24 April 2023
EMA/CHMP/57011/2023
Human Medicines Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 24-26 April 2023

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

24 April 2023, 09:00 – 19:30, virtual meeting/room 1C

25 April 2023, 08:30 – 19:30, virtual meeting/room 1C

26 April 2023, 08:30 – 19:00, 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).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Table of contents

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 24-26 April 2023. See April 2023 CHMP minutes (to be published post May 2023 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 24-26 April 2023.

1.3. Adoption of the minutes

CHMP minutes for 27-30 March 2023.

Minutes from PReparatory and Organisational Matters (PROM) meeting held on 17 April 2023.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. aripiprazole - EMEA/H/C/005929

Maintenance treatment of schizophrenia

Scope: Oral explanation

Action: Oral explanation to be held on 25 April 2023 at 14:00

List of Outstanding Issues adopted on 26.01.2023. List of Questions adopted on 13.10.2022.

2.1.2. gadopiclenol - EMEA/H/C/005626

for diagnostic: contrast-enhanced magnetic resonance imaging (MRI) to improve detection, visualisation and assist in characterisation of lesions in the central nervous system and in other body regions (including breast, liver and prostate).

Scope: Possible oral explanation

Action: Oral explanation to be held on 25 April 2023 at 11:00

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 23.06.2022.

2.1.3. gadopiclenol - EMEA/H/C/006172

for diagnostic: contrast-enhanced magnetic resonance imaging (MRI) to improve detection, visualisation and assist in characterisation of lesions in the central nervous system and in other body regions (including breast, liver and prostate).

Scope: Possible oral explanation

Action: Oral explanation to be held on 25 April 2023 at 11:00

List of Outstanding Issues adopted on 10.11.2022.

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

2.3.1. Opdivo - nivolumab - EMEA/H/C/003985/II/0117

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Martin Huber

Scope: "Extension of indication to include Opdivo in combination with platinum-based chemotherapy for neoadjuvant treatment of adult patients with resectable stage IB-IIIA non-small cell lung cancer (NSCLC), based on results from study CA209816; a randomised, open-label, phase 3 trial of nivolumab plus ipilimumab or nivolumab plus platinum-doublet chemotherapy versus platinum-doublet chemotherapy in early-stage NSCLC. 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 27.0 of the RMP has also been submitted."

Scope: Oral explanation

Action: Oral explanation to be held on 24 April 2023 at 14:00

Request for Supplementary Information adopted on 23.02.2023, 13.10.2022, 23.06.2022.

See 5.1

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. recombinant respiratory syncytial virus pre-fusion F protein, adjuvanted with AS01E - EMEA/H/C/006054

indicated for active immunisation for the prevention of lower respiratory tract disease (LRTD) caused by RSV

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.03.2023. List of Questions adopted on 24.01.2023.

3.1.2. glofitamab - Orphan - EMEA/H/C/005751

Roche Registration GmbH; treatment of diffuse large B-cell lymphoma

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 23.02.2023. List of Questions adopted on 15.09.2022.

3.1.3. pirtobrutinib - Orphan - EMEA/H/C/005863

Eli Lilly Nederland B.V.; treatment of mantle cell lymphoma (MCL)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 23.02.2023. List of Questions adopted on 13.10.2022.

3.1.4. lenadogene nolparvovec - Orphan - ATMP - EMEA/H/C/005047

GenSight Biologics S.A.; treatment of vision loss due to Leber Hereditary Optic Neuropathy (LHON)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 09.12.2022. List of Questions adopted on 19.02.2021.

3.1.5. futibatinib - Orphan - EMEA/H/C/005627

Taiho Pharma Netherlands B.V.; treatment of cholangiocarcinoma

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 23.02.2023. List of Questions adopted on 15.09.2022.

3.1.6. miglustat - EMEA/H/C/005695

treatment of adults aged 18 years and older with a confirmed diagnosis of Pompe disease

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 10.11.2022, 15.09.2022. List of Questions adopted on 24.03.2022.

3.1.7. sugammadex - EMEA/H/C/006083

Reversal of neuromuscular blockade induced by rocuronium or vecuronium in adults

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 30.03.2023. List of Questions adopted on 15.12.2022.

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

3.2.1. mavacamten - EMEA/H/C/005457

treatment of symptomatic obstructive hypertrophic cardiomyopathy

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 15.12.2022, 21.07.2022. List of Questions adopted on 27.01.2022.

3.2.2. degarelix acetate - EMEA/H/C/006048

treatment of prostate cancer

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 10.11.2022.

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 Outstanding Issues adopted on 27.01.2022, 16.12.2021, 14.10.2021. List of Questions adopted on 24.06.2021.

3.2.4. pegfilgrastim - EMEA/H/C/005587

treatment of neutropenia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 24.02.2022.

3.2.5. gefapixant - EMEA/H/C/005476

treatment of refractory or unexplained chronic cough

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 27.01.2022, 16.12.2021, 14.10.2021. List of Questions adopted on 24.06.2021.

3.2.6. natalizumab - EMEA/H/C/005752

Therapy for active relapsing remitting multiple sclerosis (RRMS)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 10.11.2022.

3.2.7. ganaxolone - Orphan - EMEA/H/C/005825

Marinus Pharmaceuticals Emerald Limited; treatment of epileptic seizures associated with cyclindependent kinase-like 5 deficiency disorder (CDD)

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 26.01.2023. List of Questions adopted on 25.01.2022.

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

3.3.1. respiratory syncytial virus vaccines - EMEA/H/C/006027

Accelerated assessment

prevention of respiratory tract disease

Scope: List of questions

Action: For adoption

3.3.2. azacitidine - EMEA/H/C/006154

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

Scope: List of questions

Action: For adoption

3.3.3. Zoonotic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted, prepared in cell cultures) - EMEA/H/C/006052

Active immunisation for the prevention of disease caused by the influenza A virus H5N1 subtype contained in the vaccine

Scope: List of questions

Action: For adoption

3.3.4. germanium (68ge) chloride / gallium (68ga) chloride - EMEA/H/C/006053

indicated for in vitro radiolabelling of specific carrier molecules to be used for positron emission tomography (PET) imaging

Scope: List of questions

Action: For adoption

3.3.5. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted, prepared in cell cultures) - EMEA/H/C/006051

Prophylaxis of influenza

Scope: List of questions

Action: For adoption

3.3.6. omecamtiv mecarbil - EMEA/H/C/006112

treatment of adult patients with symptomatic chronic heart failure and reduced ejection fraction less than 30%

Scope: List of questions

Action: For adoption

3.3.7. bevacizumab - EMEA/H/C/005723

Treatment of neovascular (wet) age-related macular degeneration (nAMD).

Scope: List of questions

Action: For adoption

3.3.8. nintedanib - EMEA/H/C/006179

treatment of idiopathic pulmonary fibrosis (IPF), chronic fibrosing interstitial lung diseases (ILDs) and lung diseases (ILDs) systemic sclerosis associated interstitial lung disease (SSc-ILD)

Scope: List of questions

Action: For adoption

3.3.9. omaveloxolone - Orphan - EMEA/H/C/006084

Reata Ireland Limited; Treatment of Friedreich's ataxia

Scope: List of questions

Action: For adoption

3.3.10. talquetamab - PRIME - Orphan - EMEA/H/C/005864

Accelerated assessment

Janssen-Cilag International N.V.; monotherapy treatment of adult patients with relapsed and refractory multiple myeloma

Scope: List of questions

Action: For adoption

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

No items

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

3.5.1. Sohonos - palovarotene - Orphan - EMEA/H/C/004867

Ipsen Pharma; treatment of fibrodysplasia ossificans progressiva

Scope: List of questions for an ad-hoc expert group; draft list of experts for the AHEG

Action: For adoption

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

Opinion adopted on 26.01.2023. List of Outstanding Issues adopted on 15.09.2022. List of Questions adopted on 16.09.2021.

3.5.2. Lagevrio - molnupiravir - EMEA/H/C/005789

Merck Sharp & Dohme B.V.; treatment of coronavirus disease 2019 (COVID-19)

Scope: Re-examination timetable

Action: For adoption

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

Opinion adopted on 23.02.2023. List of Outstanding Issues adopted on 22.04.2022. List of Questions adopted on 24.02.2022, 16.12.2021.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. ivosidenib - Orphan - EMEA/H/C/006174

Les Laboratoires Servier; treatment of acute myeloid leukaemia

Scope: Withdrawal of marketing authorisation application

Action: For information

Opinion adopted on 23.02.2023. List of Outstanding Issues adopted on 15.12.2022. List of Questions adopted on 21.07.2022.

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. Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/X/0078/G

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Armando Genazzani, Co-Rapporteur: Finbarr Leacy, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Extension application to add a new strength of 75 mg of lumacaftor and 94 mg of ivacaftor fixed dose combination granules, grouped with a type II variation (C.I.6.a).

C.I.6: Extension of indication to include treatment of cystic fibrosis for children aged 1 to less than 2 years of age who are homozygous for the F508del mutation in the CFTR gene, based on final results from study 122, a 2-part study of CF subjects 1 to <2 years of age homozygous for F508del. As a consequence, sections 4.1, 4.2, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 11.2 of the RMP has also been submitted."

Action: For adoption

List of Outstanding Issues adopted on 23.02.2023. List of Questions adopted on 13.10.2022.

4.1.2. Tenkasi - oritavancin - EMEA/H/C/003785/X/0036

Menarini International Operations Luxembourg S.A.

Rapporteur: Janet Koenig, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension application to add a new strength of 1200 mg for powder for concentrate for solution for infusion. The RMP (version 4) is updated in accordance."

Action: For adoption

List of Outstanding Issues adopted on 23.02.2023. List of Questions adopted on 21.07.2022.

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

No items

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

4.3.1. Azacitidine Accord - azacitidine - EMEA/H/C/005147/X/0013

Accord Healthcare S.L.U.

Rapporteur: Hrefna Gudmundsdottir, PRAC Rapporteur: Menno van der Elst

Scope: "Extension application to introduce a new pharmaceutical form associated with a new strength (10 mg/ml powder for solution for infusion) and a new route of administration (intravenous use). The RMP version 2 is updated in accordance."

Action: For adoption

4.3.2. Entyvio - vedolizumab - EMEA/H/C/002782/X/0075

Takeda Pharma A/S

Rapporteur: Armando Genazzani

Scope: quality variation

Action: For adoption

4.3.3. Kaftrio - ivacaftor / tezacaftor / elexacaftor - Orphan - EMEA/H/C/005269/X/0033

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber

Scope: "Extension application to add a new pharmaceutical form (granules) associated with 2 new strengths (60 mg/40 mg/80 mg and 75 mg/50 mg/100 mg) to support a new indication in a combination regimen with ivacaftor for the treatment of cystic fibrosis (CF) in paediatric patients aged 2 to less than 6 years who have at least one F508del mutation in the CFTR gene. The new indication is only applicable to the new granules pharmaceutical form. As a consequence of the line extension, the PI for the film coated tablets is also updated to reflect the addition of a new pharmaceutical form.
The RMP (version 6.2) has also been submitted."

Action: For adoption

4.3.4. Kalydeco - ivacaftor - EMEA/H/C/002494/X/0114/G

Vertex Pharmaceuticals (Ireland) Limited

Co-Rapporteur: Beata Maria Jakline Ullrich, PRAC Rapporteur: Monica Martinez Redondo

Scope: "Extension application to add a new strength (59.5 mg) of the granules pharmaceutical form grouped with C.I.6.a, to support a new indication in a combination regimen with ivacaftor/tezacaftor/elexacaftor for the treatment of cystic fibrosis (CF) in paediatric patients aged 2 to less than 6 years who have at least one F508del mutation in the CFTR gene (see section 5.1). The RMP (version 15.1) has also been submitted.
Type IB B.II.f.1.b
The Product information has been updated accordingly."

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. Adempas - riociguat - EMEA/H/C/002737/II/0037

Bayer AG

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension of indication to include treatment of pulmonary arterial hypertension (PAH) in paediatric patients aged 6 to less than 18 years of age with WHO Functional Class (FC) I to III in combination with endothelin receptor antagonists with or without prostanoids for Adempas, based on results from pivotal study PATENT-CHILD (study 15681); this is a Phase III, Open-label, individual dose titration study to evaluate safety, tolerability and pharmacokinetics of riociguat in children from 6 to less than 18 years of age with PAH; As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 8.1 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

Request for Supplementary Information adopted on 15.12.2022.

5.1.2. Ayvakit - avapritinib - Orphan - EMEA/H/C/005208/II/0023

Blueprint Medicines (Netherlands) B.V.

Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include treatment of adult patients with indolent systemic mastocytosis (ISM) for avapritinib based on results from the pivotal part of study BLU-285-2203 (PIONEER), this is a 3-part, randomized, double-blind, placebo-controlled, Phase 2 study to evaluate safety and efficacy of avapritinib (BLU-285) in indolent and smoldering systemic mastocytosis with symptoms inadequately controlled with standard therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.0 of the RMP has also been submitted."

Action: For adoption

5.1.3. Bimzelx - bimekizumab - EMEA/H/C/005316/II/0010

UCB Pharma S.A.

Rapporteur: Finbarr Leacy, Co-Rapporteur: Christophe Focke, PRAC Rapporteur: Liana

Gross-Martirosyan

Scope: "Extension of indication to include treatment of adults with active axial spondyloarthritis (axSpA), including non-radiographic axial spondyloarthritis (nr-axSpA) and ankylosing spondylitis (AS, radiographic axial spondyloarthritis), based on interim results from two interventional and controlled phase III clinical studies: AS0010 (BE MOBILE 1) and AS0011 (BE MOBILE 2), which provide evidence of the efficacy and safety of bimekizumab in axSpA (nr-axSpA and AS), both compared to placebo treatment. Further supportive data is provided by the results of a phase 2a exploratory study (AS0013), a phase 2b, dose-ranging study (AS0008) and its ongoing follow-on phase 2b open-label extension (OLE) study (AS0009). 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 1.2 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

Request for Supplementary Information adopted on 30.03.2023, 15.12.2022.

5.1.4. Bimzelx - bimekizumab - EMEA/H/C/005316/II/0011

UCB Pharma S.A.

Rapporteur: Finbarr Leacy, Co-Rapporteur: Christophe Focke, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Extension of indication to include treatment of active psoriatic arthritis in adult patients who have had an inadequate response or who have been intolerant to one or more DMARDs for BIMZELX, based on interim results of a Phase III study in biological DMARD naïve study participants (PA0010; BE OPTIMAL) and the final results of the Phase III study in study participants who are inadequate responders (inadequate response or intolerant) to ≤2 prior TNF inhibitors (PA0011; BE COMPLETE). Both Phase III studies are interventional studies aimed to evaluate the efficacy and safety of bimekizumab. For PA0010, the Initial Treatment Period was placebo- and no inferential active reference (adalimumab)-controlled, while PA0011 was placebo-controlled. Further supportive data comprise the results of a Phase 1 study (PA0007), a Phase 2b dose-finding study (PA0008) and a Phase 2 open label extension study (PA0009). A Phase 3 open-label extension study is currently ongoing (PA0012). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 to the SmPC have been updated. The package leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.2 rev.1. As part of the application the MAH is requesting a 1-year extension of the market protection.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 30.03.2023, 15.12.2022.

5.1.5. Cosentyx - secukinumab - EMEA/H/C/003729/II/0090

Novartis Europharm Limited

Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Monica Martinez Redondo

Scope: "Extension of indication to include treatment of Hidradenitis Suppurativa (HS) for Cosentyx, based on interim results from two Phase III studies CAIN457M2301 (SUNSHINE) and CAIN457M2302 (SUNRISE); These studies are ongoing, multi-center, randomized, double-blind, placebo-controlled, parallel group Phase 3 studies conducted to assess the short (16 weeks) and long-term (up to 52 weeks) efficacy and safety of two secukinumab dose regimens (Q2W or Q4W) compared to placebo in adult subjects with moderate to severe HS; 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 11 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 30.03.2023, 15.12.2022, 15.09.2022.

5.1.6. Epidyolex - cannabidiol - Orphan - EMEA/H/C/004675/II/0020

GW Pharma (International) B.V.

Rapporteur: Thalia Marie Estrup Blicher, Co-Rapporteur: Tomas Radimersky, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "Extension of indication to include treatment with Epidyolex (monotherapy) as adjunctive therapy of seizures associated with Lennox Gastaut syndrome (LGS) or Dravet syndrome (DS) for patients 2 years of age and older (without the restriction for use only in conjunction with clobazam), based on the previously generated data in patients treated without CLB in the LGS and DS pivotal studies re-evaluated in the context of the more recent evidence from study GWEP1521 in tuberous sclerosis complex (TSC). As a consequence, sections 4.1, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement editorial changes in the product information. Version 2.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 30.03.2023, 15.12.2022, 15.09.2022.

5.1.7. Ervebo - recombinant vesicular stomatitis virus - Zaire Ebolavirus vaccine (live) - EMEA/H/C/004554/II/0025

Merck Sharp & Dohme B.V.

Rapporteur: Christophe Focke, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include the paediatric population from 1 year to less than 18 years of age based on final results from study V920-016 (PREVAC); this is a phase 2, randomized, double-blind, placebo-controlled study of 2 leading Ebola vaccine candidates (Ad26.ZEBOV/MVA-BN-Filo and V920) and 3 vaccine strategies (Ad26.ZEBOV/MVABN-Filo, 1-dose V920, and 2 dose V920) to evaluate immunogenicity and safety in healthy children and adolescents from 1 to 17 years of age and adults 18 years of age and older. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.2 of the RMP has also been submitted. In addition, the MAH took the opportunity to update the Annex II and the list of local representatives in the Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 10.11.2022.

5.1.8. Iclusig - ponatinib - Orphan - EMEA/H/C/002695/II/0064

Incyte Biosciences Distribution B.V.

Rapporteur: Filip Josephson, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include treatment of newly diagnosed adult patients with Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL), either with Iclusig (ponatinib) in combination with chemotherapy, or with Iclusig (ponatinib) monotherapy after corticosteroid induction in patients not eligible to receive chemotherapy-based regimens, based on final results from studies AP24534-11-001 and INCB 84344-201. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 22 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 10.11.2022.

5.1.9. Jardiance - empagliflozin - EMEA/H/C/002677/II/0076

Boehringer Ingelheim International GmbH

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Maria del Pilar Rayon

Scope: "Extension of indication for Jardiance to include treatment of children aged 10 years and above with type 2 diabetes based on results from study DINAMO 1218-0091; this is a double-blind, randomised, placebo-controlled, parallel group trial to evaluate the efficacy and safety of empagliflozin and linagliptin over 26 weeks, with a double-blind active treatment safety extension period up to 52 weeks, in children and adolescents with type 2 diabetes mellitus. 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 21.0 of the RMP has also been submitted."

Action: For adoption

5.1.10. Moventig - naloxegol - EMEA/H/C/002810/II/0039

Kyowa Kirin Holdings B.V.

Rapporteur: Christophe Focke, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Update of sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to update information regarding the use of naloxegol in OIC patients with cancer-related pain based on real-world data from non-interventional studies (NACASY, KYONAL, and MOVE studies), post-marketing data, and literature. The Package Leaflet is updated accordingly. The RMP version 8 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the SmPC."

Action: For adoption

5.1.11. Opdivo - nivolumab - EMEA/H/C/003985/II/0117

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Martin Huber

Scope: "Extension of indication to include Opdivo in combination with platinum-based chemotherapy for neoadjuvant treatment of adult patients with resectable stage IB-IIIA non-small cell lung cancer (NSCLC), based on results from study CA209816; a randomised, open-label, phase 3 trial of nivolumab plus ipilimumab or nivolumab plus platinum-doublet chemotherapy versus platinum-doublet chemotherapy in early-stage NSCLC. 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 27.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 23.02.2023, 13.10.2022, 23.06.2022.

See 2.3

5.1.12. Opdivo - nivolumab - EMEA/H/C/003985/II/0125/G

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Martin Huber

Scope: "Extension of indication to include adolescent patients aged 12 years and older in treatment of advanced (unresectable or metastatic) melanoma (nivolumab monotherapy), treatment of advanced (unresectable or metastatic) melanoma (nivolumab in combination with ipilimumab) and adjuvant treatment of melanoma (nivolumab monotherapy) for Opdivo, based on results from a nonclinical biomarker study (Expression of PD-L1 (CD274), and characterization of tumour infiltrating immune cells in tumours of paediatric origin), also based on results from a Phase 1/2 clinical study (CA209070, A Phase 1/2 Study of Nivolumab (Ind# 124729) In Children, Adolescents, And Young Adults With Recurrent Or Refractory Solid Tumors As A Single Agent And In Combination With Ipilimumab) and a modelling and simulation study. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 30.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 15.12.2022.

5.1.13. Revestive - teduglutide - Orphan - EMEA/H/C/002345/II/0054/G

Takeda Pharmaceuticals International AG Ireland Branch

Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: "Extension of indication to include patients from 4 months corrected gestational aged 1 year and above. Consequently sections 4.1, 4.2, 4.8, 5.1 and 5.2 are updated. The package leaflet is updated accordingly.
Update of annex II to amend the date of completion of the post authorisation study. The MAH took the opportunity to also amend local representatives."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2022, 22.04.2022, 11.11.2021.

5.1.14. RoActemra - tocilizumab - EMEA/H/C/000955/II/0114

Roche Registration GmbH

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Gabriele Maurer

Scope: "Extension of indication to include treatment of new indication for slowing the rate of decline in pulmonary function in adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) for RoActemra, based on final results from study the pivotal Phase III study WA29767 (focuSSced) entitled, "A Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Assess the Efficacy and Safety of Tocilizumab Versus Placebo in Patients With Systemic Sclerosis" and the supportive Phase II/III study WA27788 (faSScinate) entitled, "A Phase II/III, Multicenter, Randomized, Double-blind, Placebo-controlled Study To Assess The Efficacy And Safety Of Tocilizumab Versus Placebo In Patients With Systemic Sclerosis".
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 28 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 15.12.2022.

5.1.15. Ronapreve - casirivimab / imdevimab - EMEA/H/C/005814/II/0002

Roche Registration GmbH

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include treatment of COVID-19 in hospitalised patients in adults and adolescents aged 12 years and older weighing at least 40 kg for Ronapreve; as a consequence, sections 4.2, 4.4, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and Labelling are 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 23.02.2023, 13.10.2022, 19.05.2022.

5.1.16. Spikevax - elasomeran - EMEA/H/C/005791/II/0097/G

Moderna Biotech Spain, S.L.

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: "Grouped variation:
- C.I.6.a (Type II): Extension of indication to include a 25 µg booster dose of Spikevax bivalent Original/Omicron BA.4-5 (12.5 µg elasomeran /12.5 µg davesomeran) in children aged 6 through 11 years of age; as a consequence, sections 2, 4.1, 4.2, 4.4 and 6.6 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version

6.5 of the RMP has also been submitted.
- C.I.z (Type II): Update of sections 4.8 and 5.1 of the Spikevax bivalent Original/Omicron BA.1 SmPC to add median follow-up period and D91 persistence data, based on Parts F and G (mRNA- 1273.214) of study mRNA-1273-P205 (NCT04927065), an open-label Phase 2/3 study evaluating the immunogenicity and safety of variant-targeting booster candidate vaccines. The Package Leaflet is updated accordingly.
- C.I.z (Type II): To update sections 4.8 and 5.1 of the Spikevax bivalent Original/Omicron BA.4-5 SmPC to add ADR details and clinical data, based on Part H (mRNA- 1273.222) of study mRNA-1273-P205 (NCT04927065), an open-label Phase 2/3 study evaluating the immunogenicity and safety of variant-targeting booster candidate vaccines.
In addition, the marketing authorisation holder took the opportunity to implement a number of editorial changes to the product information."

Action: For adoption

5.1.17. Vemlidy - tenofovir alafenamide - EMEA/H/C/004169/II/0040

Gilead Sciences Ireland UC

Rapporteur: Janet Koenig, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Valentina Di Giovanni

Scope: "Extension of indication to include treatment of chronic hepatitis B-infected children from 6 years and older and weighing at least 25 kilograms for Vemlidy, based on the interim results from Week 24 clinical study report (CSR) for Cohort 1 and Cohort 2 Group 1 and supporting modular summaries for the category 3 study GS-US-320-1092, 'A Randomized, Double-Blind Evaluation of the Pharmacokinetics, Safety, and Antiviral Efficacy of Tenofovir Alafenamide (TAF) in Children and Adolescent Subjects with Chronic Hepatitis B Virus Infection'. 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.
In addition, the MAH took the opportunity to update the wording in section 4.6 of the SmPC related to breastfeeding and pregnancies exposed to TAF, and to update the contact details of the local representative in Romania in the Package Leaflet.
An updated RMP version 8.2 has been provided."

Action: For adoption

Request for Supplementary Information adopted on 26.01.2023, 15.09.2022.

5.1.18. Xromi - hydroxycarbamide - EMEA/H/C/004837/II/0019

Nova Laboratories Ireland Limited

Rapporteur: Anastasia Mountaki, Co-Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Jo Robays

Scope: "Extension of indication to include the prevention of vaso-occlusive complications of sickle cell disease in children from 6 months to 2 years of age for Xromi, based on final results from the paediatric study INV543, listed as a category 3 study in the RMP; this is a single-arm, open-label, multi-center study in children with sickle cell anaemia over 6 months of age. 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 4.1 of the RMP has also been submitted."

Action: For adoption

5.1.19. Yervoy - ipilimumab - EMEA/H/C/002213/II/0100

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include in combination with nivolumab the treatment of adolescents (12 years of age and older) for advanced (unresectable or metastatic) melanoma, based on the pivotal study CA209070; this is a multicentre, open-label, single arm, phase 1/2 trial of nivolumab +/- ipilimumab in children, adolescents and young adults with recurrent or refractory solid tumours or lymphomas. 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 38.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 15.12.2022.

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

No items

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

No items

6. Medical devices

6.1. Ancillary medicinal substances - initial consultation

6.1.1. human albumin solution / gentamicin sulfate - EMEA/H/D/006141

human assisted reproductive techniques including in-vitro fertilisation procedures

Scope: Opinion

Action: For adoption

List of Questions adopted on 10.11.2022.

6.1.2. gentamicin sulfate / sargramostim / heparin sodium / insulin human - EMEA/H/D/006090

human assisted reproductive techniques including in-vitro fertilisation procedures

Scope: Request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted in March 2023.

Action: For adoption

List of Outstanding Issues adopted on 30.03.2023. List of Questions adopted on 13.10.2022.

6.2. Ancillary medicinal substances – post-consultation update

No items

6.3. Companion diagnostics - initial consultation

6.3.1. in vitro diagnostic medical device - EMEA/H/D/006255

is indicated as an aid in the selection of adult haemophilia A patients for whom valoctocogene roxaparvovec treatment is being considered

Scope: Request for supplementary information

Action: For information

6.3.2. in vitro diagnostic medical device - EMEA/H/D/006233

To determine HER2 (Human Epidermal Growth Factor Receptor 2) oncoprotein status

Scope: Opinion

Action: For adoption

Request for supplementary information adopted on 30.03.2023.

6.4. Companion diagnostics – follow-up consultation

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

8.2. Priority Medicines (PRIME)

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. Qarziba - dinutuximab beta - EMEA/H/C/003918/II/0043, Orphan

EUSA Pharma (Netherlands) B.V.

Rapporteur: Johann Lodewijk Hillege

Scope: "Update of sections 4.1, 4.2 and 5.1 of the SmPC based on final results from study APN311-202V3 listed as a Specific Obligation in the Annex II of the Product Information. This is a Phase I/II dose schedule finding study of Ch14.18/CHO continuous infusion combined with subcutaneous aldesleukin (IL-2) in patients with primary refractory or relapsed neuroblastoma. In addition, the MAH took the opportunity to update Annex II section E. The Package Leaflet is updated accordingly."

Action: For information

Request for Supplementary Information adopted on 15.09.2022.

9.1.2. Inpremzia - insulin human (rDNA) - EMEA/H/C/005331

Baxter Holding B.V.; treatment of patients with diabetes mellitus who require intravenous insulin

Rapporteur: Christian Gartner, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Withdrawal of marketing authorisation

Action: For information

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

9.1.3. Hepcludex - bulevirtide - EMEA/H/C/004854/II/0019, Orphan

Gilead Sciences Ireland Unlimited Company

Rapporteur: Filip Josephson

Scope: "Update of sections 4.8 and 5.1 of the SmPC in order to update the list of adverse drug reactions (ADRs) and efficacy information based on interim results from study MYR301 listed as a Specific Obligation in the Annex II of the Product Information; this is a Multicenter, Open-label, Randomized Phase III Clinical Study to Assess Efficacy and Safety of Bulevirtide in Patients with Chronic Hepatitis Delta. Consequently, the MAH proposes a switch from conditional marketing authorisation to full marketing authorisation given the fulfilment of the SOB. The Package Leaflet is updated accordingly.
In addition, the MAH took the opportunity to implement editorial changes in the SmPC."

Action: For adoption

Request for Supplementary Information adopted on 15.12.2022.

9.1.4. Ofev - nintedanib - EMEA/H/C/003821/X/0052/G

Boehringer Ingelheim International GmbH

Rapporteur: Finbarr Leacy, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Type II variation - update of SmPC sections 4.2, 5.1 and 5.2 (former line extension with extension of indication in children 6 to 17 years old)."

Action: For adoption

List of Questions adopted on 26.01.2023.

9.1.5. Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0033

AstraZeneca AB

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

Scope: "Update of section 5.1 of the SmPC based on interim results from the PK/PD study listed as a specific obligation in the Annex II in order to fulfil SOB 1 and SOB 3; this is a PK and PK/PD Analysis of Intravenously Administered Andexanet after dosing to steady state with a factor Xa inhibitor, rivaroxaban or Apixaban, in healthy subjects and patients who have acute major bleeding. In addition, the MAH took the opportunity to implement editorial changes in Annex II of the SmPC. The RMP version 3.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 26.01.2023, 13.10.2022.

9.1.6. Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0056

Orexigen Therapeutics Ireland Limited

Re-examination Rapporteur: TBC

Scope: Request for re-examination, appointment of re-examination rapporteur

Action: For adoption

Opinion adopted on 30.03.2023. Request for Supplementary Information adopted on 26.01.2023, 15.09.2022, 24.03.2022.

10. Referral procedures

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

10.1.1. Adakveo - crizanlizumab - Orphan - EMEA/H/C/004874

Novartis Europharm Limited

Referral Rapporteur: Daniela Philadelphy, Referral Co-Rapporteur: Johanna Lähteenvuo

Scope: The European Commission (EC) initiated a procedure under Article 20 of Regulation (EC) No 726/2004 and requested the Agency/CHMP to assess the benefit-risk balance of the centrally authorised medicinal product Adakveo (crizanlizumab) in its approved indication. In addition, the EC requested the Agency/CHMP to considered as soon as possible whether temporary measures were necessary to protect public health.

The initiation of the review follows preliminary results from the Phase III study (CSEG101A2301, STAND) which is a specific obligation to the conditional marketing authorisation for Adakveo. The preliminary results for STAND study show no superiority of crizanlizumab over placebo in annualised rates of vaso-occlusive crises leading to a healthcare visit over the first-year post randomisation.

Action: For adoption

List of questions adopted on 26.01.2023.

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

10.2.1. Colistimethate sodium (CMS) – EMEA/H/A-5(3)/1524

Various MAHs

Referral Rapporteur: Martina Weise, Referral Co-Rapporteur: Ewa Balkowiec Iskra

Scope: revised timetable

Review of the ratio of polymyxins E1 and E2 in colistin starting material and of the

(sulfomethylation) composition profile of CMS finished product.

Action: For adoption

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

No items

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

No items

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

No items

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

No items

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

April 2023 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. Vote by proxy

No topics

14.1.2. CHMP membership

No items

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 April 2023

Action: For adoption

14.2.2. Paediatric Committee (PDCO)

Draft agenda for the April 2023 PDCO meeting

Action: For information

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

14.3.1. Biologics Working Party (BWP)

Chair: Sean Barry

Reports from BWP April 2023 meeting to CHMP for adoption:

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

Action: For adoption

14.3.2. Election of Vice-Chairperson – Biologics Working Party

A call for nominations was launched at the March 2023 PROM meeting.

Nomination(s) received

Action: For election

14.3.3. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 26 April 2023.

Action: For adoption

14.3.4. Scientific Advice Working Party (SAWP)

Chair: Paolo Foggi

Report from the SAWP meeting held on 11-14 April 2023. Table of conclusions

Action: For information

Scientific advice letters:

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

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

No items

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)*

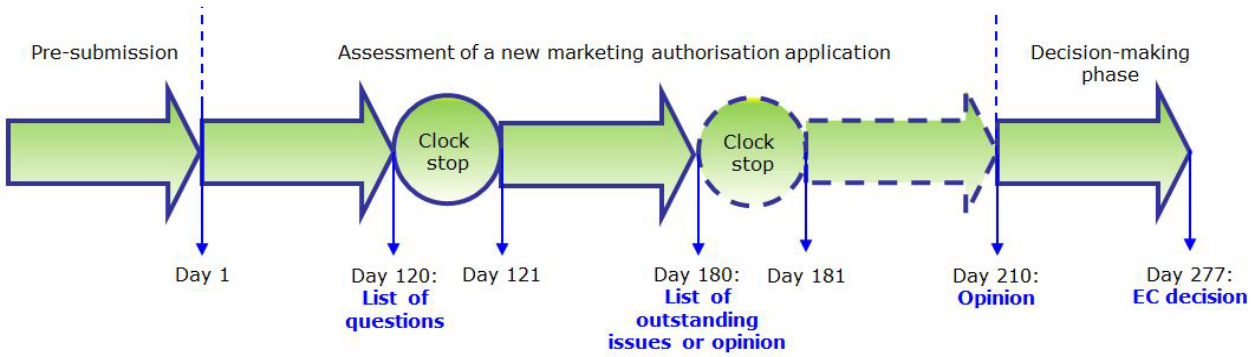
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

24 April 2023
EMA/CHMP/57013/2023

Annex to 24-26 April 2023 CHMP Agenda

Pre-submission and post-authorisations issues

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

A. PRE-SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for April 2023: **For adoption**

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

Final Outcome of Rapporteurship allocation for April 2023: **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

Ceplene - histamine dihydrochloride - EMEA/H/C/000796/S/0045
Laboratoires Delbert, Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald

ELZONRIS - tagraxofusp - EMEA/H/C/005031/S/0020, Orphan
Stemline Therapeutics B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst

SCENESSE - afamelanotide - EMEA/H/C/002548/S/0045, Orphan
Clinuvel Europe Limited, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Kigabeq - vigabatrin - EMEA/H/C/004534/R/0012
ORPHELIA Pharma SAS, Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Kirsti Villikka
Request for Supplementary Information adopted on 30.03.2023.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Braftovi - encorafenib -
EMEA/H/C/004580/R/0029
Pierre Fabre Medicament, Rapporteur: Janet Koenig, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Rugile Pilviniene
Request for Supplementary Information adopted on 23.02.2023.

Buvidal - buprenorphine -
EMEA/H/C/004651/R/0021
Camurus AB, Rapporteur: Finbarr Leacy, PRAC Rapporteur: Tiphaine Vaillant

Deferiprone Lipomed - deferiprone -
EMEA/H/C/004710/R/0011
Lipomed GmbH, Generic, Generic of Ferriprox, Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Tiphaine Vaillant
Request for Supplementary Information adopted on 23.02.2023.

Delstrigo - doravirine / lamivudine / tenofovir disoproxil -
EMEA/H/C/004746/R/0034
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ana Sofia Diniz Martins

Gefitinib Mylan - gefitinib -
EMEA/H/C/004826/R/0008
Mylan Pharmaceuticals Limited, Generic, Generic of Iressa, Rapporteur: Margareta Bego, PRAC Rapporteur: Ulla Wändel Liminga

Jivi - damoctocog alfa pegol -
EMEA/H/C/004054/R/0027
Bayer AG, Rapporteur: Thalia Marie Estrup Blicher, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Menno van der Elst

Lenalidomide Accord - lenalidomide -
EMEA/H/C/004857/R/0021
Accord Healthcare S.L.U., Generic, Generic of Revlimid, Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Tiphaine Vaillant

Mektovi - binimetinib -
EMEA/H/C/004579/R/0024
Pierre Fabre Medicament, Rapporteur: Janet Koenig, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Inês Ribeiro-Vaz

Request for Supplementary Information adopted on 23.02.2023.

Pelgraz - pegfilgrastim - EMEA/H/C/003961/R/0040
Accord Healthcare S.L.U., Rapporteur: Sol Ruiz, Co-Rapporteur: Petr Vrbata, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 30.03.2023.

Pifeltro - doravirine - EMEA/H/C/004747/R/0027
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ana Sofia Diniz Martins

Venclyxto - venetoclax - EMEA/H/C/004106/R/0046
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva Jirsová

Verzenios - abemaciclib - EMEA/H/C/004302/R/0025
Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Inês Ribeiro-Vaz
Request for Supplementary Information adopted on 30.03.2023.

VEYVONDI - vonicog alfa - EMEA/H/C/004454/R/0027
Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Mari Thorn
Request for Supplementary Information adopted on 23.02.2023.

Ziextenzo - pegfilgrastim - EMEA/H/C/004802/R/0025
Sandoz GmbH, Rapporteur: Christian Gartner, Co-Rapporteur: Simona Badoi, PRAC Rapporteur: Menno van der Elst

B.2.3. Renewals of Conditional Marketing Authorisations

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/R/0029, Orphan, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur:

Rune Kjeken, Co-Rapporteur: Heli Suila, CHMP Coordinator: Ingrid Wang, PRAC Rapporteur: Ulla Wändel Liminga	
Blenrep - belantamab mafodotin - EMEA/H/C/004935/R/0017, Orphan GlaxoSmithKline (Ireland) Limited, Rapporteur: Johanna Lähteenvuo, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Ulla Wändel Liminga	
Dovprela - pretomanid - EMEA/H/C/005167/R/0015, Orphan Mylan IRE Healthcare Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Liana Gross-Martirosyan	
Hepcludex - bulevirtide - EMEA/H/C/004854/R/0024, Orphan Gilead Sciences Ireland Unlimited Company, Rapporteur: Filip Josephson, PRAC Rapporteur: Adam Przybylkowski	
Idefirix - imlifidase - EMEA/H/C/004849/R/0014, Orphan Hansa Biopharma AB, Rapporteur: Martina Weise, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst	
ROCTAVIAN - valoctocogene roxaparvovec - EMEA/H/C/005830/R/0003, Orphan, ATMP BioMarin International Limited, Rapporteur: Violaine Closson Carella, Co-Rapporteur: Silke Dorner, CHMP Coordinator: Jean-Michel Race, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 21.04.2023.	Request for supplementary adopted with a specific timetable.
Rozlytrek - entrectinib - EMEA/H/C/004936/R/0015 Roche Registration GmbH, Rapporteur: Armando Genazzani, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 30.03.2023.	

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 11-14 April 2023 PRAC:

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its April 2023 meeting:

EMEA/H/C/PSUSA/00009329/202208
(vemurafenib)
CAPS:
Zelboraf (EMEA/H/C/002409) (vemurafenib), Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "17/08/2019 To: 16/08/2022"

EMEA/H/C/PSUSA/00010055/202209
(alemtuzumab)
CAPS:
Lemtrada (EMEA/H/C/003718) (alemtuzumab), Sanofi Belgium, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Anette Kirstine Stark, "12/09/2021 To: 12/09/2022"

EMEA/H/C/PSUSA/00010118/202209
(midazolam (oromucosal solution, treatment of prolonged, acute, convulsive seizures))
CAPS:
BUCCOLAM (EMEA/H/C/002267) (midazolam), Laboratorios Lesvi S.L., Rapporteur: Johann Lodewijk Hillege
NAPS:
NAPs - EU
PRAC Rapporteur: Liana Gross-Martirosyan, "09/09/2019 To: 09/09/2022"

EMEA/H/C/PSUSA/00010366/202209
(naltrexone / bupropion)
CAPS:
Mysimba (EMEA/H/C/003687) (naltrexone hydrochloride / bupropion hydrochloride), Orexigen Therapeutics Ireland Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, "09/09/2021 To: 09/09/2022"

EMEA/H/C/PSUSA/00010780/202209
(cemiplimab)
CAPS:
LIBTAYO (EMEA/H/C/004844) (cemiplimab),

Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Menno van der Elst, "28/09/2021To: 27/09/2022"

EMEA/H/C/PSUSA/00010880/202209
(bupivacaine/meloxicam)
CAPS:
ZYNRELEF (EMEA/H/C/005205) (bupivacaine / meloxicam), Heron Therapeutics, B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Liana Gross-Martirosyan, "24/03/2022 To: 23/09/2022"

EMEA/H/C/PSUSA/00010882/202209
(amikacin (centrally authorised product only))
CAPS:
ARIKAYCE liposomal (EMEA/H/C/005264) (amikacin), Insmed Netherlands B.V., Rapporteur: Jayne Crowe, PRAC Rapporteur: Jean-Michel Dogné, "28/09/2021 To: 27/09/2022"

EMEA/H/C/PSUSA/00010940/202209
(ponesimod)
CAPS:
PONVORY (EMEA/H/C/005163) (ponesimod), Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Anette Kirstine Stark, "18/03/2022 To: 17/09/2022"

EMEA/H/C/PSUSA/00010954/202209
(idecabtagene vicleucel)
CAPS:
Abecma (EMEA/H/C/004662) (idecabtagene vicleucel), Bristol-Myers Squibb Pharma EEIG, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang, PRAC Rapporteur: Ulla Wändel Liminga, "26/03/2022 To: 25/09/2022"

EMEA/H/C/PSUSA/00010961/202209
(pralsetinib)
CAPS:
GAVRETO (EMEA/H/C/005413) (pralsetinib), Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Ulla Wändel Liminga, "05/03/2022To: 03/09/2022"

B.4. EPARs / WPARs

BIMERVAX - sars-cov-2 virus, variants b.1.351-b.1.1.7, spike protein, receptor	For information only. Comments can be sent to

binding domain fusion heterodimer - EMEA/H/C/006058 Hipra Human Health S.L., immunisation to prevent COVID-19 caused by SARS-CoV-2, New active substance (Article 8(3) of Directive No 2001/83/EC)	the PL in case necessary.
Briumvi - ublituximab - EMEA/H/C/005914 Propharma Group The Netherlands B.V., treatment of relapsing forms of multiple sclerosis (RMS), 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.
Dabigatran Etexilate Accord - dabigatran etexilate - EMEA/H/C/005639 Accord Healthcare S.L.U., prevention of venous thromboembolic events, Generic, Generic of Pradaxa, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Epysqli - eculizumab - EMEA/H/C/006036 Samsung Bioepis NL B.V., treatment of paroxysmal nocturnal haemoglobinuria, 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.
Lacosamide Adroiq - lacosamide - EMEA/H/C/006047 Extrovis EU Ltd., treatment of epilepsy, Generic, Generic of Vimpat, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Omvoh - mirikizumab - EMEA/H/C/005122 Eli Lilly Nederland B.V., treatment of moderately to severely active ulcerative colitis, 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.
Pedmarqsi - sodium thiosulfate - EMEA/H/C/005130, PUMA Fennec Pharmaceuticals (EU) Limited, for the prevention of ototoxicity induced by cisplatin (CIS) chemotherapy in patients 1 month to < 18 years of age with localized, non-metastatic, solid tumours., 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.
Qaialdo - spironolactone - EMEA/H/C/005535 Nova Laboratories Ireland Limited, management of refractory oedema, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Sugammadex Adroiq - sugammadex -	For information only. Comments can be sent to

EMEA/H/C/006046 Extrovis EU Ltd., reversal of neuromuscular blockade induced by rocuronium or vecuronium, Generic, Generic of Bridion, Generic application (Article 10(1) of Directive No 2001/83/EC)	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

Advate - octocog alfa - EMEA/H/C/000520/II/0119/G Takeda Manufacturing Austria AG, Rapporteur: Jan Mueller-Berghaus	
Bexsero - meningococcal group B vaccine (recombinant, component, adsorbed) - EMEA/H/C/002333/II/0118 GSK Vaccines S.r.l, Rapporteur: Filip Josephson Opinion adopted on 14.04.2023.	Positive Opinion adopted by consensus on 14.04.2023.
Grepid - clopidogrel - EMEA/H/C/001059/II/0054 Pharmathen S.A., Generic, Generic of Plavix, Rapporteur: Kristina Nadrah Request for Supplementary Information adopted on 26.01.2023, 15.09.2022.	
Idefirix - imlifidase - EMEA/H/C/004849/II/0013, Orphan Hansa Biopharma AB, Rapporteur: Martina Weise Opinion adopted on 14.04.2023.	Positive Opinion adopted by consensus on 14.04.2023.
Instanyl - fentanyl - EMEA/H/C/000959/II/0075 Takeda Pharma A/S, Rapporteur: Alexandre Moreau Opinion adopted on 14.04.2023. Request for Supplementary Information adopted on 02.03.2023.	Positive Opinion adopted by consensus on 14.04.2023.
Ivabradine Zentiva - ivabradine - EMEA/H/C/004117/II/0014 Zentiva k.s., Generic, Generic of Procoralan, Rapporteur: Tomas Radimersky Request for Supplementary Information adopted on 12.01.2023.	

Kevzara - sarilumab - EMEA/H/C/004254/II/0036/G Sanofi Winthrop Industrie, Rapporteur: Jan Mueller-Berghaus	
Luminity - perflutren - EMEA/H/C/000654/II/0042/G Lantheus EU Limited, Rapporteur: Finbarr Leacy Request for Supplementary Information adopted on 15.12.2022.	
LUTATHERA - lutetium (177Lu) oxodotreotide - EMEA/H/C/004123/II/0039, Orphan Advanced Accelerator Applications, Rapporteur: Janet Koenig Request for Supplementary Information adopted on 26.01.2023.	
Mounjaro - tirzepatide - EMEA/H/C/005620/II/0004/G Eli Lilly Nederland B.V., Rapporteur: Martina Weise	
Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0036/G Roche Registration GmbH, Rapporteur: Thalia Marie Estrup Blicher Opinion adopted on 20.04.2023. Request for Supplementary Information adopted on 09.02.2023.	Positive Opinion adopted by consensus on 20.04.2023.
Ontruzant - trastuzumab - EMEA/H/C/004323/II/0045 Samsung Bioepis NL B.V., Rapporteur: Karin Janssen van Doorn Opinion adopted on 14.04.2023.	Positive Opinion adopted by consensus on 14.04.2023.
POTELIGEO - mogamulizumab - EMEA/H/C/004232/II/0018, Orphan Kyowa Kirin Holdings B.V., Rapporteur: Johann Lodewijk Hillege	
POTELIGEO - mogamulizumab - EMEA/H/C/004232/II/0019/G, Orphan Kyowa Kirin Holdings B.V., Rapporteur: Johann Lodewijk Hillege	
POTELIGEO - mogamulizumab - EMEA/H/C/004232/II/0020, Orphan Kyowa Kirin Holdings B.V., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 14.04.2023.	Request for supplementary information adopted with a specific timetable.

Surgiflo Haemostatic Matrix Kit - human thrombin - EMEA/H/D/002301/II/0033/G Ferrosan Medical Devices A/S, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 20.04.2023.	Request for supplementary information adopted with a specific timetable.
Taltz - ixekizumab - EMEA/H/C/003943/II/0049/G Eli Lilly and Co (Ireland) Limited, Rapporteur: Kristina Dunder Opinion adopted on 20.04.2023.	Positive Opinion adopted by consensus on 20.04.2023.
Vyepti - eptinezumab - EMEA/H/C/005287/II/0005/G H. Lundbeck A/S, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 20.04.2023. Request for Supplementary Information adopted on 09.02.2023.	Positive Opinion adopted by consensus on 20.04.2023.
Vyepti - eptinezumab - EMEA/H/C/005287/II/0008 H. Lundbeck A/S, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 20.04.2023.	Positive Opinion adopted by consensus on 20.04.2023.
Vyvgart - efgartigimod alfa - EMEA/H/C/005849/II/0004/G, Orphan Argenx, Rapporteur: Thalia Marie Estrup Blicher Opinion adopted on 14.04.2023. Request for Supplementary Information adopted on 16.02.2023.	Positive Opinion adopted by consensus on 14.04.2023.
Zessly - infliximab - EMEA/H/C/004647/II/0028 Sandoz GmbH, Rapporteur: Eva Skovlund Opinion adopted on 14.04.2023.	Positive Opinion adopted by consensus on 14.04.2023.
Zutectra - human hepatitis B immunoglobulin - EMEA/H/C/001089/II/0058 Biotest Pharma GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 14.04.2023.	Positive Opinion adopted by consensus on 14.04.2023.
WS2365 **Ambirix-**	

EMEA/H/C/000426/WS2365/0125 **Bexsero-** **EMEA/H/C/002333/WS2365/0119** **Cervarix-** **EMEA/H/C/000721/WS2365/0119** **Fendrix-** **EMEA/H/C/000550/WS2365/0081** **Infanrix hexa-** **EMEA/H/C/000296/WS2365/0326** **Synflorix-** **EMEA/H/C/000973/WS2365/0176** **Twinrix Adult-** **EMEA/H/C/000112/WS2365/0160** **Twinrix Paediatric-** **EMEA/H/C/000129/WS2365/0161** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke	
WS2444 **Lixiana-EMEA/H/C/002629/WS2444/0044** **Roteas-EMEA/H/C/004339/WS2444/0031** Daiichi Sankyo Europe GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro	
WS2461/G **Blitzima-** **EMEA/H/C/004723/WS2461/0065/G** **Truxima-** **EMEA/H/C/004112/WS2461/0068/G** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz	

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

ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0035 Baxalta Innovations GmbH, Rapporteur: Daniela Philadelphy, "Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on anaphylactic reaction and to add anaphylactic reaction to the list of adverse drug reactions (ADRs) with frequency Not Known, based on the cumulative review of MAH global database and literature search. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information." Request for Supplementary Information adopted on 14.04.2023.	Request for supplementary information adopted with a specific timetable.

Cosentyx - secukinumab - EMEA/H/C/003729/II/0097 Novartis Europharm Limited, Rapporteur: Outi Mäki-Ikola, "Update of section 4.8 of the SmPC in order to add pyoderma gangrenosum to the list of adverse drug reactions (ADRs) with frequency not known based on a systematic review of the MAH safety database, clinical trial data, literature search and epidemiological evaluation. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to include a Notification 61(3)."	
Darzalex - daratumumab - EMEA/H/C/004077/II/0066, Orphan Janssen-Cilag International N.V., Rapporteur: Aaron Sosa Mejia, "Submission of the final report from subgroup analysis of subjects with body weight >120 kg in ongoing randomized studies (MMY1004, MMY3012, MMY2040, and AMY3001) to further characterize the impact of body weight >120 kg on exposure and efficacy outcomes."	
Dupixent - dupilumab - EMEA/H/C/004390/II/0068 Sanofi Winthrop Industrie, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.8 and 5.1 of the SmPC to include long-term safety and efficacy information in children based on final results from study LTS14424 - EXCURSION. This is an interventional one-year study, to evaluate the long-term safety and tolerability of dupilumab in children 6 to 11 years of age with asthma, who participated in a previous dupilumab asthma clinical study EFC14153." Opinion adopted on 14.04.2023. Request for Supplementary Information adopted on 19.01.2023.	Positive Opinion adopted by consensus on 14.04.2023.
Enbrel - etanercept - EMEA/H/C/000262/II/0249 Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 4.6 of the SmPC in order to update information on breast feeding exposure based on the cumulative review of etanercept specific pharmacology, safety database and published medical literature. The Package Leaflet is updated accordingly. In addition, the MAH is taking this opportunity	Request for supplementary information adopted with a specific timetable.

to correct minor administrative and typographical changes to the SmPC, Labelling and Package Leaflet. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 14.04.2023, 12.01.2023.	
Evrysdi - risdiplam - EMEA/H/C/005145/II/0011, Orphan Roche Registration GmbH, Rapporteur: Bruno Sepodes, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to delete an existing warning on "Use with SMA gene therapy" and to update the safety profile and efficacy data in patients previously treated with other SMA-modifying therapies based on the 24-month primary analysis data from study BP39054 (JEWELFISH); this is a multicenter, open-label study to investigate the safety, tolerability, and pharmacokinetics/pharmacodynamics of risdiplam in adult and paediatric patients with SMA. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Opinion adopted on 20.04.2023. Request for Supplementary Information adopted on 26.01.2023.	Positive Opinion adopted by consensus on 20.04.2023.
Fintepla - fenfluramine - EMEA/H/C/003933/II/0018, Orphan UCB Pharma SA, Rapporteur: Thalia Marie Estrup Blicher, "Update of sections 4.8 and 5.1 of the SmPC in order to update the summary of the safety profile and list of adverse drug reactions for Dravet Syndrome and to update clinical efficacy information, following the assessment of the Article 46 procedure LEG/009 based on final results from study 3 (study 1501/1502 part 2). The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 14.04.2023.	Request for supplementary information adopted with a specific timetable.
Galafold - migalastat - EMEA/H/C/004059/II/0038, Orphan Amicus Therapeutics Europe Limited, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 5.2 of the SmPC in order to modify administration instructions and to update the pharmacokinetic information based on study AT1001-045; a randomized, open-label, 6-way	

crossover study to evaluate the relative bioavailability of the 150-mg migalastat hydrochloride (HCl) capsule taken with caffeinated and sweetened beverages versus taken with water in healthy volunteers. The Package Leaflet and Labelling are updated accordingly. In addition, the MAH took the opportunity to introduce some minor editorial changes and additional corrections to the SmPC referring to prior regulatory procedures II/0030 and II/0034."	
GONAL-f - follitropin alfa - EMEA/H/C/000071/II/0158 Merck Europe B.V., Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 4.4 of the SmPC in order to align the wording with current clinical practice and to remove Estradiol and follicle number thresholds associated with signs of Ovarian Hyperstimulation Syndrome (OHSS), based on literature and clinical guidelines. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes to the SmPC." Request for Supplementary Information adopted on 20.04.2023.	Request for supplementary information adopted with a specific timetable.
Hepcludex - bulevirtide - EMEA/H/C/004854/II/0019, Orphan Gilead Sciences Ireland Unlimited Company, Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC in order to update the list of adverse drug reactions (ADRs) and efficacy information based on interim results from study MYR301 listed as a Specific Obligation in the Annex II of the Product Information; this is a Multicenter, Open-label, Randomized Phase III Clinical Study to Assess Efficacy and Safety of Bulevirtide in Patients with Chronic Hepatitis Delta. Consequently, the MAH proposes a switch from conditional marketing authorisation to full marketing authorisation given the fulfilment of the SOB. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the SmPC." Request for Supplementary Information adopted on 15.12.2022.	See 9.1

HEPLISAV B - hepatitis B surface antigen - EMEA/H/C/005063/II/0023 Dynavax GmbH, Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to add 'injection site pruritus' to the list of adverse drug reactions (ADRs) with frequency 'uncommon', based on post-marketing surveillance. In addition, the MAH took the opportunity to introduce minor changes to the PI."	
Invokana - canagliflozin - EMEA/H/C/002649/II/0062 Janssen-Cilag International N.V., Rapporteur: Martina Weise, "Update of section 4.5 of the SmPC in order to add drug-drug interaction information with lithium, based on a safety review. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted on 14.04.2023.	Request for supplementary information adopted with a specific timetable.
LIVTENCITY - maribavir - EMEA/H/C/005787/II/0002/G, Orphan Takeda Pharmaceuticals International AG Ireland Branch, Rapporteur: Janet Koenig, "Grouped application consisting of 1) Submission of the final report from study TAK-620-1020. This is a Phase I open-label, randomized, crossover, partially fixed sequence, single-center study to evaluate the pharmacokinetic (PK) profile, safety, and tolerability of maribavir administered to healthy adult subjects of Japanese descent and matched healthy adult, non-Hispanic, Caucasian subjects; 2) Submission of the final report from study TAK 620 1025. This is a Phase I, open-Label, randomized, crossover study to evaluate the effect of food on maribavir pharmacokinetics in healthy adult participants."	
LUTATHERA - lutetium (177Lu) oxodotreotide - EMEA/H/C/004123/II/0038, Orphan Advanced Accelerator Applications, Rapporteur: Janet Koenig, "Update of sections 2, 4.2, 4.4, 4.5, 4.6, 4.8, 4.9, 5.1, 5.2, 5.3, 6.2, 6.4, 6.5, 6.6, 11 and 12 of the SmPC to align the Lutathera product information to that of the latest Core Data Sheet (CDS) version 2.0. In	

addition, the MAH is taking the opportunity to propose additional corrections and changes to align with the QRD template. This application is also used as an opportunity to propose editorial updates to the product information (PI) to improve the language throughout the SmPC and patient leaflet." Request for Supplementary Information adopted on 01.12.2022.	
Olumiant - baricitinib - EMEA/H/C/004085/II/0038 Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC to update efficacy information following the CHMP assessment of procedure R/0025 based on final results from study I4V-MC-JADY (JADY; RA BEYOND); This is a long-term extension study: a Phase 3, Multicenter Study to Evaluate the Long-Term Safety and Efficacy of Baricitinib in Patients with Rheumatoid Arthritis." Request for Supplementary Information adopted on 20.04.2023.	Request for supplementary information adopted with a specific timetable.
Perjeta - pertuzumab - EMEA/H/C/002547/II/0066 Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, "To update sections 4.8 and 5.1 to reflect updated overall survival data and cardiac safety data, based on interim results from study BO25126 (APHINITY): A randomized multicenter, double-blind, placebo-controlled comparison of chemotherapy plus trastuzumab plus placebo versus chemotherapy plus trastuzumab plus pertuzumab as adjuvant therapy in patients with operable HER2-positive primary breast cancer. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce editorial changes."	
Qarziba - dinutuximab beta - EMEA/H/C/003918/II/0043, Orphan EUSA Pharma (Netherlands) B.V., Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.1, 4.2 and 5.1 of the SmPC based on final results from study APN311-202V3 listed as a Specific Obligation in the Annex II of the Product Information. This is a Phase I/II dose schedule finding study of Ch14.18/CHO continuous infusion combined with	

subcutaneous aldesleukin (IL-2) in patients with primary refractory or relapsed neuroblastoma. In addition, the MAH took the opportunity to update Annex II section E. The Package Leaflet is updated accordingly. ” Request for Supplementary Information adopted on 15.09.2022.	
Qutenza - capsaicin - EMEA/H/C/000909/II/0057 Grunenthal GmbH, Rapporteur: Bruno Sepodes, "Update of sections 4.4 and 4.8 of the SmPC in order to add `Third Degree Burn´ to the list of adverse drug reactions (ADRs) with frequency not known, based on a validated safety signal and post-marketing data; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes to the Package Leaflet.” Request for Supplementary Information adopted on 23.02.2023.	
Saphnelo - anifrolumab - EMEA/H/C/004975/II/0007 AstraZeneca AB, Rapporteur: Outi Mäki-Ikola, "Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC based on final results from study D3461C00009 listed as an additional pharmacovigilance activity in the RMP; this is a multicentre, randomised, double-blind, placebo-controlled Phase III extension study to characterise the long-term safety and tolerability of anifrolumab in adult subjects with active systemic lupus erythematosus. In addition, the MAH took the opportunity to implement minor changes to sections 4.2 and 6.6 of the SmPC and to the Package Leaflet.” Request for Supplementary Information adopted on 14.04.2023.	Request for supplementary information adopted with a specific timetable.
Segluromet - ertugliflozin / metformin hydrochloride - EMEA/H/C/004314/II/0017 Merck Sharp & Dohme B.V., Rapporteur: Kristina Dunder, "To include significant changes to sections 4.4 and 4.8 of the SmPC and section 4 of the Package Leaflet for the medicinal product Segluromet, containing the active substances Ertugliflozin L-pyroglutamic acid and Metformin hydrochloride, regarding the risk for vitamin B12 deficiency. The topic was assessed as part of mutual	Positive Opinion adopted by consensus on 14.04.2023.

recognition procedures (FR/H/0181/001-3) for the mono-component containing metformin product (Glucophage). The current proposed update of the product information for ertugliflozin/metformin combination product (Segluromet) is the same as for the mono-component product containing metformin. In addition, the MAH proposed minor editorial changes to the PI. The proposed update of the PI for the medicinal product Segluromet, containing the active substances Ertugliflozin L-pyroglutamic acid and Metformin hydrochloride." Opinion adopted on 14.04.2023. Request for Supplementary Information adopted on 09.02.2023.	
Tecovirimat SIGA - tecovirimat - EMEA/H/C/005248/II/0005 SIGA Technologies Netherlands B.V., Rapporteur: Jayne Crowe, "Update of section 4.2 of the SmPC in order to introduce a new posology regimen for those with a body weight of 120 kg and above based on final results from study SIGA-246-022 and study report 865, which is a PopPK modelling and simulation report. Study SIGA-246-022 is a multiple-dose, open-label, safety, tolerability, and pharmacokinetic study of tecovirimat in adults weighing more than 120 kg. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."	
Twynsta - telmisartan / amlodipine - EMEA/H/C/001224/II/0046/G Boehringer Ingelheim International GmbH, Rapporteur: Martina Weise, "C.I.4: Update of section 4.8 of the SmPC in order to add 'hyponatraemia' to the list of adverse drug reactions (ADRs) with frequency 'rare'; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI, update the list of local representatives in the Package Leaflet and bring the PI in line with the latest QRD template version 10.3. C.I.z: Update of section 4.9 of the SmPC in order to add the risk of non-cardiogenic pulmonary oedema for amlodipine in case of overdose; the Package Leaflet is updated	

accordingly.”	
Vargatef - nintedanib - EMEA/H/C/002569/II/0047/G Boehringer Ingelheim International GmbH, Rapporteur: Aaron Sosa Mejia, “Grouped application containing: C.I.4: Update of sections 4.2, 5.1 and 5.2 of the SmPC in order to update information regarding the paediatric population based on results from study 1199-0337; this is a double blind, randomised, placebo-controlled trial to evaluate the dose-exposure and safety of nintedanib on top of standard of care for 24 weeks, followed by open label treatment with nintedanib of variable duration, in children and adolescents (6 to 17 year-old) with clinically significant fibrosing interstitial lung disease. The Package Leaflet is updated accordingly. C.I.4: Update of sections 4.2 and 5.2 of the SmPC in order to improve the recommendation for the administration of nintedanib based on food compatibility data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to introduce minor editorial changes to the PI.” Request for Supplementary Information adopted on 26.01.2023.	
Vokanamet - canagliflozin / metformin - EMEA/H/C/002656/II/0067/G Janssen-Cilag International N.V., Rapporteur: Martina Weise, “C.I.4: Update of section 4.5 of the SmPC in order to add drug-drug interaction information with lithium, based on a safety review. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. C.I.4: Update of section 4.8 of the SmPC in order to update the frequency for ‘vitamin B12 deficiency’ in the list of adverse drug reactions (ADRs) to ‘common’, based on a safety review. The Package Leaflet is updated accordingly.” Request for Supplementary Information adopted on 14.04.2023.	Request for supplementary information adopted with a specific timetable.
Yselty - linzagolix choline - EMEA/H/C/005442/II/0005 Theramex Ireland Limited, Rapporteur: Finbarr Leacy, “Submission of the final report from	Positive Opinion adopted by consensus on 14.04.2023.

study 22-OBE2109-001. This is a Phase I, open-label, single-dose, single-sequence, crossover drug-drug interaction study designed to evaluate the effect of linzagolix on the PK of the OATP1B1 substrate pitavastatin in healthy female subjects." Opinion adopted on 14.04.2023.	
Zejula - niraparib - EMEA/H/C/004249/II/0037, Orphan GlaxoSmithKline (Ireland) Limited, Rapporteur: Ingrid Wang, "Update of section 5.2 of the SmPC in order to update information on absorption based on results from food effect study 3000-01-004; this is an Open-Label, Randomized-Sequence, Multicenter, Single-Crossover Study to Assess the Relative Bioavailability and Bioequivalence of Niraparib Tablet Formulation Compared to Niraparib Capsule Formulation in Patients with Advanced Solid Tumors." Request for Supplementary Information adopted on 15.12.2022.	
ZYNRELEF - bupivacaine / meloxicam - EMEA/H/C/005205/II/0011 Heron Therapeutics, B.V., Rapporteur: Alexandre Moreau, "C.I.4. To update SmPC section 4.2 and the package leaflet to provide more detailed advice for health care professionals (HCPs) on suturing, especially relating to monofilament sutures and Zynrelef." Opinion adopted on 20.04.2023.	Positive Opinion adopted by consensus on 20.04.2023.
WS2321 **CONTROLOC Control- EMEA/H/C/001097/WS2321/0040** **PANTOZOL Control- EMEA/H/C/001013/WS2321/0042** **SOMAC Control- EMEA/H/C/001098/WS2321/0041** Takeda GmbH, Lead Rapporteur: Larisa Gorobets, "Update of sections 4.4 and 4.8 of the SmPC in order to add "Severe Cutaneous Adverse Reactions (SCARs)" information and to add "Acute Generalized Exanthematous Pustulosis (AGEP)" to the list of adverse drug reactions (ADRs) with frequency "not know" based on post-marketing experience, adverse reaction databases and literature; the Package Leaflet is updated accordingly. In addition, the MAH proposes to update section	

4.5 of the SmPC to introduce information regarding Drug-Laboratory Interactions. Furthermore, the MAH took the opportunity to implement editorial changes and to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 23.02.2023, 24.11.2022, 06.10.2022.	
WS2415 **Vfend-EMEA/H/C/000387/WS2415/0148** Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC to include increased risk of skin toxicity with concomitant use of voriconazole and methotrexate and potentially other drugs associated with ultraviolet (UV) reactivation to the current warning on photosensitivity skin reactions, based on post-marketing data and literature. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes to section 4.4 and 4.5 of the SmPC."	
WS2442 **Exelon-EMEA/H/C/000169/WS2442/0143** **Prometax-EMEA/H/C/000255/WS2442/0144** Novartis Europharm Limited, Lead Rapporteur: Alexandre Moreau, "Update of sections 4.4 and 4.5 of the SmPC in order to strengthen the existing warning on QT prolongation based on post-marketing data and literature; the Package Leaflet is updated accordingly." Opinion adopted on 14.04.2023.	Positive Opinion adopted by consensus on 14.04.2023.
WS2450/G **Glyxambi-EMEA/H/C/003833/WS2450/0051/G** **Synjardy-EMEA/H/C/003770/WS2450/0070/G** Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "C.I.4: Update of sections 4.2 and 4.4 of the SmPC in order to modify administration instructions to the elderly, amend an existing warning for the elderly and remove the warning for 'Cardiac Failure' in order to align with the Jardiance Product Information; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.	

C.I.z: Update of section 4.4 of the SmPC in order to introduce a rewording related to use in patients with type 1 diabetes in order to align with the Jardiance Product Information; the Package Leaflet is updated accordingly."	

B.5.3. CHMP-PRAC assessed procedures

AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0042 Sanofi Winthrop Industrie, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Submission of the final report of the open-label extension period for study EFC11759, listed as a category 3 study in the RMP. This is a two-year, multicentre, randomized, double-blind, placebo-controlled, parallel group trial to evaluate efficacy, safety, tolerability and pharmacokinetics of teriflunomide administered orally once daily in paediatric patients with relapsing forms of multiple sclerosis (MS) followed by an open-label extension. The RMP version 8.1 has also been submitted." Opinion adopted on 14.04.2023. Request for Supplementary Information adopted on 16.03.2023.	Positive Opinion adopted by consensus on 14.04.2023.
AYVAKYT - avapritinib - EMEA/H/C/005208/II/0022, Orphan Blueprint Medicines (Netherlands) B.V., Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations and to update pharmacokinetic information for use in patients with severe hepatic impairment based on the final results from study BLU-285-0107 listed as a category 3 study in the RMP; this is a phase 1, open-label, single-dose study to investigate the influence of severe hepatic impairment on the pharmacokinetics of avapritinib. The package leaflet is updated accordingly. The RMP version 3.0 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.3." Request for Supplementary Information adopted on 23.02.2023.	
Brukinsa - zanubrutinib - EMEA/H/C/004978/II/0009	Request for supplementary information adopted with a specific timetable.

BeiGene Ireland Ltd, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Menno van der Elst, "Submission of the final report from study BGB-3111-113 - A Drug-Drug Interaction Study of Zanubrutinib with Moderate and Strong CYP3A Inhibitors in Patients With B-Cell Malignancies, listed as a category 3 study in the RMP. The RMP version 3.0 has also been submitted." Request for Supplementary Information adopted on 14.04.2023.	
GIVLAARI - givosiran - EMEA/H/C/004775/II/0011/G, Orphan Alnylam Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber, "Update of section 5.3 of the SmPC based on final results from study AS1-GLP18-007 listed as a category 3 study in the RMP; This is a 104-week Subcutaneous Injection Carcinogenicity Study in Sprague Dawley Rats. Update of section 5.3 of the SmPC based on final results from study AS1-GLP18-004; This is a 26-week Subcutaneous Injection Carcinogenicity Study in TgRasH2 Mice. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 14.04.2023, 12.01.2023, 29.09.2022.	Request for supplementary information adopted with a specific timetable.
Imnovid - pomalidomide - EMEA/H/C/002682/II/0047, Orphan Bristol-Myers Squibb Pharma EEIG, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Monica Martinez Redondo, "Update of section 4.4 of the SmPC, Annex IID and Article 127a and the tools/documents included in the Educational Healthcare Professional Kit, in order to harmonise the terminology utilised in the RMP and PI documents relating to the safety concern of teratogenicity and its risk minimisation measure of the Pregnancy Prevention Plan across the 3 IMiDs. These proposed changes will only have a limited impact on the National Competent Authority (NCA)-approved content/text of the educational materials, and the key messages to the HCP and patients. Furthermore, the regulatory obligations regarding the PPP will not be impacted. The updated RMP version 16 was provided."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 14.04.2023, 09.02.2023, 27.10.2022.	
Kisplyx - lenvatinib - EMEA/H/C/004224/II/0052 Eisai GmbH, Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: David Olsen, "Update of section 4.8 of the SmPC based on pooled safety data including results of study 307, an ongoing, multicentre, randomised, open-label study that is being conducted to compare the efficacy and safety of lenvatinib in combination with everolimus or pembrolizumab versus sunitinib as first-line (1L) treatment in adults with advanced renal cell carcinoma (RCC). The provision of the CSR addresses the post-authorisation measure MEA/FSR 009.3. The Package Leaflet is updated accordingly. An updated RMP version 15.0 has been submitted." Opinion adopted on 14.04.2023. Request for Supplementary Information adopted on 09.02.2023, 29.09.2022.	Positive Opinion adopted by consensus on 14.04.2023.
Mayzent - siponimod - EMEA/H/C/004712/II/0020 Novartis Europharm Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Maria del Pilar Rayon, "Update of sections 4.4 and 4.8 of the SmPC in order to add "Progressive multifocal leukoencephalopathy (PML)" to the list of adverse drug reactions (ADRs) with frequency "not know" based on post-marketing data. The Annex II (Physician's Checklist), and Package Leaflet are updated accordingly. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to update the text regarding herpes viral infection in the Package Leaflet in alignment with the currently approved SmPC." Request for Supplementary Information adopted on 14.04.2023.	Request for supplementary information adopted with a specific timetable.
Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0094 Sanofi B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Nathalie Gault, "Update of section 4.2 of the SmPC in order to add home infusion upon request by PRAC following the assessment of PSUSA/00000086/202109 I based on a cumulative search of the MAH Global Pharmacovigilance database and literature. The Package Leaflet and Annex II are updated	

accordingly. The RMP version 10.0 has also been submitted.”	
Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0095 Sanofi B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Nathalie Gault, “Update of sections 4.4 and 5.2 of the SmPC in order to update a warning on immunogenicity. The RMP version 10.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI.” Request for Supplementary Information adopted on 14.04.2023.	Request for supplementary information adopted with a specific timetable.
Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0033 AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, “Update of section 5.1 of the SmPC based on interim results from the PK/PD study listed as a specific obligation in the Annex II in order to fulfil SOB 1 and SOB 3; this is a PK and PK/PD Analysis of Intravenously Administered Andexanet after dosing to steady state with a factor Xa inhibitor, rivaroxaban or Apixaban, in healthy subjects and patients who have acute major bleeding. In addition, the MAH took the opportunity to implement editorial changes in Annex II of the SmPC. The RMP version 3.0 has also been submitted.” Request for Supplementary Information adopted on 26.01.2023, 13.10.2022.	
Rekovelle - follitropin delta - EMEA/H/C/003994/II/0037/G Ferring Pharmaceuticals A/S, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Menno van der Elst, “Grouped application comprising two type II variations as follows: - Update of sections 4.1, 4.2, 4.4, 4.5 and 5.1 of the SmPC to update the safety information following final results from study 000304 (BEYOND). This is a randomised, controlled, open label, parallel group, multicentre trial comparing the efficacy and safety of individualised FE 999049 (follitropin delta) dosing, using a long GnRH agonist protocol and a GnRH antagonist protocol in women undergoing controlled ovarian stimulation. - Update of section 4.8 of the SmPC, including the tabulation of adverse drug reactions based	

on pooled safety data from studies ESTHER-1, ESTHER-2, 000273, 000145, BEYOND and RAINBOW. The updated 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."	
Revlimid - lenalidomide - EMEA/H/C/000717/II/0123 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, "Update of section 4.4 of the SmPC, Annex IID and Article 127a and the tools/documents included in the Educational Healthcare Professional Kit, in order to harmonise the terminology utilised in the RMP and PI documents relating to the safety concern of teratogenicity and its risk minimisation measure of the Pregnancy Prevention Plan across the 3 IMiDs. These proposed changes will only have a limited impact on the National Competent Authority (NCA)-approved content/text of the educational materials, and the key messages to the HCP and patients. Furthermore, the regulatory obligations regarding the PPP will not be impacted. The MAH is also taking the opportunity to update the RMP with PASS Protocol milestones. The updated RMP version 38 was provided." Request for Supplementary Information adopted on 14.04.2023, 09.02.2023, 27.10.2022.	Request for supplementary information adopted with a specific timetable.
Simponi - golimumab - EMEA/H/C/000992/II/0109 Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the Package Leaflet in order to update the Instructions for Use (IFU) for the pre-filled pen." Request for Supplementary Information adopted on 26.01.2023.	
Stelara - ustekinumab - EMEA/H/C/000958/II/0096 Janssen-Cilag International N.V., Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald, "Update of section 5.1 of the SmPC in order to update information with the 4-year clinical data in patients with ulcerative colitis based on the final report from study	

CNTO1275UCO3001 listed as a category 3 study in the RMP; this is a phase 3, randomized, double blind, placebo-controlled, parallel-group, multicenter study to evaluate the safety and efficacy of ustekinumab induction and maintenance therapy in subjects with moderately to severely active ulcerative colitis. The RMP version 23.1 has also been submitted. In addition, the MAH took the opportunity to introduce a correction to the PI." Request for Supplementary Information adopted on 26.01.2023.	
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0077/G Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Inês Ribeiro-Vaz, "Grouped application comprising two type II variations as follows: - Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add dose modification advice and new warning for two new important identified risks of immune-mediated myelitis and immune-mediated facial paresis and to add facial paresis and myelitis to the list of adverse drug reactions (ADRs) with frequency Rare following a safety signal based on the cumulative review of the MAH safety database and literature search. - Update of section 4.8 of the SmPC in order to add dry mouth to the list of adverse drug reactions (ADRs) with frequency Common, based on the results from study WO39210 (IMmotion010), a multicenter, randomized, placebo-controlled, double-blind study evaluating the efficacy and safety of atezolizumab versus placebo in patients with renal cell carcinoma (RCC) who are at high risk of disease recurrence following resection. The Annex II and Package Leaflet are updated accordingly. The RMP version 26.0 has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes to the SmPC and to update the list of local representatives in the Package Leaflet."	
Thalidomide BMS - thalidomide - EMEA/H/C/000823/II/0076 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine	Request for supplementary information adopted with a specific timetable.

Vaillant, "Update of section 4.4 of the SmPC, Annex IID and Article 127a and the tools/documents included in the Educational Healthcare Professional Kit, in order to harmonise the terminology utilised in the RMP and PI documents relating to the safety concern of teratogenicity and its risk minimisation measure of the Pregnancy Prevention Plan across the 3 IMiDs. These proposed changes will only have a limited impact on the National Competent Authority (NCA)-approved content/text of the educational materials, and the key messages to the HCP and patients. Furthermore, the regulatory obligations regarding the PPP will not be impacted. The MAH is also taking the opportunity to update the RMP with PASS Protocol milestones, and to make some editorial changes in the labelling. The updated RMP version 20 was provided." Request for Supplementary Information adopted on 14.04.2023, 09.02.2023, 27.10.2022.	
WS2421 **Edistride-** **EMEA/H/C/004161/WS2421/0059** **Forxiga-** **EMEA/H/C/002322/WS2421/0080** AstraZeneca AB, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Mari Thorn, "Submission of final results from non-clinical mechanistic model studies listed as a category 3 PASS in the RMP. These are non-clinical studies aiming to further investigate underlying mechanisms of diabetes ketoacidosis (DKA) in association with dapagliflozin. The RMP version 29 has also been submitted." Opinion adopted on 14.04.2023.	Positive Opinion adopted by consensus on 14.04.2023.

B.5.4. PRAC assessed procedures

PRAC Led **Arixtra - fondaparinux sodium -** **EMEA/H/C/000403/II/0087** Mylan Ire Healthcare Limited, PRAC Rapporteur: Mari Thorn, PRAC-CHMP liaison: Kristina Dunder, "To update section 4.8 of the SmPC to update the ADR table following the assessment of PSUSA (EMEA/H/C/PSUSA/00001467/202112). The Package Leaflet is updated accordingly." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 14.04.2023.	
PRAC Led **Fintepla - fenfluramine - EMEA/H/C/003933/II/0017, Orphan** UCB Pharma SA, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of an updated RMP version 2.10 in order to implement a targeted follow-up questionnaire (FUQ) to further improve the collection of follow-up information on cases of vascular heart disease (VHD) and pulmonary arterial hypertension (PAH) suggested by PRAC following the assessment of procedure EMEA/H/C/PSUSA/00010907/202112." Request for Supplementary Information adopted on 14.04.2023, 12.01.2023.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Kengrexal - cangrelor - EMEA/H/C/003773/II/0031** Chiesi Farmaceutici S.p.A., PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Armando Genazzani, "Submission of the final report from study ARCANGELO (itAlian pRospective study on CANGrELOr), listed as a category 3 study in the RMP. This is a multicentre observational, prospective cohort study including patients with acute coronary syndromes undergoing percutaneous coronary intervention who receive cangrelor i.v. transitioning to either clopidogrel, prasugrel or ticagrelor per os. The primary objective is to assess the safety of cangrelor in a real-world setting, when administered in patients with acute coronary syndromes undergoing percutaneous coronary intervention (PCI). The safety of cangrelor is based on the incidence of any haemorrhage at 30 days post-PCI. The RMP version 5.1 has also been submitted." Request for Supplementary Information adopted on 14.04.2023.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0092** Sanofi B.V., PRAC Rapporteur: Nathalie Gault, PRAC-CHMP liaison: Alexandre Moreau, "Update of sections 4.6 and 5.3 of the SmPC in order to update information on pregnancy, lactation and fertility following the request by PRAC in the AR	Positive Opinion adopted by consensus on 14.04.2023.

for MEA/024.17 and MEA/025.17 and in PSUSA/00000086/202109; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Opinion adopted on 14.04.2023. Request for Supplementary Information adopted on 01.12.2022.	
PRAC Led **NutropinAq - somatropin - EMEA/H/C/000315/II/0077** Ipsen Pharma, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Thalia Marie Estrup Blicher, "Submission of an updated RMP version 4.0 in order to remove some of the safety concerns in compliance with GVP Module V Revision 2. In addition, the MAH took the opportunity to add data from final clinical study report of International Cooperative Growth Study (iNCGS) registry (non-interventional study) and exposure and safety information." Request for Supplementary Information adopted on 14.04.2023, 12.01.2023.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Stocrin - efavirenz - EMEA/H/C/000250/II/0130** Merck Sharp & Dohme B.V., Duplicate, Duplicate of Sustiva, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "Submission of an updated RMP version 9.0 in accordance with the new template and thereby to remove safety concerns." Opinion adopted on 14.04.2023. Request for Supplementary Information adopted on 12.01.2023.	Positive Opinion adopted by consensus on 14.04.2023.
PRAC Led **Synagis - palivizumab - EMEA/H/C/000257/II/0131** AstraZeneca AB, PRAC Rapporteur: Marie Louise Schougaard Christiansen, PRAC-CHMP liaison: Thalia Marie Estrup Blicher, "Submission of an updated RMP in order to remove from the list of safety concerns "Anaphylaxis, Anaphylactic shock, and Hypersensitivity" and "Medication error of mixing lyophilised and liquid palivizumab before injection". In addition, the MAH took the opportunity to apply the revised template. RMP version 2.3 is	Positive Opinion adopted by consensus on 14.04.2023.

approved with this procedure." Opinion adopted on 14.04.2023. Request for Supplementary Information adopted on 16.03.2023, 01.12.2022.	
PRAC Led **Tecovirimat SIGA - tecovirimat - EMEA/H/C/005248/II/0006** SIGA Technologies Netherlands B.V., PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of substantial updates to the protocol of study SIGA-246-021 listed as a specific obligation in the Annex II of the Product Information in order to reflect the transfer of sponsorship from SIGA Technologies, Inc. to the NIH Division of Microbiology and Infection Disease protocol. This is a phase 4, observational field study to evaluate safety and clinical benefit in tecovirimat-treated patients following exposure to variola virus and clinical diagnosis of smallpox disease. The Annex II and the RMP submitted version 1.2 are updated accordingly." Request for Supplementary Information adopted on 14.04.2023.	Request for supplementary information adopted with a specific timetable.
PRAC Led **TOBI Podhaler - tobramycin - EMEA/H/C/002155/II/0053, Orphan** Viatris Healthcare Limited, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 8.0 following the request by PRAC in the AR for PSUSA/00009315/202106 in order to update it based on the guidance provided in the GVP and to remove the safety concerns as well as to reflect the finalisation of study CTBM100C2407 and the transfer of ownership." Opinion adopted on 14.04.2023. Request for Supplementary Information adopted on 01.12.2022.	Positive Opinion adopted by consensus on 14.04.2023.
PRAC Led **VPRIV - velaglucerase alfa - EMEA/H/C/001249/II/0061** Takeda Pharmaceuticals International AG Ireland Branch, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of an updated RMP version 12 in order to remove certain risks from the list of safety concerns."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 14.04.2023, 09.02.2023.

PRAC Led
WS2402
Advagraf-
EMEA/H/C/000712/WS2402/0069
Modigraf-
EMEA/H/C/000954/WS2402/0045
Astellas Pharma Europe B.V., Lead PRAC Rapporteur: Eamon O Murchu, PRAC-CHMP liaison: Jayne Crowe, "C.I.11.z - To update the EU Risk Management Plan with the new TPRI final study submission milestone, related to procedure EMEA/H/C/000712/MEA030 and EMEA/H/C/000954/MEA022 (study F506-PV-0001)."
Request for Supplementary Information adopted on 16.03.2023.

B.5.5. CHMP-CAT assessed procedures

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0027, Orphan, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang
Request for Supplementary Information adopted on 24.03.2023.

Alofisel - darvadstrocel - EMEA/H/C/004258/II/0045/G, Orphan, ATMP
Takeda Pharma A/S, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder

ROCTAVIAN - valoctocogene roxaparvovec - EMEA/H/C/005830/II/0004/G, Orphan, ATMP
BioMarin International Limited, Rapporteur: Violaine Closson Carella, CHMP Coordinator: Jean-Michel Race

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

PRAC Led
Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0059, ATMP
Amgen Europe B.V, CHMP Coordinator: Jan

Mueller-Berghaus, PRAC Rapporteur: Gabriele Maurer, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 10 in order to update and reclassify identified risk of 'Disseminated herpetic infection' based on the cumulative assessment of literature review and MAH Global Safety Database and to remove studies 20180062 and 20180099 from Planned and Ongoing Studies from the list of Pharmacovigilance Plan studies in the Annex II." Request for Supplementary Information adopted on 20.01.2023.	

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

WS2372/G **Suboxone-** **EMEA/H/C/000697/WS2372/0056/G** Indivior Europe Limited, Lead Rapporteur: Janet Koenig Opinion adopted on 20.04.2023.	Positive Opinion adopted by consensus on 20.04.2023.
WS2414/G **Mircera-** **EMEA/H/C/000739/WS2414/0093/G** **NeoRecormon-** **EMEA/H/C/000116/WS2414/0119/G** Roche Registration GmbH, Lead Rapporteur: Martina Weise Opinion adopted on 14.04.2023.	Positive Opinion adopted by consensus on 14.04.2023.
WS2433 **Hexacima-** **EMEA/H/C/002702/WS2433/0145** **Hexyon-** **EMEA/H/C/002796/WS2433/0149** Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus	
WS2447/G **Fluenz Tetra-** **EMEA/H/C/002617/WS2447/0126/G** **Pandemic influenza vaccine H5N1 AstraZeneca-** **EMEA/H/C/003963/WS2447/0061/G** AstraZeneca AB, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 14.04.2023.	Positive Opinion adopted by consensus on 14.04.2023.
WS2448	Request for supplementary information adopted

Filgrastim Hexal-EMEA/H/C/000918/WS2448/0069 Zarzio-EMEA/H/C/000917/WS2448/0070 Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 14.04.2023.	with a specific timetable.
WS2455/G Ongentys-EMEA/H/C/002790/WS2455/0058/G Ontilyv-EMEA/H/C/005782/WS2455/0013/G Bial - Portela & Cª, S.A., Lead Rapporteur: Martina Weise	

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

Supemtek - influenza quadrivalent vaccine (rDNA) - EMEA/H/C/005159/II/0009 Sanofi Pasteur, Rapporteur: Jan Mueller-Berghaus, "Update of section 5.1 of the SmPC in order to update the efficacy information based on final results from study VAP00003 listed as a category 3 study in the RMP; this is a phase 4, multi-center, modified-cluster randomized study to assess the effectiveness of Flublok Quadrivalent vaccine compared to standard dose inactivated influenza vaccine in adults. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted on 15.12.2022.	The MAH withdrew the application on 30.03.2023
LUTATHERA - lutetium (177Lu) oxodotreotide - EMEA/H/C/004123/II/0039, Orphan Advanced Accelerator Applications, Rapporteur: Janet Koenig Request for Supplementary Information adopted on 26.01.2023.	The MAH withdrew the application on 20.04.2023

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

in vitro diagnostic medical device - EMEA/H/D/006232
to detect rearrangements involving the ALK gene via fluorescence

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

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

Adtralza - tralokinumab - EMEA/H/C/005255/X/0007
LEO Pharma A/S, Rapporteur: Jayne Crowe, PRAC Rapporteur: Kimmo Jaakkola, "Extension application to add a new strength of 300 mg (150 mg/ml) tralokinumab solution for injection in pre-filled pen for subcutaneous administration.
The RMP (version 1.1) is updated accordingly."
List of Questions adopted on 30.03.2023.

in vitro diagnostic medical device - EMEA/H/D/006233
To determine HER2 (Human Epidermal Growth Factor Receptor 2) oncoprotein status
Request for Supplementary Information adopted on 30.03.2023.

latanoprost - EMEA/H/C/005933
Reduction of elevated intraocular pressure (IOP)
List of Questions adopted on 26.01.2023.

Erleada - apalutamide - EMEA/H/C/004452/X/0028/G
Janssen-Cilag International N.V., Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Tiphaine Vaillant, "Extension application to add a new strength (240 mg) film-coated tablets grouped with the IB variation (C.I.z).
The RMP (version 6.1) has also been submitted.
C.I.z (IB): to align the SmPC/PL for Erleada 60 mg with the SmPC/PL proposed for the registration of the new Erleada film-coated

tablet strength, 240 mg.
The PL for Erleada 60 mg is proposed to be updated to ensure consistency.
In addition, few minor revisions are proposed to the SmPC for Erleada 60 mg, to align the SmPC proposed for the 240 mg strength:
- SmPC sections 5.1 and 5.2: Orthographic corrections
- SmPC section 6.5: Further details on the description of the current packaging have been added, this change does not result from a change to the container.
- SmPC Section 6.6: The title of the section has been aligned with QRD template."
List of Questions adopted on 30.03.2023.

fezolinetant - EMEA/H/C/005851
treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause
List of Questions adopted on 26.01.2023.

Xolair - omalizumab - EMEA/H/C/000606/X/0115/G
Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Mari Thorn"Extension application to add a new strength of 300 mg (150 mg/ml) for Xolair solution for injection grouped with quality type II, IB and IAIN variations. The RMP (version 17.0) is updated in accordance.
List of Questions adopted on 15.12.2022.

zilucoplan - EMEA/H/C/005450, Orphan
UCB Pharma S.A., treatment of generalised myasthenia gravis in adults
List of Questions adopted on 26.01.2023.

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

Chenodeoxycholic acid Leadiant - chenodeoxycholic acid - EMEA/H/C/004061/S/0022, Orphan
Leadiant GmbH, Rapporteur: Anastasia Mountaki, PRAC Rapporteur: Adam Przybylkowski

DECTOVA - zanamivir - EMEA/H/C/004102/S/0016
GlaxoSmithKline Trading Services Limited, Rapporteur: Ingrid Wang, PRAC Rapporteur: Ulla Wändel Liminga

Elaprase - idursulfase -
EMEA/H/C/000700/S/0111
Takeda Pharmaceuticals International AG Ireland Branch, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan

Firdapse - amifampridine -
EMEA/H/C/001032/S/0075
SERB SA, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

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

Adakveo - crizanlizumab -
EMEA/H/C/004874/R/0014, Orphan
Novartis Europharm Limited, Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Jo Robays

Besremi - ropeginterferon alfa-2b -
EMEA/H/C/004128/R/0031
AOP Orphan Pharmaceuticals GmbH, Rapporteur: Janet Koenig, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Inês Ribeiro-Vaz

Bevespi Aerosphere - glycopyrronium / formoterol fumarate dihydrate -
EMEA/H/C/004245/R/0017
AstraZeneca AB, Rapporteur: Kristina Dunder, Co-Rapporteur: Finbarr Leacy, PRAC Rapporteur: Jan Neuhauser

Erleada - apalutamide -
EMEA/H/C/004452/R/0030
Janssen-Cilag International N.V., Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Elita Poplavska, PRAC Rapporteur: Tiphaine Vaillant

TECFIDERA - dimethyl fumarate -
EMEA/H/C/002601/R/0083
Biogen Netherlands B.V., Rapporteur: Martina Weise, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Martin Huber

Vantobra - tobramycin -
EMEA/H/C/005086/R/0009
PARI Pharma GmbH, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

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

ASPAVELI - pegcetacoplan - EMEA/H/C/005553/II/0011, Orphan Swedish Orphan Biovitrum AB (publ), Rapporteur: Alexandre Moreau, Co-Rapporteur: Selma Arapovic Dzakula, PRAC Rapporteur: Kimmo Jaakkola, "Extension of indication to include treatment of adult patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) not previously treated with a complement inhibitor for ASPAVELI, based on final results from study APL2-308. This is a Phase III, randomized, open-label, comparator-controlled study that enrolled adult patients with PNH who had not been treated with a complement inhibitor. 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 1.1 of the RMP has also been submitted."	
Beyfortus - nirsevimab - EMEA/H/C/005304/II/0005 AstraZeneca AB, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Kimmo Jaakkola, "Extension of indication to include treatment of children up to 24 months of age who remain vulnerable to severe Respiratory Syncytial Virus (RSV) disease through their second RSV season for BEYFORTUS, based on interim results from studies D5290C00005 and D5290C00008. Study D5290C00005 (MEDLEY) is a Phase II/III, randomized, double-blind, placebo-controlled study to evaluate the safety of Beyfortus in high-risk children. Study D5290C00008 (MUSIC) is a Phase II, open-label, uncontrolled, single-dose study to evaluate the safety and tolerability, pharmacokinetics, and occurrence of antidrug antibody for Beyfortus in immunocompromised children ≤ 24 months of Age. 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 accordingly. Version 2.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the	

Package Leaflet.”	
Fluad Tetra - influenza vaccine (surface antigen, inactivated, adjuvanted) - EMEA/H/C/004993/II/0043 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, “Extension of indication to include adults 50 years of age and older for Fluad Tetra, based on final results from study V118_23; this is a phase 3, randomized, observer-blind, controlled, multicenter, clinical study to evaluate immunogenicity and safety of an MF59-adjuvanted quadrivalent subunit inactivated influenza vaccine in comparison with a licensed quadrivalent influenza vaccine, in adults 50 to 64 years of age. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Labelling and Package Leaflet are updated in accordance. Version 2.9 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to the PI.”	
JEMPERLI - dostarlimab - EMEA/H/C/005204/II/0023 GlaxoSmithKline (Ireland) Limited, Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Inês Ribeiro-Vaz, “Extension of indication to include in combination with platinum-containing chemotherapy the treatment of adult patients with mismatch repair deficient (dMMR)/ microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer (EC) and who are candidates for systemic therapy, based on results from study 213361 (RUBY) Part 1, listed as a Specific Obligation in the Annex II; this is a phase 3, randomized, double-blind, multicenter study of dostarlimab (TSR-042) plus carboplatin-paclitaxel versus placebo plus carboplatin-paclitaxel in patients with recurrent or primary advanced endometrial cancer. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Annex II and Package Leaflet are updated in accordance. Version 3.0 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to the PI. As part of the application, the MAH is requesting	

a 1-year extension of the market protection."
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

LIVMARLI - maralixibat - EMEA/H/C/005857/II/0003/G, Orphan
Mirum Pharmaceuticals International B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Adam Przybylkowski, "Grouped variation consisting of:
1) Extension of indication to include treatment of Progressive Familial Intrahepatic Cholestasis (PFIC) in patients 2 months of age and older for LIVMARLI, based on results from studies MRX-502, LUM001-501, MRX-503, MRX-800 and MRX-801; MRX-502 is an international, multicenter, randomized, double-blind, placebo-controlled, parallel group Phase 3 study that evaluated the efficacy and safety of maralixibat in PFIC participants aged >12 months to <18 years on a proposed dosage of up to 600 µg/kg BID over 6 months. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and Annex II are updated in accordance. Version 2.0 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes.
2) B.I.b.1.b "
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Advate - octocog alfa - EMEA/H/C/000520/II/0120/G
Takeda Manufacturing Austria AG, Rapporteur: Jan Mueller-Berghaus

Apexxnar - pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - EMEA/H/C/005451/II/0014/G
Pfizer Europe MA EEIG, Rapporteur: Daniela Philadelphy

COMIRNATY - tozinameran - EMEA/H/C/005735/II/0178
BioNTech Manufacturing GmbH, Rapporteur:

Filip Josephson

Eylea - aflibercept - EMEA/H/C/002392/II/0086
Bayer AG, Rapporteur: Alexandre Moreau

Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0053/G, Orphan
Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia

LIVMARLI - maralixibat - EMEA/H/C/005857/II/0002, Orphan
Mirum Pharmaceuticals International B.V., Rapporteur: Martina Weise

Ontruzant - trastuzumab - EMEA/H/C/004323/II/0046/G
Samsung Bioepis NL B.V., Rapporteur: Karin Janssen van Doorn

Pazenir - paclitaxel - EMEA/H/C/004441/II/0014
ratiopharm GmbH, Generic, Generic of Abraxane, Rapporteur: Daniela Philadelphy

Pluvicto - lutetium (177Lu) vipivotide tetraxetan - EMEA/H/C/005483/II/0003
Novartis Europharm Limited, Rapporteur: Janet Koenig

Spikevax - elasomeran - EMEA/H/C/005791/II/0100/G
Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus

Surgiflo Haemostatic Matrix Kit - human thrombin - EMEA/H/D/002301/II/0034/G
Ferrosan Medical Devices A/S, Rapporteur: Jan Mueller-Berghaus

TOBI Podhaler - tobramycin - EMEA/H/C/002155/II/0057/G, Orphan
Viatris Healthcare Limited, Rapporteur: Johann Lodewijk Hillege

Toujeo - insulin glargine - EMEA/H/C/000309/II/0121/G
Sanofi-Aventis Deutschland GmbH, Duplicate, Duplicate of Lantus, Rapporteur: Johann Lodewijk Hillege

TRODELVY - sacituzumab govitecan - EMEA/H/C/005182/II/0023/G
Gilead Sciences Ireland UC, Rapporteur: Jan

Mueller-Berghaus

TRODELVY - sacituzumab govitecan - EMEA/H/C/005182/II/0024/G
Gilead Sciences Ireland UC, Rapporteur: Jan Mueller-Berghaus

Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0119/G
MCM Vaccine B.V., Rapporteur: Christophe Focke

VidPrevtyn Beta - SARS-CoV-2, B.1.351 variant, prefusion Spike delta TM protein, recombinant - EMEA/H/C/005754/II/0003
Sanofi Pasteur, Rapporteur: Jan Mueller-Berghaus

Voxzogo - vosoritide - EMEA/H/C/005475/II/0007, Orphan
BioMarin International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Zane Neikena

Zinplava - bezlotoxumab - EMEA/H/C/004136/II/0038/G
Merck Sharp & Dohme B.V., Rapporteur: Jan Mueller-Berghaus

WS2479
Hexacima-
EMEA/H/C/002702/WS2479/0146
Hexyon-
EMEA/H/C/002796/WS2479/0150
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

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

CABOMETYX - cabozantinib - EMEA/H/C/004163/II/0032
Ipsen Pharma, Rapporteur: Ingrid Wang, "Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on Vanishing Bile Duct Syndrome (VBDS), to add embolism arterial to the list of adverse drug reactions (ADRs) with frequency Uncommon and to add vanishing bile duct syndrome to the list of adverse drug reactions (ADRs) with frequency Not known based on the cumulative review of the global safety database and literature search.

The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Dupixent - dupilumab - EMEA/H/C/004390/II/0071

Sanofi Winthrop Industrie, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC in order to support the longer-term (5-year) safety of dupilumab in adults with moderate-to-severe Atopic Dermatitis (AD) based on final results from study R668-AD-1225 listed as a specific PASS category 3 study in the RMP.
The study R668-AD-1225 was a phase 3, multicenter, open-label extension (OLE) study of dupilumab in adults with moderate-to-severe atopic dermatitis (AD) who had previously participated in dupilumab clinical trials. The main objective of this study is to assess the long-term safety of dupilumab administered in adult patients with AD."

Dupixent - dupilumab - EMEA/H/C/004390/II/0072

Sanofi Winthrop Industrie, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update the safety and efficacy information relevant to patients with hand and foot Atopic Dermatitis based on the results from study R668-AD-1924. This is a Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy and Safety of Dupilumab in Adult and Adolescent Patients with Moderate-to-Severe Atopic Hand and Foot Dermatitis."

Kanuma - sebelipase alfa - EMEA/H/C/004004/II/0044, Orphan

Alexion Europe SAS, Rapporteur: Karin Janssen van Doorn, "Update of sections 4.2 and 6.6 of the SmPC in order to limit the 1-hour infusion time only to those patients receiving the 1 mg/kg dose and to modify the table for 'recommended infusion volumes' to address the USP endotoxin limit. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Kisqali - ribociclib -

EMEA/H/C/004213/II/0041/G

Novartis Europharm Limited, Rapporteur: Filip Josephson, "Grouped application comprising two type II variations as follows:
- Update of section 5.2 of the SmPC in order to update absorption information based on final results from study CLEE011A2117, a Phase I, single center, two-period, two-treatment, open label, randomized crossover study to investigate the absolute bioavailability of a single oral dose of 600 mg of ribociclib relative to an intravenous (i.v.) infusion of 150 mg ribociclib in healthy subjects.
- Update of sections 4.2 and 4.5 of the SmPC in order to update the recommended dose modification when ribociclib is administered in combination with CYP3A4 inhibitors and update the drug-drug interaction information on substances that may increase ribociclib plasma concentrations based on the updated PBPK modelling.
In addition, the MAH took this opportunity to introduce minor editorial changes to the Package Leaflet."

Koselugo - selumetinib - EMEA/H/C/005244/II/0013, Orphan

AstraZeneca AB, Rapporteur: Alexandre Moreau, "Update of sections 4.2 and 5.2 of the SmPC in order to update the recommended dosage regimen to remove the fasting state and update pharmacokinetic information, based on the final results from study D1346C00015; this is a phase 1, single-arm, sequential study to evaluate the effect of food on the gastrointestinal tolerability and pharmacokinetics of selumetinib after multiple doses in adolescent children with neurofibromatosis type 1 (NF1) related plexiform neurofibromas (PN). The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Nexviadyme - avalglucosidase alfa - EMEA/H/C/005501/II/0008

Sanofi B.V., Rapporteur: Christian Gartner, "Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to update the list of adverse drug reactions (ADRs) and to update the safety and efficacy information, based on interim results

from the open-label extension period of study EFC14028 as well as pooled safety and immunogenicity data. EFC14028 is a phase 3 randomized, multicenter, multinational, double-blinded study comparing the efficacy and safety of repeated biweekly infusions of avalglucosidase alfa and alglucosidase alfa in treatment naïve patients with late-onset Pompe disease. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."	
NUVAXOVID - Covid-19 vaccine (recombinant, adjuvanted) - EMEA/H/C/005808/II/0048/G Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege	
Orgovyx - relugolix - EMEA/H/C/005353/II/0012 Accord Healthcare S.L.U., Rapporteur: Johann Lodewijk Hillege, "Update of section 4.5 of the SmPC based on final results from study MVT-601-9039; this is an In vitro Interaction Study of Relugolix with human OATP2B1 Uptake Transporter."	
Paxlovid - nirmatrelvir / ritonavir - EMEA/H/C/005973/II/0040/G Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, "Grouped application comprising two type II variations as follows: - Update of section 4.3 of the SmPC in order to add 'Mineralocorticoid receptor antagonists: finerenone' and 'Opioid antagonists: naloxegol' under Medicinal products that are highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening reactions and to add 'primidone' and 'Cystic fibrosis transmembrane conductance regulator potentiators: lumacaftor/ivacaftor' under Medicinal products that are potent CYP3A inducers where significantly reduced nirmatrelvir/ritonavir plasma concentrations may be associated with the potential for loss of virologic response and possible resistance based on the review of the PI for a number of medicines from different drug classes that are metabolized by CYP3A4 or CYP2D6, transported by P-gp, or induce CYP3A4.	

- Update of section 4.5 of the SmPC in order to add drug-drug interaction information with Alpha1-adrenoreceptor antagonist, Analgesics, Antiarrhythmics, Anticoagulants, Anticonvulsants, Anti-HIV, Anti-infectives, β2-agonist (long acting), Calcium channel antagonists, Cardiovascular agents and Migraine medicinal products, to add drug-drug interaction information with Cystic fibrosis transmembrane conductance regulator potentiators, Dipeptidyl peptidase 4 (DPP4) inhibitors, Janus kinase (JAK) inhibitors, Mineralocorticoid receptor antagonists, Muscarinic receptor antagonists, Neuropsychiatric agents and Opioid antagonists and order to remove cross reference to section 4.4 from information regarding coadministration of Paxlovid with Antidepressants based on the review of the PI for a number of medicines from different drug classes that are metabolised by CYP3A4 or CYP2D6, transported by P-gp, or induce CYP3A4."	
Paxlovid - nirmatrelvir / ritonavir - EMEA/H/C/005973/II/0042 Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, "Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update efficacy, safety and pharmacokinetic information, based on updated results from studies C4671005 (EPIC-HR), C4671002 (EPIC-SR) and C4671006 (EPIC-PEP) as well as a supplemental report to Pop PK analysis PMAR-EQDD-C467a-DP4-1323, following the reanalysis of data after the removal of data related to four sites from the Paxlovid data analysis."	
RINVOQ - upadacitinib - EMEA/H/C/004760/II/0034 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, "Submission of the final report from study M13-542, listed as a category 3 study in the RMP. This is a phase 3, randomized, double-blind study comparing upadacitinib (ABT-494) to placebo on stable conventional synthetic disease-modifying anti rheumatic drugs (csDMARDs) in subjects with moderately to severely active rheumatoid arthritis with inadequate response or intolerance to biologic DMARDs (bDMARDs)."	
RINVOQ - upadacitinib - EMEA/H/C/004760/II/0035	

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, "Submission of the final report from study M13-549 listed as a category 3 study in the RMP. This is a Phase III, Randomized, Double-Blind Study Comparing Upadacitinib (ABT-494) to Placebo in Subjects with Moderately to Severely Active Rheumatoid Arthritis Who Are on a Stable Dose of Conventional Synthetic Disease-Modifying Anti Rheumatic Drugs (csDMARDs) and Have an Inadequate Response to csDMARDs."

Scemblix - asciminib - EMEA/H/C/005605/II/0004/G, Orphan

Novartis Europharm Limited, Rapporteur: Janet Koenig, "Grouped application comprising two type II variations as follows:
- Submission of the final reports from study DMPK-R2200470 (REC). This is an in vitro evaluation of inducibility of OATP1V1, MDR1 and CYP3A4 by asciminib using human hepatocytes.
- Submission of the final report from study DMPK-R2270399 (REC). This is a physiologically based PK modelling and simulations to characterize the effect of cyclodextrins on the exposure of asciminib."

Spinraza - nusinersen - EMEA/H/C/004312/II/0029, Orphan

Biogen Netherlands B.V., Rapporteur: Bruno Sepodes, "Update of section 5.3 of the SmPC in order to update non-clinical information based on final results from study P058-17-02. This is a 24-month carcinogenicity study when administered by subcutaneous injection in mouse."

Xultophy - insulin degludec / liraglutide - EMEA/H/C/002647/II/0049

Novo Nordisk A/S, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to add dysgeusia to the list of adverse drug reactions (ADRs) with frequency uncommon based on post-marketing data and literature. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update section 4.9 of the SmPC to update overdose information and to amend Annex A."

Zokinvy - lonafarnib - EMEA/H/C/005271/II/0004, Orphan

EigerBio Europe Limited, Rapporteur: Johann

Lodewijk Hillege, "Update of sections 4.2, 4.4, 4.5 and 6.6 of the SmPC in order to update drug-drug interaction information based on final results from Drug-Drug Interaction study EIG-LNF-021. This is a phase I, single-center, two period, single sequence, study to assess the effects of lonafarnib autoinhibition following multiple-dose lonafarnib and the effects of a nonspecific CYP2C9 inhibitor on multiple-dose lonafarnib pharmacokinetics in healthy subjects. The Package Leaflet is updated accordingly."	
WS2467 **Adrovance-** **EMEA/H/C/000759/WS2467/0051** **FOSAVANCE-** **EMEA/H/C/000619/WS2467/0054** **VANTAVO-** **EMEA/H/C/001180/WS2467/0041** Organon N.V., Lead Rapporteur: Christian Gartner, "Update of sections 4.4 and 4.8 of the SmPC in order to include information on the risk of low-energy fractures in bones other than femur based on post-marketing case reports and the literature. The Package Leaflet and Labelling are updated accordingly. In addition, the MAH the opportunity to update the list of local representatives in the Package Leaflet, to bring the PI in line with the latest QRD template and to introduce editorial changes."	
WS2489/G **Kinzalmono-** **EMEA/H/C/000211/WS2489/0119/G** **Micardis-** **EMEA/H/C/000209/WS2489/0127/G** **Pritor-** **EMEA/H/C/000210/WS2489/0132/G** Boehringer Ingelheim International GmbH, Lead Rapporteur: Armando Genazzani, "Grouped application consisting of: C.I.4: Update of section 4.8 of the SmPC in order to include "hyponatremia" to the list of adverse drug reactions (ADRs) with frequency "rare", based on post marketing data and literature; C.I.z (Type IB unforeseen): Update of section 4.2 of the SmPC to include the possibility of using the combination of telmisartan and amlodipine for lowering blood pressure based on literature;	

C.I.z (Type IB unforeseen): Update of section 4.7 of the SmPC to replace the terms "dizziness" and "drowsiness" by "syncope" and "vertigo" to align with adverse reactions table in section 4.8 of SmPC. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, bring the PI in line with the latest QRD template version 10.3 and to implement editorial changes to the SmPC."	
WS2492 **Glyxambi-** **EMEA/H/C/003833/WS2492/0052** **Synjardy-** **EMEA/H/C/003770/WS2492/0071** Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "Submission of the final report from study PASS 1245-0137 listed as a category 3 study in the RMP. This is a multicentre international randomised parallel group double-blind placebo-controlled clinical trial of EMPAgliflozin once daily to assess cardiorenal outcomes in patients with chronic kidney disease."	

B.6.10. CHMP-PRAC assessed procedures

Enhertu - trastuzumab deruxtecan - **EMEA/H/C/005124/II/0031** Daiichi Sankyo Europe GmbH, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Inês Ribeiro-Vaz, "Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update safety, efficacy and pharmacokinetic information based on data from study DS8201-A-U301 and study DS8201-A-U302. Study U301 was a Phase 3, randomized, 2-arm, open-label, multicenter study designed to compare the safety and efficacy of T-DXd vs TPC in HER2-positive, unresectable and/or metastatic BC subjects who were resistant or refractory to T-DM1. Study U302 was a Phase 3, multicenter, randomized, open-label, 2-arm, active-controlled study in subjects with unresectable and/or metastatic HER2-positive (IHC 3+ or ISH-positive) BC previously treated with trastuzumab plus taxane in the advanced/metastatic setting or who had progressed within 6 months after neoadjuvant or adjuvant treatment involving a regimen	

including trastuzumab plus taxane. The Package Leaflet and Annex II are updated accordingly. The updated RMP version 4.1 has also been submitted."	
Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0130 AstraZeneca AB, Rapporteur: Christophe Focke, PRAC Rapporteur: Jean-Michel Dogné, "Submission of the final report from study MA-VA-MEDI3250-1116 (A Case Control Study of the Effectiveness of Q/LAIV Versus Inactivated Influenza Vaccine and No Vaccine in Subjects 2 to 17 Years of Age) listed as a category 3 study in the RMP. This was an observational study. The objective of this study was to evaluate the effectiveness of Q/LAIV compared to IIV or no vaccine in community-dwelling subjects 2 to 17 years of age against laboratory-confirmed influenza. The RMP version 11.0 has also been submitted."	
Veklury - remdesivir - EMEA/H/C/005622/II/0050 Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, PRAC Rapporteur: Eva Jirsová, "Update of sections 4.2, 4.4, 4.8 and 5.2 of the SmPC in order to address the safety of remdesivir and its metabolites in patients with hepatic impairment and to update information on hepatic and coagulation laboratory abnormalities based on final results from study GS US 540 9014: "A phase 1 open-label, adaptive, single-dose study to evaluate the pharmacokinetics of remdesivir and its metabolite(s) in subjects with normal hepatic function and hepatic impairment", listed as a category 3 study in the RMP, and on safety data from post-marketing and clinical trials experience. The Package Leaflet is updated accordingly. The RMP version 5.4 has also been submitted. In addition, the MAH took the opportunity submit Minor Linguistic Amendments (MLA) for Veklury."	
XOSPATA - gilteritinib - EMEA/H/C/004752/II/0013, Orphan Astellas Pharma Europe B.V., Rapporteur: Ingrid Wang, PRAC Rapporteur: Martin Huber, "Update of sections 4.2 and 5.2 in order to update the information on renal impairment based on final	

results from study 2215-CL-0114, listed as a category 3 study in the RMP. Study 2215-CL-0114 is a phase 1, single-dose, open-label study to investigate the effect of renal impairment on gilteritinib pharmacokinetics, safety and tolerability in 9 participants with severe renal impairment compared to 8 participants with normal renal function.
The RMP version 4.0 has also been submitted.
In addition, the MAH took the opportunity to introduce editorial changes."

B.6.11. PRAC assessed procedures

PRAC Led
CABOMETYX - cabozantinib - EMEA/H/C/004163/II/0033
Ipsen Pharma, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report from study F-FR-60000-001 (CASSIOPE) listed as a category 3 study in the RMP. This is a prospective, non-imposed and non-interventional study of cabozantinib tablets in adults with advanced renal cell carcinoma (RCC) following prior vascular endothelial growth factor (VEGF)-targeted therapy. The RMP version 7.0 has also been submitted."

PRAC Led
Eurartesim - piperaquine tetraphosphate / artenimol - EMEA/H/C/001199/II/0040/G
Alfasigma S.p.A., PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "C.I.13: Submission of the final report from the effectiveness evaluation survey for Eurartesim (protocol no. 3366) listed as a category 3 study in the RMP. This is a European multi-centre online survey to assess physician understanding of the revised edition of the educational material. Consequential changes to RMP version 16.1 have been implemented.
C.I.11.b: Submission of an updated RMP version 16.1 in order to delete "Severe Malaria" from the Missing Information."

PRAC Led
EXJADE - deferasirox - EMEA/H/C/000670/II/0085
Novartis Europharm Limited, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre

Moreau, "Submission of an updated RMP version 21.0 in order to include the physician survey CICL670A2429 as a PASS category 3, based on the submission of a draft version of the protocol for the physician survey CICL670A2429. The Annex IID is updated to remove one sentence related to 'surveillance programme' and to introduce a minor correction."

PRAC Led

JCOVDEN - COVID-19 vaccine Janssen (Ad26.COV2.S) - EMEA/H/C/005737/II/0071/G

Janssen-Cilag International N.V., PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Grouped application consisting of:
1) Submission of the final study report of a clinical TTS characterisation study listed as a category 3 study in the RMP. This is a Test Pre- and Post-Vaccination Serum Across All Populations Using Clinical Samples From Ad26-based Company Vaccine Studies Other Than Ad26.COV2.S;
2) Submission of the Addendum to final CSR of the study VAC31518COV2001 listed as a category 3 study in the RMP. This is a randomized, double-blind, placebo-controlled Phase 2a study to evaluate a range of dose levels and vaccination intervals of Ad26.COV2.S in healthy adults aged 18 to 55 years, and adults aged 65 years and older. The RMP version 6.1 has also been submitted."

PRAC Led

JCOVDEN - COVID-19 vaccine Janssen (Ad26.COV2.S) - EMEA/H/C/005737/II/0072/G

Janssen-Cilag International N.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Update of section 4.4 of the SmPC in order to add a new warning on pericarditis and myocarditis and update of section 4.8 of the SmPC to add myocarditis and pericarditis to the list of adverse drug reactions (ADRs) with frequency not known based on post-marketing data and three observational claims databases in US. The Package Leaflet is updated accordingly. The RMP version 6.2 has also been submitted. In addition, the MAH took the

opportunity to update the ATC Code as amended by the WHO."

PRAC Led

Nexium Control - esomeprazole - EMEA/H/C/002618/II/0038

GlaxoSmithKline Dungarvan Ltd, PRAC Rapporteur: Rugile Pilviniene, PRAC-CHMP liaison: Vilma Petrikaite, "Submission of an updated RMP version 2.0 in order to update the list of safety concerns to meet the definition of important risk and missing information provided in GVP Module V Rev. 2"

PRAC Led

Olumiant - baricitinib - EMEA/H/C/004085/II/0039/G

Eli Lilly Nederland B.V., PRAC Rapporteur: Adam Przybylkowski, PRAC-CHMP liaison: Ewa Balkowiec Iskra, "Submission of the final reports from studies I4V-MC-B016 and I4V-MC-B011 listed as category 3 non-interventional PASS studies in the RMP. B016 is a drug utilisation study for the assessment of off-label use of baricitinib in the paediatric population in the United Kingdom. B011 is a retrospective cohort study to assess the safety of baricitinib compared with other therapies used in the treatment of rheumatoid arthritis in Nordic countries. The RMP version 19.1 has also been submitted."

PRAC Led

Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0144

Boehringer Ingelheim International GmbH, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Thalia Marie Estrup Blicher, "Submission of the final report from the Human Factors Study (007-HFE-009035), listed as a category 3 study in the RMP; this is a non-interventional study to assess the effectiveness of a training video to mitigate potential medication errors during the reconstitution and dosing of the dabigatran etexilate paediatric oral solution."

PRAC Led

Revlimid - lenalidomide - EMEA/H/C/000717/II/0126

Bristol-Myers Squibb Pharma EEIG, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP

liaison: Alexandre Moreau, "Submission of the final report from study CC-5013-MDS-010 listed as an obligation in the Annex II of the Product Information. This is a prospective non-interventional post-authorisation safety study (PASS), designed as a disease registry of patients with transfusion dependent IPSS low or intermediate-1-risk myelodysplastic syndromes (MDS) and isolated del(5q). Section D of the Annex II and the RMP (version 39) are updated accordingly."

PRAC Led
WS2483
Lixiana-EMEA/H/C/002629/WS2483/0045
Roteas-EMEA/H/C/004339/WS2483/0032
Daiichi Sankyo Europe GmbH, Lead PRAC Rapporteur: Nathalie Gault, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final report from DSE-EDO-04-14-EU (Non-Interventional Study on Edoxaban Treatment in Routine Clinical Practice for Patients with Non-Valvular Atrial Fibrillation, ETNA-AF Europe), listed as a category 3 study in the RMP (MEA 006). This is a multicentre, prospective, non-interventional, observational PASS. The RMP version 15.1 has also been submitted."

PRAC Led
WS2487
Humalog-
EMEA/H/C/000088/WS2487/0199
Liprolog-
EMEA/H/C/000393/WS2487/0159
Eli Lilly Nederland B.V., Lead PRAC Rapporteur: Mari Thorn, PRAC-CHMP liaison: Kristina Dunder, "To remove severe hypoglycemia as a result of incorrect or incomplete data provided to a compatible software application which is listed as an important potential risk for the Tempo Pen and all associated risk minimisation measures, following PRAC assessment of F3Z-MC-B030 PASS protocol (EMA/PRAC/781358/2022, 29 September 2022)."

B.6.12. CHMP-CAT assessed procedures

Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0018/G, ATMP

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Concetta Quintarelli, CHMP Coordinator: Armando Genazzani

CARVYKTI - ciltacabtagene autoleucel - EMEA/H/C/005095/II/0016, Orphan, ATMP
Janssen-Cilag International NV, Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0070/G, Orphan, ATMP
Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

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

WS2427/G
Silodosin Recordati- EMEA/H/C/004964/WS2427/0011/G
Silodyx- EMEA/H/C/001209/WS2427/0051/G
Urorec- EMEA/H/C/001092/WS2427/0054/G
Recordati Ireland Ltd, Generic, Generic of Urorec, Lead Rapporteur: Margareta Bego

WS2445
Ambirix- EMEA/H/C/000426/WS2445/0127
Cervarix- EMEA/H/C/000721/WS2445/0122
Fendrix- EMEA/H/C/000550/WS2445/0082
Infanrix hexa- EMEA/H/C/000296/WS2445/0329
Synflorix- EMEA/H/C/000973/WS2445/0180
Twinrix Adult- EMEA/H/C/000112/WS2445/0162
Twinrix Paediatric- EMEA/H/C/000129/WS2445/0163
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Kristina Dunder

WS2456/G
Infanrix hexa-
EMEA/H/C/000296/WS2456/0328/G
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke

WS2458
Juluca-EMEA/H/C/004427/WS2458/0051
Tivicay-EMEA/H/C/002753/WS2458/0087
Triumeq-
EMEA/H/C/002754/WS2458/0112
ViiV Healthcare B.V., Lead Rapporteur: Janet Koenig

WS2466
Fluenz Tetra-
EMEA/H/C/002617/WS2466/0128
Pandemic influenza vaccine H5N1
AstraZeneca-
EMEA/H/C/003963/WS2466/0063
AstraZeneca AB, Lead Rapporteur: Christophe Focke

WS2468/G
Hexacima-
EMEA/H/C/002702/WS2468/0148/G
Hexyon-
EMEA/H/C/002796/WS2468/0152/G
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

WS2469
Hexacima-
EMEA/H/C/002702/WS2469/0147
Hexyon-
EMEA/H/C/002796/WS2469/0151
MenQuadfi-
EMEA/H/C/005084/WS2469/0023
Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus

WS2472
Afinitor-
EMEA/H/C/001038/WS2472/0085
Votubia-
EMEA/H/C/002311/WS2472/0081
Novartis Europharm Limited, Lead Rapporteur: Janet Koenig

WS2473
ProQuad-
EMEA/H/C/000622/WS2473/0161

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. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

E.2. Time Tables – starting & ongoing procedures: For information

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

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

G. ANNEX G

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

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

G.2. PRIME

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

G.2.1. List of procedures concluding at 23-26 April 2023 CHMP plenary:

G.2.2. List of procedures starting in April 2023 for May 2023 CHMP adoption of outcomes

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