/H/C/PSUSA/00000235/202009. The Package Leaflet is updated accordingly."

PRAC Led

Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0038

AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Christophe Focke, "Submission of the final report from study MS1222-0003 ''Assessment of anti-PF4 antibodies prior to, and following, vaccination with AZD1222" listed as a category 3 study in the RMP. This is a study where sera of vaccinated individuals in study D8110C00001 are tested to elucidate whether vaccination with Vaxzevria leads to increased levels of circulating anti-PF4 antibodies, a key component of the hypothesized mechanism underlying thrombosis with thrombocytopenia syndrome (TTS)."

PRAC Led

Xeljanz - tofacitinib - EMEA/H/C/004214/II/0044

Pfizer Europe MA EEIG, Rapporteur: Armando Genazzani, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "C.I.3.b - Update of sections 4.4, 4.8 and 5.1 to add warnings and safety data on serious infections, viral reactivation, non-melanoma skin cancer and fractures. This is based on the final results from study A3921133

listed as a category 3 study in the RMP; this is a post-authorisation safety study conducted to evaluate the safety of tofacitinib 5mg and 10 mg compared to TNFi in adults' subjects aged ≥50 years with moderately or severely active RA and with at least 1 additional CV risk factor. The Package Leaflet is updated accordingly. The RMP version 21.1 has also been submitted. In addition, the MAH took the opportunity to update the Outer carton (section 4 for oral solution) to include a total volume of 240 mL as requested following the completion of the procedure EMEA/H/C/004214/X/0024/G."	
PRAC Led **WS2158** **Exviera-EMEA/H/C/003837/WS2158/0051** **Viekirax-EMEA/H/C/003839/WS2158/0063** AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "To update the Annex IID study milestone due date for the hepatocellular carcinoma (HCC) recurrence post-authorisation safety study (B20-146) following the EMA's recommendation on 6 July 2021. In addition, the MAH is taking the opportunity to introduce few minor linguistic and typographical corrections in the Summary of Product Characteristics (SmPCs) for the Hungarian, Latvian and Romanian translations of the Exviera product information."	

B.6.12. CHMP-CAT assessed procedures

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

WS2131 **Herceptin-EMEA/H/C/000278/WS2131/0176** **Kadcyla-EMEA/H/C/002389/WS2131/0060**	

Phesgo-EMEA/H/C/005386/WS2131/0009
Roche Registration GmbH, Lead Rapporteur: Jan Mueller-Berghaus

WS2139
Hexacima-EMEA/H/C/002702/WS2139/0121
Hexyon-EMEA/H/C/002796/WS2139/0125
Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus

WS2147
Infanrix hexa-EMEA/H/C/000296/WS2147/0306
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke

WS2161
Mircera-EMEA/H/C/000739/WS2161/0085
NeoRecormon-EMEA/H/C/000116/WS2161/0114
Roche Registration GmbH, Lead Rapporteur: Martina Weise

WS2171
Glyxambi-EMEA/H/C/003833/WS2171/0040
Synjardy-EMEA/H/C/003770/WS2171/0058
Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "To update section 4.8 of the SmPC and section 4 of the PL to include the side effect 'constipation' in order to align with the Jardiance PI following approval of EMEA/H/C/002677/II/0055."

WS2172
Aprovel-EMEA/H/C/000141/WS2172/0186
CoAprovel-EMEA/H/C/000222/WS2172/0205
Karvea-EMEA/H/C/000142/WS2172/0188
Karvezide-EMEA/H/C/000221/WS2172/0205
sanofi-aventis groupe, Lead Rapporteur: Maria Concepcion Prieto Yerro

WS2176
Enurev Breezhaler-EMEA/H/C/002691/WS2176/0039
Seebri Breezhaler-EMEA/H/C/002430/

WS2176/0039
Tovanor Breezhaler-EMEA/H/C/002690/ WS2176/0043
Novartis Europharm Limited, Lead Rapporteur: Kirstine Moll Harboe, "To update the PI for Seebri Breezhaler (glycopyrronium bromide) and its two duplicates, Enurev Breezhaler and Tovanor Breezhaler in line with current QRD template v10.2, Rev. 1 and QRD template v10.1 as follows:
- Package leaflet is updated to include Northern Ireland in the list of the local representatives of the Marketing Authorisation Holder (QRD v10.2)
- ANNEX II (C and D sections) and Labelling are updated in line with the QRD template v10.1.
The MAH also updated section 4.4 (subsection 'Excipients') of the SmPC (Annex I) to change the word from "the Lapp" to "total" to align with the latest European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use' (SANTE-2017-11668), dated 22-Nov-2019.
In addition, the MAH has taken the opportunity to update the Instructions for use (IFU) in section 6.6 of the SmPC (Annex I) and also at the end of the Package leaflet."

WS2178/G
Aflunov-EMEA/H/C/002094/WS2178/ 0074/G
Foclivia-EMEA/H/C/001208/WS2178/ 0071/G
Seqirus S.r.l, Lead Rapporteur: Armando Genazzani

WS2180
Aprovel-EMEA/H/C/000141/WS2180 /0187
CoAprovel-EMEA/H/C/000222/WS2180/ 0206
Karvea-EMEA/H/C/000142/WS2180/0189
Karvezide-EMEA/H/C/000221/WS2180/ 0206
sanofi-aventis groupe, Lead Rapporteur: Maria Concepcion Prieto Yerro

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 - EMA 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. 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

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.1.1. List of procedures concluding at 11-14 October 2021 CHMP plenary:

G.1.2. List of procedures starting in October 2021 for November 2021 CHMP adoption of outcomes

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