EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 February 2023
EMA/CHMP/44874/2023 Corr.1[1]
Human Medicines Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 20-23 February 2023

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

20 February 2023, 09:00 – 19:30, virtual meeting/room 1C

21 February 2023, 08:30 – 19:30, virtual meeting/room 1C

22 February 2023, 08:30 – 19:30, virtual meeting/room 1C

23 February 2023, 08:30 – 14:00, 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).

[1] Correction in sections 8.1 and 9.1.3

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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 20-23 February 2023. See February 2023 CHMP minutes (to be published post March 2023 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 20-23 February 2023.

1.3. Adoption of the minutes

CHMP minutes for 23 -26 January 2023.

Minutes from PReparatory and Organisational Matters (PROM) meeting held on 13 February 2023.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. mavacamten - EMEA/H/C/005457

treatment of symptomatic obstructive hypertrophic cardiomyopathy

Scope: Oral explanation

Action: Oral explanation to be held on 22 February 2023 at 16:00

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

2.1.2. molnupiravir - EMEA/H/C/005789

treatment of coronavirus disease 2019 (COVID-19)

Scope: Oral explanation

Action: Oral explanation to be held on 21 February 2023 at 16:00

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

2.1.3. ruxolitinib - EMEA/H/C/005843

treatment of non-segmental vitiligo

Scope: Oral explanation

Action: Oral explanation to be held on 22 February 2023 at 14:00

List of Outstanding Issues adopted on 13.10.2022. List of Questions adopted on 24.02.2022.

2.1.4. raltegravir potassium - EMEA/H/C/005813

treatment of human immunodeficiency virus (HIV-1)

Scope: Oral explanation

Action: Oral explanation to be held on 21 February 2023 at 11:00

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

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

2.3.1. Libtayo - cemiplimab - EMEA/H/C/004844/II/0028

Regeneron Ireland Designated Activity Company (DAC)

Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include Libtayo in combination with platinum-based chemotherapy for the first-line treatment of adult patients with locally advanced NSCLC who are not candidates for definitive chemoradiation or metastatic NSCLC with no EGFR, ALK or ROS1 aberrations; as a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.0 of the RMP has also been submitted."

Scope: Oral explanation

Action: Oral explanation to be held on 22 February 2023 at 11:00

Request for Supplementary Information adopted on 15.12.2022, 21.07.2022, 22.04.2022.

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. niraparib / abiraterone acetate - EMEA/H/C/005932

treatment of adult patients with prostate cancer

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 15.12.2022. List of Questions adopted on 15.09.2022.

3.1.2. eculizumab - EMEA/H/C/005652

treatment of paroxysmal nocturnal haemoglobinuria

Scope: Opinion

Action: For adoption

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

3.1.3. pegunigalsidase alfa - Orphan - EMEA/H/C/005618

Chiesi Farmaceutici S.p.A.; treatment of Fabry disease

Scope: Opinion

Action: For adoption

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

3.1.4. sirolimus - Orphan - EMEA/H/C/005896

Plusultra pharma GmbH; Treatment of angiofibroma associated with tuberous sclerosis complex

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 22.04.2022.

3.1.5. ivosidenib - Orphan - EMEA/H/C/005936

Les Laboratoires Servier; treatment of acute myeloid leukaemia and treatment of metastatic cholangiocarcinoma

Scope: Opinion

Action: For adoption

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

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

Les Laboratoires Servier; treatment of acute myeloid leukaemia

Scope: Opinion

Action: For adoption

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

3.1.7. vadadustat - EMEA/H/C/005131

treatment of anaemia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.01.2023, 15.12.2022, 15.09.2022. List of Questions adopted on 24.03.2022.

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

3.2.1. sodium phenylbutyrate / ursodoxicoltaurine - Orphan - EMEA/H/C/005901

Amylyx Pharmaceuticals EMEA B.V.; treatment of amyotrophic lateral sclerosis (ALS)

Scope: List of outstanding issues

Action: For adoption

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

3.2.2. enalapril maleate - PUMA - EMEA/H/C/005731

treatment of heart failure

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 21.07.2022.

3.2.3. dabigatran etexilate - EMEA/H/C/005922

prevention of venous thromboembolic events

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 23.06.2022.

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

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 15.09.2022.

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

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 13.10.2022.

3.2.6. adagrasib - EMEA/H/C/006013

treatment of patients with advanced non-small cell lung cancer (NSCLC) with KRAS G12C mutation

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 15.09.2022.

3.2.7. lacosamide - EMEA/H/C/006047

treatment of epilepsy

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 15.09.2022.

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

Taiho Pharma Netherlands B.V.; treatment of cholangiocarcinoma

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 15.09.2022.

3.2.9. eculizumab - EMEA/H/C/006036

treatment of paroxysmal nocturnal haemoglobinuria

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 10.11.2022.

3.2.10. sugammadex - EMEA/H/C/006046

reversal of neuromuscular blockade induced by rocuronium or vecuronium

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 15.09.2022.

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

3.3.1. vamorolone - Orphan - EMEA/H/C/005679

Santhera Pharmaceuticals (Deutschland) GmbH; Treatment of Duchenne muscular dystrophy (DMD)

Scope: List of questions

Action: For adoption

3.3.2. cabotegravir - EMEA/H/C/005756

pre-exposure prophylaxis of HIV-1 infection

Scope: List of questions

Action: For adoption

3.3.3. lebrikizumab - EMEA/H/C/005894

Treatment of moderate-to-severe atopic dermatitis in adults and adolescents

Scope: List of questions

Action: For adoption

3.3.4. eribulin - EMEA/H/C/006134

treatment of breast cancer and liposarcoma

Scope: List of questions

Action: For adoption

3.3.5. epcoritamab - Orphan - EMEA/H/C/005985

AbbVie Deutschland GmbH & Co. KG; treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL)

Scope: List of questions

Action: For adoption

3.3.6. epinephrine - EMEA/H/C/006139

Treatment of allergic reactions (anaphylaxis) and idiopathic or exercise induced anaphylaxis

Scope: List of questions

Action: For adoption

3.3.7. ranibizumab - EMEA/H/C/006055

treatment of neovascular age-related macular degeneration (AMD)

Scope: List of questions

Action: For adoption

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

3.4.1. aripiprazole - EMEA/H/C/005929

Maintenance treatment of schizophrenia

Scope: Letter by the applicant dated 03.02.2023 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in January 2023.

Action: For adoption

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

3.4.2. germanium (68Ge) chloride / gallium (68Ga) chloride - EMEA/H/C/005165

indicated for in vitro labelling of kits for radiopharmaceutical preparation

Scope: Letter by the applicant dated 13.02.2023 requesting an extension to the clock stop to respond to the list of questions adopted in December 2021.

Action: For adoption

List of Questions adopted on 16.12.2021.

3.4.3. efbemalenograstim alfa - EMEA/H/C/005828

Reduction in the duration of neutropenia and the incidence of febrile neutropenia.

Scope: Letter by the applicant dated 17.02.2023 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in July 2022.

Action: For adoption

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

3.4.4. pegfilgrastim - EMEA/H/C/005810

Treatment of neutropenia

Scope: Letter by the applicant dated 17.02.2023 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in October 2022.

Action: For adoption

List of Outstanding Issues adopted on 13.10.2022. List of Questions adopted on 27.01.2022.

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: Re-examination request, appointment of re-examination rapporteurs

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.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

No items

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

4.2.1. 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 old 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 Questions adopted on 13.10.2022.

4.2.2. 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 Questions adopted on 21.07.2022.

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

No items

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. Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - ATMP - EMEA/H/C/004731/II/0005

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Concetta Quintarelli, CHMP Coordinator: Armando Genazzani, PRAC Rapporteur: Gabriele Maurer

Scope: "Extension of indication to include treatment of adult patients with Second-line (2L) Transplant Intended (TI) Large B-Cell Lymphoma (LBCL) for Breyanzi, based on interim analyses from pivotal study JCAR017-BCM-003; this is a global randomized multicentre Phase III Trial to compare the efficacy and safety of JCAR017 to standard of care in adult subjects with high-risk, transplant-eligible relapsed or refractory aggressive B-cell Non-Hodgkin Lymphomas (TRANSFORM); As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 09.09.2022.

5.1.2. Esbriet - pirfenidone - EMEA/H/C/002154/II/0074

Roche Registration GmbH

Rapporteur: Finbarr Leacy, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Extension of indication to include treatment of 'advanced' idiopathic pulmonary fibrosis (IPF) by the deletion of the current qualifier 'mild to moderate', based on the results from study MA29957; this is a 52-week Phase IIb, multicentre, randomised, double-blind, placebo-controlled clinical trial in IPF patients with advanced lung function impairment

(DLco < 40% of predicted) and at high risk of grade 3 pulmonary hypertension, and additional analyses performed on the original pivotal trials for pirfenidone in IPF.
As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. In addition, the MAH took the opportunity to include information in section 4.4 of the SmPC related to the content of sodium per Esbriet capsule and tablet. The Package Leaflet is updated in accordance. Version 12.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 13.10.2022, 19.05.2022.

5.1.3. Mircera - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/II/0092

Roche Registration GmbH

Rapporteur: Maria Concepcion Prieto Yerro

Scope: "Extension of indication to include treatment of paediatric patients from 3 months to less than 18 years of age requiring dialysis or not yet on dialysis and switching from another ESA to Mircera, based on final results from study NH19708; this is a single-arm, open-label, Phase II study of Mircera in patients aged 3 months to <18 years with CKD on dialysis or not yet on dialysis to generate PK, efficacy, and safety data for subcutaneous (SC) administration of Mircera. In addition, supportive data from studies NH19707, Modelling & Simulation study (study 3) and MH40258 were included. 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 introduce minor editorial changes to the PI and to update the Instruction for Use in the Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2022.

5.1.4. Nordimet - methotrexate - EMEA/H/C/003983/II/0027

Nordic Group B.V.

Rapporteur: Bruno Sepodes, PRAC Rapporteur: Martin Huber

Scope: "Extension of indication to include treatment of moderate to severe recalcitrant disabling psoriasis for Nordimet, based on literature; As a consequence, sections 4.1 and 4.2 of the SmPC were updated. The package leaflet is updated in accordance. Version 6.0 of the RMP has also been submitted."

Action: For adoption

5.1.5. 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 13.10.2022, 23.06.2022.

5.1.6. Rinvoq - upadacitinib - EMEA/H/C/004760/II/0027

AbbVie Deutschland GmbH & Co. KG

Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication to include treatment of moderately to severely active Crohn's disease in adult patients for Rinvoq, based on final results from three Phase III studies, two confirmatory placebo-controlled induction studies (study M14 431/U-EXCEED/CD-1) and study M14 433/U-EXCEL/CD-2) and a placebo-controlled maintenance/long-term extension study (study M14-430/U-ENDURE/CD-3).
M14-431 study is a Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled Induction Study of the Efficacy and Safety of Upadacitinib (ABT-494) in Subjects with Moderately to Severely Active Crohn's Disease Who Have Inadequately Responded to or are Intolerant to Biologic Therapy.
M14-433 study is a Phase III, Multicenter, Randomized, Double-Blind, Placebo Controlled Induction Study of the Efficacy and Safety of Upadacitinib (ABT-494) in Subjects with Moderately to Severely Active Crohn's Disease Who Have Inadequately Responded to or are Intolerant to Conventional and/or Biologic Therapies.
M14-430 study is an ongoing Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled Maintenance and Long-Term Extension Study of the Efficacy and Safety of Upadacitinib (ABT-494) in Subjects with Crohn's Disease Who Completed the Studies M14-431 or M14-433.
As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 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 26.01.2023, 10.11.2022.

5.1.7. 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 13.10.2022, 19.05.2022.

5.1.8. Ryeqo - relugolix / estradiol / norethisterone acetate - EMEA/H/C/005267/II/0013/G

Gedeon Richter Plc.

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Martin Huber

Scope: "Extension of indication to include treatment of moderate to severe pain associated with endometriosis for Ryeqo in adult women of reproductive age with a history of previous medical or surgical treatment for their endometriosis, based on final results from studies MVT-601-3101 and MVT-601-3102 and final results up to 104 weeks from study MVT-601-3103. Studies 3101 and 3102 are pivotal, phase III, randomised, double-blind, placebo-controlled, safety and efficacy studies to evaluate relugolix with E2 and NETA as a combination therapy for pain associated with endometriosis. Study 3103 is an open-label extension study including patients who completed one of the two pivotal studies and met the eligibility criteria, regardless of their treatment assignment in the pivotal studies. In the extension part all patients received relugolix combination therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC were updated. The Package Leaflet is updated in accordance.
Update of section 4.5 of the SmPC to update information regarding Drug-Drug Interaction based on final results of DDI studies MVT-601-54, MVT-601-55 and MVT-601-57. Study MVT-601-54 is a 2-part interventional open-label study to assess the potential effects of erythromycin on the PK of the 3 components of Ryeqo. Study MVT-601-55 is an interventional open label fixed single sequence cross-over study to assess whether a 6-hour dose separation is sufficient to mitigate absorption mediated increased exposure to relugolix and study MVT-601-057 is a 2-part study to assess the potential effect of relugolix on the PK of total dabigatran.
The updated RMP version (2.0) has also been submitted. As part of the application, the MAH also requests an extension of the market protection by one additional year.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

5.1.9. Soliris - eculizumab - Orphan - EMEA/H/C/000791/II/0126

Alexion Europe SAS

Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Monica Martinez Redondo

Scope: "Extension of indication to include treatment of paediatric patients with refractory generalised myasthenia gravis (gMG) for Soliris, based on interim results from study ECU-MG-303; this is an open-label, multicenter, phase 3 study to evaluate the efficacy, safety, pharmacokinetics and pharmacodynamics of intravenous (IV) eculizumab in paediatric patients aged 6 to less than 18 years with acetylcholine receptor-antibody (AChR-Ab) positive (+) refractory gMG. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 20.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to update section 4.8 of the SmPC in order to update the frequency of the list of adverse drug reactions (ADRs) based on cumulative safety data and to introduce minor editorial changes to the PI."

Action: For adoption

5.1.10. TachoSil - human thrombin / human fibrinogen - EMEA/H/C/000505/II/0117

Corza Medical GmbH

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

Scope: "Extension of indication to include treatment of children aged 1 month to 18 years, based on available bibliographical data, results from study TC-2402-040-SP which compared TachoSil with Surgicel Original as adjunct to primary surgical treatment in both adult and paediatric subjects, and results from study TC-019-IN; a prospective, uncontrolled study in paediatric subjects. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes in the product information. Version 0.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 26.01.2023, 15.09.2022.

5.1.11. Wegovy - semaglutide - EMEA/H/C/005422/II/0009

Novo Nordisk A/S

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Mari Thorn

Scope: "Extension of indication to include treatment of adolescents for weight management for Wegovy based on final results from study NN9536-4451; this trial was conducted to assess the effect and safety of semaglutide in the paediatric population in order to address the unmet need for treatment of adolescents ages 12 to <18 years with obesity.
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 8.0 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.2."

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

5.2.1. Bylvay - odevixibat – Orphan - EMEA/H/C/004691/II/0011

Albireo

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension of indication to include treatment of cholestasis and pruritus in Alagille syndrome (ALGS) in patients from birth and older for Bylvay, based on final results from study A4250-012 and interim results from study A4250-015. Study A4250-012 is a 24-week, randomised, double-blind, placebo-controlled Phase III study conducted in 52

patients with a genetically confirmed diagnosis of ALGS and presence of pruritus and high serum bile acid levels at baseline. Study A4250-015 is an ongoing 72-week open-label extension trial for patients who completed study A4250-012 and evaluates the long-term safety and efficacy of Bylvay in patients with ALGS. 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 2.1 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)

Update on the procedure; intervention by third party

Action: for information

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

No items

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/006201

to detect internal tandem duplication (ITD) and tyrosine kinase domain (TKD) mutations D835 and I836

Scope: Opinion

Action: For adoption

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

8.1.1. iptacopan hydrochloride - Orphan - H0005764

Novartis Europharm Limited; Treatment of Paroxysmal Nocturnal Haemoglobinuria (PNH)

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

Action: For adoption

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. COVID-19 Vaccine (inactivated, adjuvanted) Valneva - COVID-19 vaccine (inactivated, adjuvanted, adsorbed) - EMEA/H/C/006019/II/0004

Valneva Austria GmbH

Rapporteur: Daniela Philadelphy

Scope: "Update of sections 4.2 and 5.1 of the SmPC in order to include a booster dose for adults 18 to 50 years of age based on the interim results from study VLA2001-301 (Booster part); this is a randomized, observer-blind, controlled, superiority study to compare the immunogenicity of COVID-19 Vaccine (inactivated, adjuvanted) Valneva to AZD1222, where participants received a booster dose of COVID-19 vaccine Valneva; the Package Leaflet is updated accordingly."

Action: For adoption

Request for Supplementary Information adopted on 15.12.2022.

9.1.2. 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: Silvijus Abramavicius

Scope: "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 known" 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."

Action: For adoption

Request for Supplementary Information adopted on 24.11.2022, 06.10.2022.

9.1.3. Buvidal - buprenorphine - EMEA/H/C/004651/II/0017

Camurus AB

Rapporteur: Finbarr Leacy, Co-Rapporteur: Robert Porszasz, PRAC Rapporteur: Tiphaine Vaillant

Scope: "To add the new therapeutic indication of treatment of moderate to severe chronic pain in patients with opioid dependence. As a consequence, sections 4.1, 4.2, 4.5, 5.1 and 6.6 of the SmPC and sections 1, 3 and Instruction for use of the PL are updated accordingly. The updated RMP version 2.1 has also been submitted."

Withdrawal of extension of indication application.

Action: For information

Request for Supplementary Information adopted on 23.06.2022, 24.02.2022.

10. Referral procedures

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

No items

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

No items

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

No items

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

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

February 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 items

14.1.2. CHMP membership

CHMP co-opted membership

Election of a co-opted member. With his nomination as CHMP alternate for Austria, the co-opted member mandate for Christian Gartner came to an end on 31.12.2022.

The CHMP agreed that a co-opted member should be appointed in the following area of expertise: biostatistics/ clinical trial methodology. A call for nomination of a co-opted member was launched following the January 2023 plenary.

Nomination(s) received

Action: For election

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 February 2023

Action: For adoption

14.2.2. Paediatric Committee (PDCO)

PIPs reaching D30 at February 2023 PDCO

Action: For information

Report from the PDCO meeting held on 21-24 February 2023

Action: For information

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

14.3.1. Biologics Working Party (BWP)

Chair: Sol Ruiz/ Sean Barry

Reports from BWP February 2023 meeting to CHMP for adoption:

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

Action: For adoption

14.3.2. Election of Chairperson – Biologics Working Party (BWP)

Sol Ruiz`s last term will expire in February 2023. A call for nomination of a BWP chair was launched in December 2022.

Nomination(s) received

Action: For election

14.3.3. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 14-15 February 2023.

Action: For adoption

14.3.4. Scientific Advice Working Party (SAWP)

Chair: Paolo Foggi

Report from the SAWP meeting held on 06-09 February 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.

14.3.5. SAWP composition

SAWP composition for re-nomination

Action: For adoption

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Update on COVID-19

Action: For information

Explanatory notes

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

Oral explanations *(section 2)*

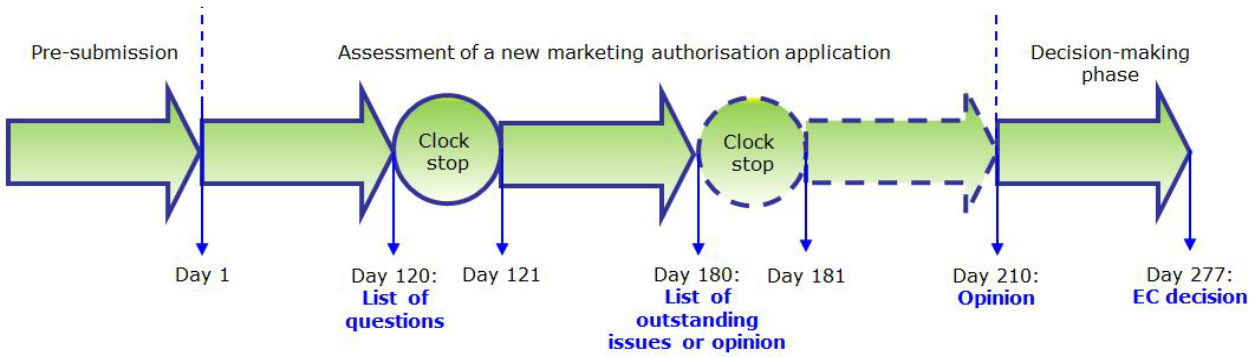
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

Initial applications *(section 3)*

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

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

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



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

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

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

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

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

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

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

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

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

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

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

Re-examination procedures *(section5.3)*

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

Withdrawal of application *(section 3.7)*

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

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

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

Pre-submission issues *(section 8)*

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

Post-authorisation issues *(section 9)*

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

Referral procedures *(section 10)*

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

Pharmacovigilance issues *(section 11)*

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

Inspections Issues *(section 12)*

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

Innovation task force *(section 13)*

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

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

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

Satellite groups / other committees *(section 14.2)*

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

Invented name issues *(section 14.3)*

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

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

20 February 2023
EMA/CHMP/44930/2023

Annex to 20-23 February 2023 CHMP Agenda

Pre-submission and post-authorisations issues

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A. PRE-SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

Final Outcome of Rapporteurship allocation for February 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

Brineura - cerliponase alfa - EMEA/H/C/004065/S/0038, Orphan
BioMarin International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Mari Thorn
Request for Supplementary Information adopted on 15.12.2022.

NYXTHRACIS - obiltoxaximab - EMEA/H/C/005169/S/0008, Orphan
SFL Pharmaceuticals Deutschland GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Liana Gross-Martirosyan

Orphacol - cholic acid - EMEA/H/C/001250/S/0048, Orphan
Laboratoires CTRS, Rapporteur: Anastasia Mountaki, PRAC Rapporteur: Sofia Trantza

Raxone - idebenone - EMEA/H/C/003834/S/0032, Orphan
Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli

Vedrop - tocofersolan -
EMEA/H/C/000920/S/0044
Recordati Rare Diseases, Rapporteur: Robert Porszasz, PRAC Rapporteur: Melinda Palfi

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Onpattro - patisiran -
EMEA/H/C/004699/R/0031, Orphan
Alnylam Netherlands B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Rhea Fitzgerald

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

Cablivi - caplacizumab -
EMEA/H/C/004426/R/0042, Orphan
Ablynx NV, Rapporteur: Filip Josephson, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Jan Neuhauser

Deferiprone Lipomed - deferiprone -
EMEA/H/C/004710/R/0011
Lipomed GmbH, Generic, Generic of Ferriprox, Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Tiphaine Vaillant

Imfinzi - durvalumab -
EMEA/H/C/004771/R/0055
AstraZeneca AB, Rapporteur: Aaron Sosa Mejia, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: David Olsen

Imnovid - pomalidomide -
EMEA/H/C/002682/R/0049, Orphan
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Monica Martinez Redondo

Kymriah - tisagenlecleucel -
EMEA/H/C/004090/R/0068, Orphan, ATMP
Novartis Europharm Limited, Rapporteur: Rune

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

Lonquex - lipegfilgrastim - EMEA/H/C/002556/R/0077
Teva B.V., Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kirsti Villikka
Request for Supplementary Information adopted on 26.01.2023.

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

Nityr - nitisinone - EMEA/H/C/004582/R/0015
Cycle Pharmaceuticals (Europe) Limited, Generic, Generic of Orfadin, Rapporteur: Jayne Crowe, PRAC Rapporteur: Amelia Cupelli
Request for Supplementary Information adopted on 26.01.2023.

VEYVONDI - vonicog alfa - EMEA/H/C/004454/R/0027
Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Mari Thorn

Vyxeos liposomal - daunorubicin / cytarabine - EMEA/H/C/004282/R/0037, Orphan
Jazz Pharmaceuticals Ireland Limited, Rapporteur: Johanna Lähteenvuo, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Inês Ribeiro-Vaz

Xerava - eravacycline - EMEA/H/C/004237/R/0023
Paion Deutschland GmbH, Rapporteur: Filip Josephson, Co-Rapporteur: Ingrid Wang, PRAC Rapporteur: Adam Przybylkowski

Yescarta - axicabtagene ciloleucel - EMEA/H/C/004480/R/0056, Orphan, ATMP
Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Claire Beuneu, CHMP Coordinators: Jan Mueller-Berghaus and Karin Janssen van Doorn, PRAC Rapporteur: Anette

Kirstine Stark

B.2.3. Renewals of Conditional Marketing Authorisations

Koselugo - selumetinib -
EMEA/H/C/005244/R/0010, Orphan
AstraZeneca AB, Rapporteur: Alexandre Moreau,
PRAC Rapporteur: Ulla Wändel Liminga

Lunsumio - mosunetuzumab -
EMEA/H/C/005680/R/0001, Orphan
Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Ulla Wändel Liminga

Ondexxya - andexanet alfa -
EMEA/H/C/004108/R/0034
AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 26.01.2023.

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 06-09 February 2023
PRAC:

Signal of interstitial lung disease (ILD)

Bosulif (CAP) – bosutinib

Rapporteur: Janet Koenig, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Martin Huber
PRAC recommendation on a variation
Action: For adoption

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

EMEA/H/C/PSUSA/00009255/202207
(perampanel)
CAPS:
Fycompa (EMEA/H/C/002434) (perampanel), Eisai GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, "21/07/2021 To: 21/07/2022"

EMEA/H/C/PSUSA/00010697/202207 (inotersen) CAPS: **Tegsedi** (EMEA/H/C/004782) (inotersen), Akcea Therapeutics Ireland Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Rhea Fitzgerald, "05/07/2021 To: 05/07/2022"	
EMEA/H/C/PSUSA/00010742/202207 (voretigene neparvovec) CAPS: **Luxturna** (EMEA/H/C/004451) (voretigene neparvovec), Novartis Europharm Limited, Rapporteur: Sol Ruiz, CHMP Coordinator: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Gabriele Maurer, "24/07/2021 To: 23/07/2022"	

B.4. EPARs / WPARs

Dapagliflozin Viatris - dapagliflozin - EMEA/H/C/006006 Viatris Limited, treatment of type 2 diabetes mellitus, heart failure and chronic kidney disease, Generic, Generic of Forxiga, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Sitagliptin/Metformin hydrochloride SUN - sitagliptin / metformin hydrochloride - EMEA/H/C/005778 Sun Pharmaceutical Industries Europe B.V., treatment of type 2 diabetes mellitus, Generic, Generic of Janumet, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
SOTYKTU - deucravacitinib - EMEA/H/C/005755 Bristol-Myers Squibb Pharma EEIG, treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy, 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.
Tolvaptan Accord - tolvaptan - EMEA/H/C/005961 Accord Healthcare S.L.U., treatment of hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH), Generic, Generic of Samsca, Generic application (Article 10(1) of Directive No	For information only. Comments can be sent to the PL in case necessary.

2001/83/EC)

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

Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0163 Amgen Europe B.V., Rapporteur: Martina Weise Request for Supplementary Information adopted on 02.02.2023.	Request for supplementary information adopted with a specific timetable.
CEVENFACTA - eptacog beta (activated) - EMEA/H/C/005655/II/0002 Laboratoire Francais du Fractionnement et des Biotechnologies, Rapporteur: Daniela Philadelphy Request for Supplementary Information adopted on 12.01.2023.	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0165/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
Cosentyx - secukinumab - EMEA/H/C/003729/II/0096 Novartis Europharm Limited, Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 19.01.2023.	
Cyramza - ramucirumab - EMEA/H/C/002829/II/0051 Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege	
Dupixent - dupilumab - EMEA/H/C/004390/II/0069/G Sanofi Winthrop Industrie, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 16.02.2023.	Positive Opinion adopted by consensus on 16.02.2023.
ECALTA - anidulafungin - EMEA/H/C/000788/II/0052/G Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege	
Enbrel - etanercept - EMEA/H/C/000262/II/0251	Positive Opinion adopted by consensus on 02.02.2023.

Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro Opinion adopted on 02.02.2023.	
Ervebo - recombinant vesicular stomatitis virus - Zaire Ebolavirus vaccine (live) - EMEA/H/C/004554/II/0030 Merck Sharp & Dohme B.V., Rapporteur: Christophe Focke Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
EVUSHELD - tixagevimab / cilgavimab - EMEA/H/C/005788/II/0006/G AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus	
Fluad Tetra - influenza vaccine (surface antigen, inactivated, adjuvanted) - EMEA/H/C/004993/II/0036 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz Opinion adopted on 02.02.2023.	Positive Opinion adopted by consensus on 02.02.2023.
Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0143 CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 16.02.2023.	Request for supplementary information adopted with a specific timetable.
IMVANEX - smallpox vaccine (live modified vaccinia virus Ankara) - EMEA/H/C/002596/II/0084/G Bavarian Nordic A/S, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 09.02.2023.	Request for supplementary information adopted with a specific timetable.
Kovaltry - octocog alfa - EMEA/H/C/003825/II/0040/G Bayer AG, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 12.01.2023.	
LifeGlobal Media - human albumin solution - EMEA/H/D/004287/II/0005/G LifeGlobal Group LLC, Rapporteur: Maria Grazia Evandri Request for Supplementary Information adopted on 12.01.2023.	
Miglustat Gen.Orph - miglustat - EMEA/H/C/004366/II/0023 Gen.Orph, Generic, Generic of Zavesca, Rapporteur: Daniela Philadelphy	Positive Opinion adopted by consensus on 09.02.2023.

Opinion adopted on 09.02.2023.	
NUVAXOVID - NVX-CoV2373 - EMEA/H/C/005808/II/0035/G Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 12.01.2023.	
NUVAXOVID - NVX-CoV2373 - EMEA/H/C/005808/II/0039/G Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 19.01.2023.	
Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0036/G Roche Registration GmbH, Rapporteur: Thalia Marie Estrup Blicher Request for Supplementary Information adopted on 09.02.2023.	Request for supplementary information adopted with a specific timetable.
Oyavas - bevacizumab - EMEA/H/C/005556/II/0019 STADA Arzneimittel AG, Duplicate, Duplicate of Alymsys, Rapporteur: Christian Gartner Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
Paxlovid - nirmatrelvir / ritonavir - EMEA/H/C/005973/II/0028/G Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race Opinion adopted on 02.02.2023. Request for Supplementary Information adopted on 17.11.2022.	Positive Opinion adopted by consensus on 02.02.2023.
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0195 CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 16.02.2023.	Request for supplementary information adopted with a specific timetable.
Replagal - agalsidase alfa - EMEA/H/C/000369/II/0122 Takeda Pharmaceuticals International AG Ireland Branch, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 16.02.2023, 12.01.2023.	Request for supplementary information adopted with a specific timetable.
Roclanda - latanoprost / netarsudil - EMEA/H/C/005107/II/0011	Request for supplementary information adopted with a specific timetable.

Santen Oy, Rapporteur: Jayne Crowe Request for Supplementary Information adopted on 09.02.2023.	
Ryeqo - relugolix / estradiol / norethisterone acetate - EMEA/H/C/005267/II/0012 Gedeon Richter Plc., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 15.12.2022.	
Sapropterin Dipharma - sapropterin - EMEA/H/C/005646/II/0010 DIPHARMA Arzneimittel GmbH, Generic, Generic of Kuvan, Rapporteur: Frantisek Drafi	
Skyrizi - risankizumab - EMEA/H/C/004759/II/0029/G AbbVie Deutschland GmbH & Co. KG, Rapporteur: Finbarr Leacy Opinion adopted on 02.02.2023.	Positive Opinion adopted by consensus on 02.02.2023.
Somavert - pegvisomant - EMEA/H/C/000409/II/0106/G Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race	
Supemtek - influenza quadrivalent vaccine (rDNA) - EMEA/H/C/005159/II/0010/G Sanofi Pasteur, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 02.02.2023.	Request for supplementary information adopted with a specific timetable.
Supemtek - influenza quadrivalent vaccine (rDNA) - EMEA/H/C/005159/II/0011/G Sanofi Pasteur, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 09.02.2023.	Request for supplementary information adopted with a specific timetable.
Tabrecta - capmatinib - EMEA/H/C/004845/II/0003/G Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa Opinion adopted on 02.02.2023.	Positive Opinion adopted by consensus on 02.02.2023.
Taltz - ixekizumab - EMEA/H/C/003943/II/0048 Eli Lilly and Co (Ireland) Limited, Rapporteur: Kristina Dunder Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
TEPADINA - thiotepa -	Request for supplementary information adopted

EMEA/H/C/001046/II/0046/G ADIENNE S.r.l. S.U., Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 09.02.2023.	with a specific timetable.
Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0042 Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 09.02.2023. Request for Supplementary Information adopted on 24.11.2022.	Positive Opinion adopted by consensus on 09.02.2023.
Vyepti - eptinezumab - EMEA/H/C/005287/II/0005/G H. Lundbeck A/S, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 09.02.2023.	Request for supplementary information adopted with a specific timetable.
Vyvgart - efgartigimod alfa - EMEA/H/C/005849/II/0004/G, Orphan Argenx, Rapporteur: Thalia Marie Estrup Blicher	
Xenpozyme - olipudase alfa - EMEA/H/C/004850/II/0002/G, Orphan Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 02.02.2023.	Request for supplementary information adopted with a specific timetable.
WS2326/G **Hexacima-** **EMEA/H/C/002702/WS2326/0138/G** **Hexyon-** **EMEA/H/C/002796/WS2326/0142/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 08.12.2022.	
WS2385/G **Fluenz Tetra-** **EMEA/H/C/002617/WS2385/0123/G** **Pandemic influenza vaccine H5N1 AstraZeneca-** **EMEA/H/C/003963/WS2385/0058/G** AstraZeneca AB, Lead Rapporteur: Christophe Focke Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
WS2390	Request for supplementary information adopted

Januvia-EMEA/H/C/000722/WS2390/0080 Ristaben-EMEA/H/C/001234/WS2390/0074 Steglujan-EMEA/H/C/004313/WS2390/0019 TESAVEL-EMEA/H/C/000910/WS2390/0080 Xelevia-EMEA/H/C/000762/WS2390/0088 Merck Sharp & Dohme B.V., Lead Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 16.02.2023.	with a specific timetable.
WS2401/G Hexacima-EMEA/H/C/002702/WS2401/0143/G Hexyon-EMEA/H/C/002796/WS2401/0147/G Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus	

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

Adtralza - tralokinumab - EMEA/H/C/005255/II/0008 LEO Pharma A/S, Rapporteur: Jayne Crowe, "To update section 4.8 of the SmPC in order to update safety information based on interim results from the ECZTEND study, listed as a category 3 study in the RMP. This is a phase 3 open-label, single-arm, multi-centre, long-term extension trial to evaluate the safety and efficacy of tralokinumab in subjects with moderate-to-severe atopic dermatitis who participated in previous tralokinumab clinical trials. In addition, the MAH is taking this opportunity to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 09.02.2023.	Request for supplementary information adopted with a specific timetable.
Amglidia - glibenclamide - EMEA/H/C/004379/II/0015, Orphan Ammtek, Rapporteur: Martina Weise, "Update of section 5.1 of the SmPC in order to update information regarding sulphonylurea effects on neurological abnormalities in children and adults with KCNJ11- and ABCC8-related neonatal diabetes based on literature."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 09.02.2023.	
Beyfortus - nirsevimab - EMEA/H/C/005304/II/0001 AstraZeneca AB, Rapporteur: Thalia Marie Estrup Blicher, "Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update efficacy information based on additional results from study D5290C00004 (MELODY); this is a Phase III Randomized, Double-blind, Placebo-controlled Study to Evaluate the Safety and Efficacy of MEDI8897, for the Prevention of Medically Attended Lower Respiratory Tract Infection Due to Respiratory Syncytial Virus in Healthy Late Preterm and Term Infants." Request for Supplementary Information adopted on 26.01.2023.	
Briviact - brivaracetam - EMEA/H/C/003898/II/0037/G UCB Pharma S.A., Rapporteur: Filip Josephson, "Grouped application comprising two variations as follows: C.I.4 - Update of section 4.6 of the SmPC in order to update information on breastfeeding following the outcome of the safety signal assessment report (SSAR). C.I.3.a - Update of section 4.8 of the SmPC to implement the wording agreed by the CHMP following the outcome of the procedure P46/009. In addition, the MAH took the opportunity to make editorial changes, to update the list of local representatives in the Package Leaflet and to bring the Package Leaflet in line with the current approved mock-up/specimen layout." Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0115 GlaxoSmithkline Biologicals SA, Rapporteur: Christophe Focke, "Submission of the final report from study HPV-027 listed as a category 3 study in the RMP to fulfil MEA/024.2; this is a long-term follow-up registry-based cohort study of HPV vaccine effectiveness against cervical pre-cancerous lesions and cervical cancer in a cohort of females previously enrolled from Finland in study HPV-008 or HPV-012, as compared to an unvaccinated population-based	Positive Opinion adopted by consensus on 09.02.2023.

reference cohort of females from Finland." Opinion adopted on 09.02.2023. Request for Supplementary Information adopted on 15.09.2022.	
Cibinqo - abrocitinib - EMEA/H/C/005452/II/0007 Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder, "To update section 5.1 of the SmPC in order to update long-term efficacy data based on the results from studies B7451012, B7451013, B7451015 and B7451029." Opinion adopted on 16.02.2023.	Positive Opinion adopted by consensus on 16.02.2023.
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0139 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC of COMIRNATY 30 µg concentrate for dispersion for injection and COMIRNATY 30 µg dispersion for injection as well as section 4.8 of the SmPC of COMIRNATY 10 µg concentrate for dispersion for injection in order to update information based on six months post (booster) dose three interim report data in patients aged 16 years of age and above from studies C4591001 and C4591031. Study C4591001 is a phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals, while study C4591031 is a phase 3 master protocol to evaluate additional dose(s) of BNT162b2 in healthy individuals previously vaccinated with BNT162b2." Request for Supplementary Information adopted on 13.10.2022.	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0160 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC of Comirnaty 10 micrograms/dose, Comirnaty 3 micrograms/dose and Comirnaty Original/Omicron BA.4-5 (5/5 micrograms)/dose in order to update safety and efficacy information 6 months post-dose 2 follow-up for children aged 5 to 11 years based on updated interim results from study C4591007 listed as a category 3 study in the RMP; this is a phase I, open-label dose-finding study to evaluate	Positive Opinion adopted by consensus on 09.02.2023.

safety, tolerability and immunogenicity and phase II/III placebo-controlled, observer-blinded safety, tolerability, and immunogenicity study of a SARS-CoV-2 RNA vaccine candidate against COVID-19 in healthy children and young adults. Update of section 5.1 of the SmPC of all Comirnaty vaccines in order to include information on the predominant circulating strains at the time of the vaccine efficacy estimate generation. In addition, the MAH took the opportunity to implement editorial changes throughout the product information." Opinion adopted on 09.02.2023.	
COVID-19 Vaccine (inactivated, adjuvanted) Valneva - SARS-CoV-2 virus, strain Wuhan hCoV-19/Italy/INMI1-isl/2020, inactivated - EMEA/H/C/006019/II/0004 Valneva Austria GmbH, Rapporteur: Daniela Philadelphy, "Update of sections 4.2 and 5.1 of the SmPC in order to include a booster dose for adults 18 to 50 years of age based on the interim results from study VLA2001-301 (Booster part); this is a randomized, observer-blind, controlled, superiority study to compare the immunogenicity of COVID-19 Vaccine (inactivated, adjuvanted) Valneva to AZD1222, where participants received a booster dose of COVID-19 vaccine Valneva; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 15.12.2022.	See 9.1
Darzalex - daratumumab - EMEA/H/C/004077/II/0064, Orphan Janssen-Cilag International N.V., Rapporteur: Aaron Sosa Mejia, "Submission of the final report from study MMY3013 (54767414MMY3013). This is a Phase III, randomized, open-label study comparing daratumumab, pomalidomide and low-dose dexamethasone (DaraPomDex) with pomalidomide and low-dose dexamethasone (PomDex) in subjects with relapsed or refractory multiple myeloma who have received at least 1 prior treatment regimen with both lenalidomide and a proteasome inhibitor and have demonstrated disease progression."	Positive Opinion adopted by consensus on 09.02.2023.

Opinion adopted on 09.02.2023.	
DuoPlavin - clopidogrel / acetylsalicylic acid - EMEA/H/C/001143/II/0065 Sanofi Winthrop Industrie, Rapporteur: Bruno Sepodes, "Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on 'drug reaction with eosinophilia and systemic symptoms (DRESS)' based on a safety evaluation report; the Package Leaflet is updated accordingly." Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
Esperoct - turoctocog alfa pegol - EMEA/H/C/004883/II/0013 Novo Nordisk A/S, Rapporteur: Daniela Philadelphy, "Update of section 4.2 of the SmPC in order to delete the statement in reference to previously untreated patients (PUPs) and section 5.1 of the SmPC in order to update information based on final results from study NN7088-3908; this is an open-label single-arm multicentre non-controlled phase 3a trial investigating safety and efficacy of turoctocog alfa pegol (N8-GP) in prophylaxis and treatment of bleeding episodes in previously untreated paediatric patients with severe haemophilia A. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted on 15.12.2022, 13.10.2022, 21.07.2022.	
Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0030 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz, "Update of section 4.8 of the SmPC in order to add Guillain Barré syndrome (GBS), syncope and pre-syncope to the list of adverse drug reactions (ADRs) based on the assessment of the global safety database; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the Package Leaflet in order to align it with the information in the SmPC." Opinion adopted on 09.02.2023. Request for Supplementary Information adopted on 01.12.2022.	Positive Opinion adopted by consensus on 09.02.2023.
IBRANCE - palbociclib - EMEA/H/C/003853/II/0040 Pfizer Europe MA EEIG, Rapporteur: Filip	Request for supplementary information adopted with a specific timetable.

Josephson, "Update of section 5.1 of the SmPC in order to update efficacy and safety information based on final OS results from study A5481008 (PALOMA-2, "A Randomized, Multicenter, Double-blind Phase 3 Study of PD-0332991 (Oral CDK 4/6 Inhibitor) Plus Letrozole Versus Placebo Plus Letrozole for the Treatment of Postmenopausal Women with ER (+), HER2 (-) Breast Cancer Who Have Not Received Any Prior Systemic Anti-Cancer Treatment For Advanced Disease") to fulfil REC 2. In addition, the MAH took the opportunity to align Annex II with the current QRD template." Request for Supplementary Information adopted on 02.02.2023.	
INREBIC - fedratinib - EMEA/H/C/005026/II/0010/G, Orphan Bristol-Myers Squibb Pharma EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sonja Hrabcik, "Update of section 4.4 of the SmPC in order to add new warnings on major adverse cardiac events (MACE), thrombosis and secondary malignancies. The updates pertain to three signals, assessed by the FDA, which were identified with another JAK inhibitor (tofacitinib) indicated in rheumatoid arthritis; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted on 26.01.2023, 10.06.2022.	
Kesimpta - ofatumumab - EMEA/H/C/005410/II/0006 Novartis Ireland Limited, Rapporteur: Thalia Marie Estrup Blicher, "Update of section 5.1 of the SmPC based on final results from pivotal studies G2301, G2302 and a meta-analysis of studies G2301 and G2302. G2301 and G2302 are two Phase III, randomized, double-blind, double-dummy, parallel-group studies comparing the efficacy and safety of ofatumumab versus teriflunomide in patients with relapsing multiple sclerosis." Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
Kisplyx - lenvatinib - EMEA/H/C/004224/II/0054 Eisai GmbH, Rapporteur: Karin Janssen van Doorn, "Submission of the latest Modelling and Simulation related data (such as PopPK and	Positive Opinion adopted by consensus on 02.02.2023.

PK/PD Analyses) following the assessment of procedure II/52 to fulfil MEA/FSR 008.1, MEA/FSR 007.3 and MEA/FSR 013.2." Opinion adopted on 02.02.2023.	
Lumeblue - methylthioninium chloride - EMEA/H/C/002776/II/0004 Alfasigma S.p.A., Rapporteur: Thalia Marie Estrup Blicher, "Update of sections 4.2 and 5.2 of the SmPC in order to introduce a new posology regimen based on scientific literature." Request for Supplementary Information adopted on 15.09.2022.	
Noxafil - posaconazole - EMEA/H/C/000610/II/0077 Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau, "C.I.4. To update section 5.2 of the SmPC for 300 mg gastro-resistant powder and solvent for oral suspension formulation (EU/1/05/320/005) to reflect the data of an in vitro dissolution study which was conducted to evaluate the impact of alcohol. The applicant took the opportunity to also include minor editorial updates to the SmPC, PI and labelling of all pharmaceutical forms." Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0035 AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC in order to remove the information referring to healthy volunteers and to add infusion related adverse reactions in bleeding patients following an internal review of the labels and based on ANNEXA-4 study. The Package Leaflet is updated accordingly. In addition, the MAH would like to take this opportunity to make some corrections in the SmPC." Request for Supplementary Information adopted on 12.01.2023.	
Orgovyx - relugolix - EMEA/H/C/005353/II/0007 Accord Healthcare S.L.U., Rapporteur: Johann Lodewijk Hillege, "Submission of the bioanalytical report of testosterone." Opinion adopted on 02.02.2023.	Positive Opinion adopted by consensus on 02.02.2023.
Orgovyx - relugolix - EMEA/H/C/005353/II/0008	Request for supplementary information adopted with a specific timetable.

Accord Healthcare S.L.U., Rapporteur: Johann Lodewijk Hillege, "Submission of the final report from study MVT-601-055; this is an open-label, fixed (single)-sequence crossover phase 1 study to assess the sufficiency of dose separation to mitigate absorption-mediated increases in exposure to relugolix resulting from inhibition of intestinal P-gp by azithromycin in healthy adult men." Request for Supplementary Information adopted on 09.02.2023.	
Orgovyx - relugolix - EMEA/H/C/005353/II/0009 Accord Healthcare S.L.U., Rapporteur: Johann Lodewijk Hillege, "Submission of the bioanalytical report for testosterone measurement in the clinical study MVT-601-3201." Request for Supplementary Information adopted on 09.02.2023.	Request for supplementary information adopted with a specific timetable.
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."	
Retsevmo - selpercatinib - EMEA/H/C/005375/II/0023 Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to introduce a new dose modification regimen in the event of 'interstitial lung disease (ILD)/pneumonitis' and to introduce it as a new warning and add it to the list of adverse drug reactions (ADRs) with frequency common, based on an internal safety review. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor formatting changes to the PI."	
Revlimid - lenalidomide - EMEA/H/C/000717/II/0124 Bristol-Myers Squibb Pharma EEIG, Rapporteur:	Positive Opinion adopted by consensus on 09.02.2023.

Alexandre Moreau, "Update of section 5.1 of the SmPC in order to update 5-year Overall Survival data following the assessment of procedure II/107 based on study CC-5013-NHL-007, A Phase 3, Double-Blind Randomized Study To Compare The Efficacy And Safety Of Rituximab Plus Lenalidomide (Cc-5013) Versus Rituximab Plus Placebo In Subjects With Relapsed/Refractory Indolent Lymphoma." Opinion adopted on 09.02.2023.	
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 in order to include a warning for vitamin B12 deficiency and to change the frequency of vitamin B12 deficiency from very rare to common, following the assessment of the medicinal product Glucophage, which also contains the active substance metformin, assessed as part of a mutual recognition procedure FR/H/0181/001-3. The same wording is used for the combination product. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted on 09.02.2023.	Request for supplementary information adopted with a specific timetable.
Simponi - golimumab - EMEA/H/C/000992/II/0107 Janssen Biologics B.V., Rapporteur: Kristina Dunder, "Update to section 5.1 of the SmPC to add the results of the final report from study MK-8259-038 (Go-BACK) in order to fulfil MEA/30.2. This is a phase 4, randomised, double-blind, parallel-group, withdrawal, post-authorisation efficacy study (PAES) of golimumab in adult participants, aged 18 to 45 years, with active non-radiographic axial spondyloarthritis. In addition, the MAH took the opportunity to update the list of local representatives." Opinion adopted on 16.02.2023. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 16.02.2023.

on 08.12.2022, 01.09.2022.	
SIRTURO - bedaquiline - EMEA/H/C/002614/II/0051, Orphan Janssen-Cilag International N.V., Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC in order to update information on breast-feeding based on new literature." Request for Supplementary Information adopted on 26.01.2023, 15.12.2022.	
Skyrizi - risankizumab - EMEA/H/C/004759/II/0028 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Finbarr Leacy, "Update of section 4.8 of the SmPC in order to add eczema, rash and urticaria to the list of adverse drug reactions (ADRs) based on a thorough evaluation of all events of rash, eczema, and urticaria, including clinical trial and post-marketing data from the global safety database; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 24.11.2022.	
TEPMETKO - tepotinib - EMEA/H/C/005524/II/0005 Merck Europe B.V., Rapporteur: Filip Josephson, "Update of sections 4.5 and 5.2 of the SmPC in order to remove interactions with 'CYP and P-gp inducers' and 'dual strong CYP3A and P-gp inhibitors, and P-gp inhibitors' and to update pharmacokinetic information based on final results from the drug-drug interaction (DDI) studies MS200095-0051 and MS200095-0053. Study MS200095-0051 is a phase 1, open-label, single-sequence, cross-over study to evaluate the effect of multiple doses of carbamazepine on single-dose tepotinib pharmacokinetics in healthy participants, while study MS200095-0053 is a phase 1, open-label, single-sequence, cross-over study to evaluate the effect of multiple doses of itraconazole on single-dose tepotinib pharmacokinetics in healthy participants. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor changes to the PI." Request for Supplementary Information adopted on 09.02.2023.	Request for supplementary information adopted with a specific timetable.
Verquvo - vericiguat -	Positive Opinion adopted by consensus on

EMEA/H/C/005319/II/0004 Bayer AG, Rapporteur: Johann Lodewijk Hillege, "Submission of updated non-clinical and clinical study reports based on the correction of the data following the re-evaluation of vericiguat metabolite M-1 (BAY 1222707) reference standard with a different analytical method." Opinion adopted on 09.02.2023.	09.02.2023.
Xolair - omalizumab - EMEA/H/C/000606/II/0118 Novartis Europharm Limited, Rapporteur: Kristina Dunder, "Update of sections 4.2, 4.8 and 5.1 of the SmPC with long-term safety and efficacy results from XTEND study (ML29510), a Phase 4, multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of omalizumab through 48 weeks in patients with CSU." Opinion adopted on 16.02.2023.	Positive Opinion adopted by consensus on 16.02.2023.
WS2312 **Kisplyx-EMEA/H/C/004224/WS2312/0053** **Lenvima-EMEA/H/C/003727/WS2312/0048** Eisai GmbH, Lead Rapporteur: Karin Janssen van Doorn, "To update of SmPC sections 4.2 and 6.6 to include the option of administering the capsules as a suspension, including instructions for the administration and preparation of the suspension. The MAH also took the opportunity to include some editorial changes to the SmPC. The package leaflets have been updated accordingly." Request for Supplementary Information adopted on 15.09.2022.	
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: Silvijus Abramavicius, "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	See 9.1

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 24.11.2022, 06.10.2022.	
WS2339/G **Keppra-** **EMEA/H/C/000277/WS2339/0198/G** UCB Pharma S.A., Lead Rapporteur: Karin Janssen van Doorn, "Grouped application comprising two type II variations as follows: C.I.4 – Update of section 4.4 of the SmPC in order to add a new warning on lack of efficacy or seizure worsening based on the cumulative review of MAH Global Safety database and published literature. C.I.4 – Update of section 4.8 of the SmPC in order to add a note on obsessive compulsive disorder in the ADR table based on the cumulative review of MAH Global Safety database, clinical studies, data from external spontaneous reporting database and published literature. The Package Leaflet is updated accordingly. In addition, the MAH proposes minor editorial changes of the labelling." Request for Supplementary Information adopted on 15.12.2022.	
WS2358 **Elebrato Ellipta-** **EMEA/H/C/004781/WS2358/0028** **Trelegy Ellipta-** **EMEA/H/C/004363/WS2358/0025** GlaxoSmithKline Trading Services Limited, Lead Rapporteur: Finbarr Leacy, "Update of sections 4.4 and 4.8 of the SmPC in order to add 'urinary retention' and 'dysuria' to the list of adverse drug reactions (ADRs) with frequency rare and to amend a warning regarding urinary retention; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and bring it in line with the latest QRD template."	Positive Opinion adopted by consensus on 16.02.2023.

Opinion adopted on 16.02.2023. Request for Supplementary Information adopted on 12.01.2023, 10.11.2022.	
WS2405 **BYANNLI-** **EMEA/H/C/005486/WS2405/0004** **Trevicta-** **EMEA/H/C/004066/WS2405/0030** **Xeplion-** **EMEA/H/C/002105/WS2405/0055** Janssen-Cilag International N.V., Lead Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC for Xeplion and Trevicta in order to modify the frequencies of the list of adverse drug reactions (ADRs) to align with the Product Information of Byannli. In addition, the MAH took the opportunity to introduce administrative corrections and minor editorial changes to the PI as well as to update the list of local representatives in the Package Leaflet."	
WS2407 **Efficib-EMEA/H/C/000896/WS2407/0110** **Janumet-** **EMEA/H/C/000861/WS2407/0109** **Ristfor-EMEA/H/C/001235/WS2407/0098** **Velmetia-** **EMEA/H/C/000862/WS2407/0115** Merck Sharp & Dohme B.V., Lead Rapporteur: Johann Lodewijk Hillege, "To include significant changes to sections 4.4 and 4.8 of the SmPC and section 4 of the Package Leaflet for the medicinal products Janumet, Velmetia, Ristfor and Efficib, containing the active substances Metformin hydrochloride and Sitagliptin phosphate in order to include a warning for vitamin B12 deficiency and to change the frequency of vitamin B12 deficiency from very rare to common following the assessment of the medicinal product Glucophage, which also contains the active substance metformin, assessed as part of a mutual recognition procedure FR/H/0181/001-3. The same wording is used for the combination product. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet for Janumet, Ristfor and Efficib and to improve the wording in section 2 of the Package Leaflet."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 09.02.2023.

B.5.3. CHMP-PRAC assessed procedures

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."

GAVRETO - pralsetinib - EMEA/H/C/005413/II/0010

Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update efficacy and safety information in the treatment of adult patients with RET fusion-positive advanced NSCLC based on final results (NSCLC indication) from study ARROW/BO42863, a Phase 1/2 Study of the Highly-selective RET Inhibitor, BLU 667, in Patients With Thyroid Cancer, Non-Small Cell Lung Cancer (NSCLC), and Other Advanced Solid Tumours listed as a specific obligation in the Annex II.
The RMP version 1.5 has also been submitted."

GIVLAARI - givosiran - EMEA/H/C/004775/II/0013/G, Orphan

Alnylam Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber, "Submission of the final reports from studies ALN-AS1-003 (study 003) and ALN-AS1-002 (study 002) listed as a category 3 studies in the RMP. Study 003 is a phase 3 randomized, double-blind, placebo-controlled multicenter

study with an open-label extension to evaluate the efficacy and safety of givosiran in patients with acute hepatic porphyrias, while study 002 is a multicenter, open-label extension study to evaluate the long-term safety and clinical activity of subcutaneously administered ALN AS1 in patients with acute intermittent porphyria who have completed a previous clinical study with ALN-AS1. The RMP version 2.2 has also been submitted." Request for Supplementary Information adopted on 13.10.2022.	
IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0059, Orphan CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update information and amend the frequencies of adverse drug reactions (ADRs) based on the final results from study CSL654_3003 listed as a category 3 study in the RMP; this is an open-label, multicentre, uncontrolled study to evaluate the safety, pharmacokinetics and clinical response of rIX-FP with regard to the prevention and treatment of bleeding in previously untreated patients (PUPs) with Haemophilia B. The Package Leaflet is updated accordingly. The RMP version 4.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 12.01.2023, 27.10.2022, 10.06.2022.	
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	Request for supplementary information adopted with a specific timetable.

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 on 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, multicenter, 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." Request for Supplementary Information adopted on 09.02.2023, 29.09.2022.	Request for supplementary information adopted with a specific timetable.
Lucentis - ranibizumab - EMEA/H/C/000715/II/0101 Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update information on preterm infants based on final results from study CRFB002H2301E (RAINBOW extension), listed as a PAES in the Annex II; this is an extension study to evaluate the long-term efficacy and safety of ranibizumab compared with laser therapy for the treatment of infants born prematurely with retinopathy of prematurity. The Annex II and Package Leaflet are updated accordingly. The RMP version 22.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
NexoBrid - concentrate of proteolytic enzymes enriched in bromelain - EMEA/H/C/002246/II/0057, Orphan MediWound Germany GmbH, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber,	

"Submission of the 24-months' CSR addendum of the MW2010-03-02 (DETECT) category 1 study; a multicentre, multinational, randomized, controlled, assessor blinded study, performed in subjects with thermal burns, to evaluate the efficacy and safety of NexoBrid compared to gel vehicle and compared to standard of care. The provision of the CSR addresses the post-authorisation measure ANX 001.7. An updated RMP version 8.0 was provided as part of the application." Request for Supplementary Information adopted on 10.11.2022.	
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 09.02.2023, 27.10.2022.	Request for supplementary information adopted with a specific timetable.
Sancuso - granisetron - EMEA/H/C/002296/II/0061 Kyowa Kirin Holdings B.V., Rapporteur: Silvijus Abramavicius, PRAC Rapporteur: Rugile Pilviniene, "Update of sections 4.4, 4.6, 4.7, 4.8, 4.10 and 5.3 of the SmPC in order to add 'Serotonin syndrome' and 'Application site Reactions' to the list of adverse drug reactions (ADRs) with frequency unknow; as well as 'Application site Irritation' with frequency 'Uncommon' based on post-marketing data and literature. The MAH also proposes to update	Positive Opinion adopted by consensus on 09.02.2023.

sections 4.4 and 4.5 of the SmPC to add drug-drug interaction information with buprenorphine/Opioids and serotonergic medicinal products based on post-marketing data and literature. The Package Leaflet has been updated accordingly. The RMP version 5 has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes in the SmPC." Opinion adopted on 09.02.2023. Request for Supplementary Information adopted on 01.12.2022.	
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0074 Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Inês Ribeiro-Vaz, "Submission of the final report from study MO39171 listed as a category 3 study in the RMP in order to fulfil MEA/008. This is a Phase III/IV, Single Arm, multicenter, interventional study of Atezolizumab to Investigate Long-term Safety and Efficacy in previously treated Patients with Locally Advanced or Metastatic Non-small Cell Lung Cancer. The RMP version 25.1 has also been agreed." Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
Thalidomide BMS - thalidomide - EMEA/H/C/000823/II/0076 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, and to make some editorial changes in the labelling.	Request for supplementary information adopted with a specific timetable.

The updated RMP version 20 was provided." Request for Supplementary Information adopted on 09.02.2023, 27.10.2022.	
Vabysmo - faricimab - EMEA/H/C/005642/II/0002 Roche Registration GmbH, Rapporteur: Jayne Crowe, PRAC Rapporteur: Inês Ribeiro-Vaz, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information and to update the warnings and the list of adverse drug reactions (ADRs), based on longer-term results from studies GR40306 (TENAYA) and GR40844 (LUCERNE); these are phase 3, multicenter, randomized, double-masked, active comparator-controlled, 112-week studies to evaluate the efficacy and safety of faricimab in patients with neovascular age-related macular degeneration (nAMD); the Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."	
Vaxzevria - COVID 19 vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0084/G AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, "Submission of an updated RMP version 6 succession 3 in order to request the discontinuation of the category 1 study D8111C00010 and remove it from the Annex II; this is an interventional safety study of AZD1222 vaccine in immunocompromised adults. In addition, the important potential risk of 'Nervous system disorders, including immune mediated neurological conditions' has been amended to 'Immune mediated neurological conditions', due dates of additional pharmacovigilance activities have been updated and other editorial wordings of the RMP have been implemented." Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
Veklury - remdesivir - EMEA/H/C/005622/II/0044/G Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, PRAC Rapporteur: Eva Jirsová, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to change posology recommendations for patients with renal	

impairment, remove an existing warning on renal impairment and update the safety and efficacy information based on final results from studies GS US 540 5912 and GS-US-540-9015, listed as category 3 studies in the RMP. Study GS US 540 5912 is a phase 3 randomized, double-blind, placebo-controlled, parallel group, multicenter study evaluating the efficacy and safety of remdesivir in participants with severely reduced kidney function who were hospitalized for COVID-19, while study GS-US-540-9015 is a phase 1, multicenter, open-label, single-dose study to evaluate the single-dose PK of remdesivir in participants with normal and impaired renal function. The Package Leaflet is updated accordingly. The RMP version 5.1 has also been submitted. In addition, the MAH took the opportunity to introduce minor edits to the PI."

Zeposia - ozanimod - EMEA/H/C/004835/II/0016

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maria del Pilar Rayon, "Update of sections 4.2 and 5.2 of the SmPC in order to add a dose adjustment after completion of the dose escalation regimen in patients with mild or moderate chronic hepatic impairment (Child-Pugh class A or B) based on the final results from study RPC-1063-CP-004; this is a Phase I, multicenter, open-label study to evaluate the effect of mild or moderate hepatic impairment on the multiple-dose pharmacokinetics of ozanimod. The Package Leaflet is updated accordingly. The updated RMP version 5.0 has also been submitted."
Request for Supplementary Information adopted on 26.01.2023.

B.5.4. PRAC assessed procedures

PRAC Led

Aldurazyme - laronidase - EMEA/H/C/000477/II/0085

Genzyme Europe BV, PRAC Rapporteur: Nathalie Gault, PRAC-CHMP liaison: Alexandre Moreau, "To update section 4.2 of the SmPC in order to modify the administration instructions following the assessment of procedure PSUSA/00001830/202104 based on literature

review. The Package Leaflet is updated accordingly. The RMP version 1.0 has also been submitted.”	
PRAC Led **Brintellix - vortioxetine - EMEA/H/C/002717/II/0037** H. Lundbeck A/S, PRAC Rapporteur: Jo Robays, PRAC-CHMP liaison: Karin Janssen van Doorn, “Submission of the final report from study PASS 16034N listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study (PASS) of vortioxetine in Europe - An analysis of European automated healthcare databases. The RMP version 4.0 has also been submitted.” Opinion adopted on 09.02.2023. Request for Supplementary Information adopted on 27.10.2022, 07.07.2022.	Positive Opinion adopted by consensus on 09.02.2023.
PRAC Led **Darzalex - daratumumab - EMEA/H/C/004077/II/0063, Orphan** Janssen-Cilag International N.V., Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Inês Ribeiro-Vaz, PRAC-CHMP liaison: Bruno Sepodes, “Update of section 4.4 of the SmPC in order to update the warnings and precautions for myocardial infarction and ocular events following PSUSA/00010498/202111, based on the cumulative review of the relevant cases retrieved from the MAH’s global safety database, clinical database, epidemiological evaluation and literature review. The Package Leaflet is updated accordingly.” Opinion adopted on 09.02.2023. Request for Supplementary Information adopted on 01.12.2022.	Positive Opinion adopted by consensus on 09.02.2023.
PRAC Led **Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0063** Merck Sharp & Dohme B.V., PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Karin Janssen van Doorn, “Update of section 4.6 of the SmPC in order to include additional information on exposure during pregnancy, based on the final report of the US Pregnancy Registry, listed as a category 3 study in the RMP; the Package Leaflet is updated	Request for supplementary information adopted with a specific timetable.

accordingly. The RMP version 5.1 has also been submitted." Request for Supplementary Information adopted on 09.02.2023.	
PRAC Led **Insuman - insulin human - EMEA/H/C/000201/II/0142** Sanofi-Aventis Deutschland GmbH, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Karin Janssen van Doorn, "Submission of the final report from study HUBIN-C-06380 listed as a category 3 study in the RMP. This is an observational prospective PASS designed to gain additional longitudinal and long-term safety data related to the use of Insuman Implantable 400 IU/mL via an IP implantable pump in a European observational cohort of patients with type 1 diabetes. The updated RMP version 5.0 was agreed during the procedure." Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
PRAC Led **JCOVDEN - COVID-19 vaccine Janssen (Ad26.COV2.S) - EMEA/H/C/005737/II/0065** Janssen-Cilag International N.V., PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 5.3 in order to update the clinical exposure and risk sections. In addition, the study VAC31518COV3018 is removed from the RMP. This is an interventional clinical trial to evaluate the immunogenicity and safety of Jcovden in immunocompromised patients." Opinion adopted on 09.02.2023. Request for Supplementary Information adopted on 01.12.2022.	Positive Opinion adopted by consensus on 09.02.2023.
PRAC Led **Mycamine - micafungin - EMEA/H/C/000734/II/0047** Astellas Pharma Europe B.V., PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Update of the RMP to include the results of the non-interventional PASS as an Effectiveness Check of the Prescriber Checklist for Mycamine (micafungin): 9463-PV-0002. Version 23.2 of the RMP is approved with this procedure. Annex IID of the PI is also updated to delete the additional risk minimisation measures (prescriber´s checklist)."	Positive Opinion adopted by consensus on 09.02.2023.

Opinion adopted on 09.02.2023. Request for Supplementary Information adopted on 01.12.2022, 01.09.2022.	
PRAC Led **Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0054** Orexigen Therapeutics Ireland Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of the final report from study NB-542 listed as a category 3 PASS in the RMP. This is a cross-sectional survey aimed to evaluate the effectiveness of the Mysimba Physician Prescribing Checklist (PPC) among physicians in the EU. The RMP version 12.6 has also been submitted." Opinion adopted on 09.02.2023. Request for Supplementary Information adopted on 29.09.2022, 10.06.2022, 10.02.2022.	Positive Opinion adopted by consensus on 09.02.2023.
PRAC Led **Obizur - susoctocog alfa - EMEA/H/C/002792/II/0049** Baxalta Innovations GmbH, PRAC Rapporteur: Gabriele Maurer, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report for study 241501 listed as a category 2 study in the RMP in order to fulfil SOB/001.4. This is a prospective and retrospective, non-interventional post-authorisation safety study (PASS) to evaluate the safety and effectiveness of Obizur in real-life practice. The RMP version 6.0 has also been submitted." Opinion adopted on 09.02.2023. Request for Supplementary Information adopted on 29.09.2022.	Positive Opinion adopted by consensus on 09.02.2023.
PRAC Led **Praluent - alirocumab - EMEA/H/C/003882/II/0077** Sanofi Winthrop Industrie, PRAC Rapporteur: Gabriele Maurer, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from the PASS study ALIROC08577. This is a non-interventional drug utilisation study of alirocumab in special populations using two U.S. healthcare databases." Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
PRAC Led	Positive Opinion adopted by consensus on

RAVICTI - glycerol phenylbutyrate - EMEA/H/C/003822/II/0044, Orphan Immedica Pharma AB, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Armando Genazzani, "Submission of the final report from study HZNP-RAV-401 "European Post-Authorization Registry for RAVICTI (glycerol phenylbutyrate) Oral Liquid in Partnership with the European Registry and Network for Intoxication Type Metabolic Diseases (E-IMD)", listed as a category 3 study in the RMP. The RMP version 7.4 has also been submitted." Opinion adopted on 09.02.2023.	09.02.2023.
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 on 09.02.2023.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Zydelig - idelalisib - EMEA/H/C/003843/II/0056** Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the final report from study GS-EU-313-4172 listed as a category 3 study in the RMP. This is a non-interventional study to assess the safety profile of idelalisib in patients with refractory follicular lymphoma (FL) with primary objective to assess the overall safety profile of idelalisib monotherapy in patients with refractory FL." Opinion adopted on 09.02.2023. Request for Supplementary Information adopted on 01.12.2022.	Positive Opinion adopted by consensus on 09.02.2023.
PRAC Led **WS2387 Rixathon- EMEA/H/C/003903/WS2387/0063 Riximyo- EMEA/H/C/004729/WS2387/0064** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus, Lead PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Thalia Marie	Positive Opinion adopted by consensus on 09.02.2023.

Estrup Blicher, "Submission of the final report from study GP13-501 following procedure EMEA/H/C/PSUSA/00002652/201811. This is a prospective, open-label, single-arm, non-interventional, multicenter study describing the effectiveness and safety of biosimilar rituximab administered in combination with CHOP chemotherapy for the treatment of patients with previously untreated CD20-positive diffuse large B-cell lymphoma in current clinical practice." Opinion adopted on 09.02.2023.	
PRAC Led **WS2406** **Glyxambi-** **EMEA/H/C/003833/WS2406/0049** **Jardiance-** **EMEA/H/C/002677/WS2406/0075** **Synjardy-** **EMEA/H/C/003770/WS2406/0068** Boehringer Ingelheim International GmbH, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Blanca Garcia-Ochoa, "Submission of the final results from the PASS 1245-96 listed as a category 3 study in the RMP for Jardiance and Synjardy; this is a post-authorisation safety study in patients with T2DM to assess the risk of acute liver injury, acute kidney injury and chronic kidney disease, severe complications of urinary tract infection, genital infections, and diabetic ketoacidosis among patients treated with empagliflozin compared to patients treated with DPP-4 inhibitors. The RMP versions for Jardiance (RMP version 20.0), Synjardy (RMP version 13.0) and Glyxambi (RMP version 8.0) have also been submitted." Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.

B.5.5. CHMP-CAT assessed procedures

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0022/G, Orphan, ATMP Bristol-Myers Squibb Pharma EEIG, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang	
Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0007/G, ATMP Bristol-Myers Squibb Pharma EEIG, Rapporteur: Concetta Quintarelli, CHMP Coordinator:	

Armando Genazzani
Opinion adopted on 17.02.2023.
Request for Supplementary Information adopted on 09.12.2022.

Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0009, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Concetta Quintarelli, CHMP Coordinator: Armando Genazzani
Opinion adopted on 17.02.2023.
Request for Supplementary Information adopted on 09.12.2022.

Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0013/G, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Concetta Quintarelli, CHMP Coordinator: Armando Genazzani

Upstaza - eladocagene exuparvovec - EMEA/H/C/005352/II/0004/G, Orphan, ATMP
PTC Therapeutics International Limited, Rapporteur: Maura O'Donovan, CHMP Coordinator: Finbarr Leacy
Request for Supplementary Information adopted on 09.12.2022.

Upstaza - eladocagene exuparvovec - EMEA/H/C/005352/II/0005/G, Orphan, ATMP
PTC Therapeutics International Limited, Rapporteur: Maura O'Donovan, CHMP Coordinator: Finbarr Leacy
Request for Supplementary Information adopted on 20.01.2023.

WS2389/G
Tecartus- EMEA/H/C/005102/WS2389/0031/G
Yescarta- EMEA/H/C/004480/WS2389/0059/G
Kite Pharma EU B.V., Lead Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

B.5.6. CHMP-PRAC-CAT assessed procedures

Libmeldy - atidarsagene autotemcel - EMEA/H/C/005321/II/0011/G, Orphan,

ATMP Orchard Therapeutics (Netherlands) B.V., Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege, PRAC Rapporteur: Gabriele Maurer, "Grouped application (Clinical & Quality) consisting of: Type II (C.I.4): Update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC; the Package Leaflet and Labelling are updated accordingly. In addition, the MAH took the opportunity to remove ANX/002 from the Annex II and to introduce minor editorial changes to the PI. The RMP version 1.3 has also been submitted." Request for Supplementary Information adopted on 09.12.2022.	

B.5.7. PRAC assessed ATMP procedures

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

WS2351 **Fiasp-EMEA/H/C/004046/WS2351/0032** **NovoMix-EMEA/H/C/000308/WS2351/0113** **NovoRapid-EMEA/H/C/000258/WS2351/0144** Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
WS2353 **Saxenda-EMEA/H/C/003780/WS2353/0035** **Victoza-EMEA/H/C/001026/WS2353/0065** Novo Nordisk A/S, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
WS2357 **Actraphane-EMEA/H/C/000427/WS2357/0093** **Actrapid-EMEA/H/C/000424/WS2357/0086** **Actrapid-EMEA/H/W/005779/WS2357/0002** **Insulatard-EMEA/H/C/000441/WS2357/0091** **Insulatard-EMEA/H/W/005780/WS2357/0002** **Levemir-EMEA/H/C/000528/WS2357/0106**	Positive Opinion adopted by consensus on 09.02.2023.

Mixtard- **EMEA/H/C/000428/WS2357/0094** **Protaphane-** **EMEA/H/C/000442/WS2357/0090** **Ryzodeg-** **EMEA/H/C/002499/WS2357/0051** **Tresiba-EMEA/H/C/002498/WS2357/0058** **Xultophy-** **EMEA/H/C/002647/WS2357/0047** Novo Nordisk A/S, Lead Rapporteur: Thalia Marie Estrup Blicher Opinion adopted on 09.02.2023.	
WS2371 **Infanrix hexa-** **EMEA/H/C/000296/WS2371/0320** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
WS2384 **Infanrix hexa-** **EMEA/H/C/000296/WS2384/0322** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
WS2391 **Fluenz Tetra-** **EMEA/H/C/002617/WS2391/0124** **Pandemic influenza vaccine H5N1 AstraZeneca-** **EMEA/H/C/003963/WS2391/0059** AstraZeneca AB, Lead Rapporteur: Christophe Focke Opinion adopted on 02.02.2023.	Positive Opinion adopted by consensus on 02.02.2023.
WS2393 **Infanrix hexa-** **EMEA/H/C/000296/WS2393/0321** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.
WS2404 **Stayveer-** **EMEA/H/C/002644/WS2404/0038** **Tracleer-** **EMEA/H/C/000401/WS2404/0103** Janssen-Cilag International N.V., Lead Rapporteur: Alexandre Moreau Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.

WS2411/G **Copalia HCT-** **EMEA/H/C/001159/WS2411/0104/G** **Dafiro HCT-** **EMEA/H/C/001160/WS2411/0106/G** **Exforge HCT-** **EMEA/H/C/001068/WS2411/0103/G** Novartis Europharm Limited, Lead Rapporteur: Thalia Marie Estrup Blicher	
WS2416 **Filgrastim Hexal-** **EMEA/H/C/000918/WS2416/0068** **Zarzio-EMEA/H/C/000917/WS2416/0069** Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "C.I.2.a - To amend the Product Information (section 4.4) to align with the updated reference product, Neupogen, Product Information published by the Irish Pharmaceutical Healthcare Association on 11-Oct-2022, by deleting the transient cytogenic abnormalities in normal donors following G-CSF use. Furthermore, the MAH took the opportunity to introduce some minor changes (to correct typographical errors and align symbols with the PI of the reference product) and to conduct the: - Alignment to the current QRD template (version 10.3) - Alignment to the current Appendix I, II and III - Alignment to the Annex to the Commission Guideline on `Excipients in the labelling and package leaflet of medicinal products for human use' - Alignment to the current `Compilation of QRD decisions on stylistic matters in product information." Opinion adopted on 09.02.2023.	Positive Opinion adopted by consensus on 09.02.2023.

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

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

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

in vitro diagnostic medical device - **EMEA/H/D/006233**

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

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

piflufolastat (18F) - EMEA/H/C/005520
imaging in patients undergoing oncologic diagnostic procedures when increased expression of prostate specific membrane antigen is a diagnostic target
List of Questions adopted on 10.11.2022.

dabigatran etexilate - EMEA/H/C/006023
Prevention of venous thromboembolic events
List of Questions adopted on 21.07.2022.

Entresto - sacubitril / valsartan - EMEA/H/C/004062/X/0044/G
Novartis Europharm Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Anette Kirstine Stark, "Extension application to introduce a new pharmaceutical form associated with two new strengths (6 mg/6 mg granules in capsule for opening and 15 mg/16 mg granules in capsule for opening), grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment of children and adolescents aged one year or older with chronic heart failure with left ventricular systolic dysfunction, based on the results of study PANORAMA-HF (CLCZ696B2319); a multicenter, open-label, study to evaluate safety, tolerability, pharmacokinetics and pharmacodynamics of sacubitril/valsartan followed by a 52-week randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of sacubitril/valsartan compared with enalapril in paediatric patients from 1 month to < 18 years of age with heart failure due to systemic left ventricle systolic dysfunction. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.2 of the SmPC are being updated and the Package Leaflet is updated accordingly. In addition, an updated RMP version 4.0 was provided as part of the application. Further, the MAH requested a one-year extension of the market protection."
List of Questions adopted on 10.11.2022.

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

in vitro diagnostic medical device - EMEA/H/D/006201
to detect internal tandem duplication (ITD) and tyrosine kinase domain (TKD) mutations D835 and I836 in the FLT3 gene
Request for Supplementary Information adopted on 26.01.2023.

Neparvis - sacubitril / valsartan - EMEA/H/C/004343/X/0042/G
Novartis Europharm Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Anette Kirstine Stark, "Extension application to introduce a new pharmaceutical form associated with two new strengths (6 mg/6 mg granules in capsule for opening and 15 mg/16 mg granules in capsule for opening), grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment of children and adolescents aged one year or older with chronic heart failure with left ventricular systolic dysfunction, based on the results of Study PANORAMA-HF (CLCZ696B2319); a multicenter, open-label, study to evaluate safety, tolerability, pharmacokinetics and pharmacodynamics of sacubitril/valsartan followed by a 52-week randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of sacubitril/valsartan compared with enalapril in paediatric patients from 1 month to < 18 years of age with heart failure due to systemic left ventricle systolic dysfunction. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.2 of the SmPC are being updated and the Package Leaflet is updated accordingly. In addition, an updated RMP version 4.0 was provided as part of the application. Further, the MAH requested a one-year extension of the market protection."
List of Questions adopted on 10.11.2022.
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

tislelizumab - EMEA/H/C/005919, Orphan
Novartis Europharm Limited, treatment of adult patients with unresectable, recurrent, locally advanced or metastatic oesophageal squamous cell carcinoma after prior chemotherapy

List of Questions adopted on 21.07.2022.

Sogroya - somapacitan - EMEA/H/C/005030/X/0006/G, Orphan
Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber, "Extension application to add a new strength of 15 mg/1.5 mL solution for injection in pre-filled pen grouped with a type II variation C.I.6 to add a new indication 'Replacement of endogenous growth hormone (GH) in children and adolescents with growth failure due to growth hormone deficiency (GHD)', based on results from the completed main 52-week period of the confirmatory phase 3 trial (4263), supported with long-term data from the phase 2 trial (4172), up to week 208 completed. As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly. A revised RMP version 3.0 was provided as part of the application."
List of Questions adopted on 10.11.2022.

sugammadex - EMEA/H/C/006083
Reversal of neuromuscular blockade induced by rocuronium or vecuronium in adults
List of Questions adopted on 15.12.2022.

tislelizumab - EMEA/H/C/005542
treatment of locally advanced or metastatic non-squamous non-small cell lung cancer in adults, treatment of locally advanced or metastatic squamous non-small cell lung cancer in adults, locally advanced or metastatic non-small cell lung cancer after prior chemotherapy in adults
List of Questions adopted on 21.07.2022.

alpelisib - EMEA/H/C/005468, Orphan
Novartis Europharm Limited, treatment of patients with severe manifestations of PIK3CA-related overgrowth spectrum
List of Questions adopted on 10.11.2022.

atogepant monohydrate - EMEA/H/C/005871
Prophylaxis of migraine in adults who have at least 4 migraine days per month.
List of Questions adopted on 10.11.2022.

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

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

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

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

Kinpeygo - budesonide - EMEA/H/C/005653/R/0003, Orphan
STADA Arzneimittel AG, Rapporteur: Christian Gartner, PRAC Rapporteur: Marie Louise Schougaard Christiansen

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
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
Rozlytrek - entrectinib - EMEA/H/C/004936/R/0015 Roche Registration GmbH, Rapporteur: Armando Genazzani, PRAC Rapporteur: Menno van der Elst
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
Ziextenzo - pegfilgrastim - EMEA/H/C/004802/R/0025 Sandoz GmbH, Rapporteur: Christian Gartner, Co-Rapporteur: Simona Badoi, PRAC Rapporteur: Menno van der Elst

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

AYVAKYT - avapritinib - EMEA/H/C/005208/II/0023, Orphan Blueprint Medicines (Netherlands) B.V., Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst, "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."

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

Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Maria del Pilar Rayon, "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."

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, "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."

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, "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."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Bexsero - meningococcal group B vaccine (recombinant, component, adsorbed) - EMEA/H/C/002333/II/0118
GSK Vaccines S.r.l, Rapporteur: Filip Josephson

Budesonide/Formoterol Teva Pharma B.V. - budesonide / formoterol fumarate dihydrate - EMEA/H/C/004882/II/0012/G
Teva Pharma B.V., Duplicate, Duplicate of DuoResp Spiromax, Rapporteur: John Joseph Borg, PRAC Rapporteur: Marie Louise Schougaard Christiansen

EVUSHELD - tixagevimab / cilgavimab - EMEA/H/C/005788/II/0007/G
AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus

Hepcludex - bulevirtide - EMEA/H/C/004854/II/0023/G, Orphan
Gilead Sciences Ireland Unlimited Company, Rapporteur: Filip Josephson

Idefirix - imlifidase - EMEA/H/C/004849/II/0013, Orphan
Hansa Biopharma AB, Rapporteur: Martina Weise

Instanyl - fentanyl - EMEA/H/C/000959/II/0075
Takeda Pharma A/S, Rapporteur: Alexandre Moreau

Lunsumio - mosunetuzumab - EMEA/H/C/005680/II/0002/G, Orphan
Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia

Methylthioninium chloride Proveblue - methylthioninium chloride - EMEA/H/C/002108/II/0055/G
Provepharm SAS, Rapporteur: Kristina Dunder

Nuceiva - botulinum toxin type a - EMEA/H/C/004587/II/0029

Evolus Pharma B.V., Rapporteur: Finbarr Leacy

Ontruzant - trastuzumab - EMEA/H/C/004323/II/0045
Samsung Bioepis NL B.V., Rapporteur: Karin Janssen van Doorn

QUVIVIQ - daridorexant - EMEA/H/C/005634/II/0007/G
Idorsia Pharmaceuticals Deutschland GmbH, Rapporteur: Alexandre Moreau

Taltz - ixekizumab - EMEA/H/C/003943/II/0049/G
Eli Lilly and Co (Ireland) Limited, Rapporteur: Kristina Dunder

Vyepti - eptinezumab - EMEA/H/C/005287/II/0008
H. Lundbeck A/S, Rapporteur: Jan Mueller-Berghaus

Zessly - infliximab - EMEA/H/C/004647/II/0028
Sandoz GmbH, Rapporteur: Eva Skovlund

Zutectra - human hepatitis B immunoglobulin - EMEA/H/C/001089/II/0058
Biotest Pharma GmbH, Rapporteur: Jan Mueller-Berghaus

B.6.9. 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."

Dovprela - pretomanid - EMEA/H/C/005167/II/0013, Orphan
Mylan IRE Healthcare Limited, Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC in order to update frequency

information of several adverse drug reactions (ADRs) as well as to update clinical efficacy information based on final results from study ZeNix (NC007) listed as a specific obligation (SOB/001) in the Annex II. This is a Phase III Partially-Blinded, Randomized Trial Assessing the Safety and Efficacy of Various Doses and Treatment Durations of Linezolid plus Bedaquiline and Pretomanid in Participants with Pulmonary Infection of Either Extensively DrugResistant Tuberculosis (XDRTB), pre-XDR-TB or Treatment Intolerant or NonResponsive Multi-Drug Resistant Tuberculosis (MDRTB)-ZeNix study. The Annex II and Package Leaflet are updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the SmPC and to update the list of local representatives in the Package Leaflet."	
Fintepla - fenfluramine - EMEA/H/C/003933/II/0018, Orphan Zogenix ROI Limited, 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."	
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."	
Imnovid - pomalidomide - EMEA/H/C/002682/II/0050, Orphan Bristol-Myers Squibb Pharma EEIG, Rapporteur: Blanca Garcia-Ochoa, "Update of section 5.1 of the SmPC in order to update efficacy and safety information following the assessment of	

II/0031/G based on OS results from study CC-4047-MM-007 listed as PAES in the Annex II; this is to further investigate the efficacy of pomalidomide in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior treatment regimen including lenalidomide."	
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."	
Jevtana - cabazitaxel - EMEA/H/C/002018/II/0049 Sanofi Winthrop Industrie, Rapporteur: Alexandre Moreau, "Update of sections 4.6 and 5.3 of the SmPC in order to introduce a genotoxicity mechanism update and a contraception update based on the safety working party recommendations on the duration of contraception following the end of treatment with a genotoxic drug. The Package Leaflet is updated accordingly."	
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."	
Lynparza - olaparib - EMEA/H/C/003726/II/0059	

AstraZeneca AB, Rapporteur: Alexandre Moreau, "Submission of the final report from study AME02164. This is a Genetic Toxicity Evaluation using a Bacterial Reverse Mutation Test with Salmonella typhimurium LT2 Strains TA1535, TA1537, TA98 and TA100, and Escherichia coli WP2 Strain uvrA/pKM101."	
Methylthioninium chloride Proveblue - methylthioninium chloride - EMEA/H/C/002108/II/0056 Provepharm SAS, Rapporteur: Kristina Dunder, "Update of section 4.5 of the SmPC in order to add information regarding potential increase of the risk of serotonin syndrome when used in combination with opioids, as well as, to add information regarding the potent reversible MAO Inhibitory activity of Methylthioninium chloride based on post-marketing data and literature; the Package Leaflet is updated accordingly."	
MVABEA - Ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005343/II/0018/G Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, "Grouped application comprising three type II variations as follows: - Update of sections 4.8 and 5.1 of the SmPC in order to add crying, screaming and hyperhidrosis to the list of adverse drug reactions (ADRs) in children with frequency very common, common and common, respectively and to add immunogenicity data from study VAC52150EBL2004 (PREVAC), listed as a study 3 in the agreed PIP. This was a randomized, double-blind, placebo-controlled, parallel-group Phase 2 study conducted at multiple sites in West Africa to investigate the immunogenicity and safety of 3 Ebola vaccine regimens versus placebo in adults (aged ≥18 years), adolescents (aged 12-17 years), and children (2 age strata: 5-11 years and 1-4 years) who never received a candidate Ebola vaccine (self-report) and had no history of Ebola virus disease (self-report). - Update of sections 4.2, 4.8 and 5.1 of the SmPC to add interim safety and immunogenicity data from study VAC52150EBL2005, a study conducted by the MAH in infants 4-11 months of age. - Update of sections 4.2, 4.8 and 5.1 of the SmPC to add final safety and immunogenicity	

data from study VAC52150EBL2011, a study in which an Ad26.ZEBOV booster dose was evaluated in children 1 to 11 years of age (at the time of first vaccination in EBL3001). The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce editorial changes and update the contact details of the local representatives in the Package Leaflet."

Ocaliva - obeticholic acid - EMEA/H/C/004093/II/0038, Orphan

Advanz Pharma Limited, Rapporteur: Blanca Garcia-Ochoa, "Update of sections 4.8 and 5.1 of the SmPC in order to update clinical information based on final results from studies 747-302 and 747-401, listed as specific obligations in the Annex II, as well as results from real-world evidence (RWE) studies evaluating analyses of hepatic clinical outcomes. Study 747-302 is a confirmatory double-blind, randomised, placebo-controlled multicentre study investigating the clinical benefit associated with Ocaliva treatment in patients with PBC who are either unresponsive or intolerant to UDCA treatment based on clinical endpoints, while study 747-401 is a double-blind, randomised, placebo-controlled study evaluating the safety and pharmacokinetics of Ocaliva in patients with PBC and moderate to severe hepatic impairment. The Annex II and Package Leaflet are updated accordingly."

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."

Paxlovid - nirmatrelvir / ritonavir - EMEA/H/C/005973/II/0036

Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, "Update of sections 4.4 and 4.5 of the SmPC in order to include a warning related to Immunosuppressants and to update the

information regarding co-administration with Immunosuppressants following the assessment of procedure II/0010/G based on the cumulative review of the spontaneous reports of over-exposure/over-toxicity of immunosuppressants and literature review. In addition, the MAH took this opportunity to introduce minor editorial changes to the Package Leaflet."

Plegridy - peginterferon beta-1A - EMEA/H/C/002827/II/0068

Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, "Update of section 4.6 of the SmPC in order to update the information relating to secretion in human milk based on the results from study US-PEG-15-10936, a prospective, open label, post marketing study that measured Plegridy concentrations in breast milk in 6 lactating patients with Multiple Sclerosis.
In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet."

Rydapt - midostaurin - EMEA/H/C/004095/II/0029, Orphan

Novartis Europharm Limited, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.8 of the SmPC in order to add "Acute febrile neutrophilic dermatosis (Sweet syndrome)" to the list of adverse drug reactions (ADRs) with frequency not known based on pre-clinical data, clinical trial datasets, scientific literature and safety databases. The Package Leaflet is updated accordingly."

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."

SARCLISA - isatuximab - EMEA/H/C/004977/II/0020

Sanofi Winthrop Industrie, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update an existing warning on 'second primary malignancies', update the list of adverse drug reactions (ADRs) and update the efficacy and safety information based on final OS analysis from ICARIA study (EFC14335), following a recommendation by the CHMP during the initial MAA. This is a phase 3 randomized, open-label, multicenter study designed to assess the efficacy, safety and pharmacokinetics (PK) of isatuximab in combination with pomalidomide and low-dose dexamethasone (IPd) compared with pomalidomide and low-dose dexamethasone (Pd) in patients with refractory or relapsed and refractory multiple myeloma."

Synagis - palivizumab - EMEA/H/C/000257/II/0132

AstraZeneca AB, Rapporteur: Thalia Marie Estrup Blicher, "Update of sections 4.2 and 5.1 of the SmPC in order to update safety information based on results from safety data evaluations from multiple sources, including the clinical study W00-350, post-Marketing Clinical Surveillance Programme (REACH), literature searches and the AstraZeneca Global Patient Safety database."

TAGRISSO - osimertinib - EMEA/H/C/004124/II/0050

AstraZeneca AB, Rapporteur: Blanca Garcia-Ochoa, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to modify the posology recommendations in the case of toxic epidermal necrolysis (TEN), add it as a new warning and add it to the list of adverse drug reactions (ADRs) with frequency uncommon and to update the frequency of interstitial lung disease (ILD) based on an internal safety information review. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Trajenta - linagliptin - EMEA/H/C/002110/II/0049

Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, "Update of

sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update information on the paediatric population based on final results from study DINAMO 1218-0091; this is a Phase III 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. The Package Leaflet is updated accordingly."	
Vipidia - alogliptin - EMEA/H/C/002182/II/0035 Takeda Pharma A/S, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update paediatric information following positive opinion of procedure P46/013 and confirmation of full compliance of PIP EMEA-000496-PIP01-08-M08 based on reports from study studies SYR-322_104 and SYR-322_309. 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 editorial changes."	
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."	
Xevudy - sotrovimab - EMEA/H/C/005676/II/0014 Glaxosmithkline Trading Services Limited, Rapporteur: Thalia Marie Estrup Blicher, "Update sections 4.4 and 5.1 of the SmPC to update information on epitope conservation and activity of sotrovimab against pseudotyped virus encoding epitope variants as well as to update information on the in vitro activity of sotrovimab	

in a pseudotyped virus assay against the Omicron BA.4.6 spike variant, the Omicron BQ.1.1 spike variant and the Omicron BQ.1, BF.7, BA.2.75.2 and XBB.1 spike variants based on final results from studies PC-7831-0143 v15, PC-22-0130, PC-22-0142, PC-22-0145. In addition, the MAH took the opportunity implement editorial changes in the SmPC."	
Xevudy - sotrovimab - EMEA/H/C/005676/II/0015 Glaxosmithkline Trading Services Limited, Rapporteur: Thalia Marie Estrup Blicher, "Update of section 5.1 of the SmPC in order to update clinical information based on a systematic literature review of observational studies evaluating the real world effectiveness of sotrovimab for treatment of SARS-CoV-2 infection during the period when the SARS-CoV-2 Omicron BA.2 sub-variant was dominant."	
Yselty - linzagolix choline - EMEA/H/C/005442/II/0005 Theramex Ireland Limited, Rapporteur: Finbarr Leacy, "Submission of the final report from 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."	
ZABDENO - Ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005337/II/0015/G Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, "Grouped application comprising three type II variations as follows: - Update of sections 4.8 and 5.1 of the SmPC in order to add crying, screaming and hyperhidrosis to the list of adverse drug reactions (ADRs) in children with frequency very common, common and common, respectively and to add immunogenicity data from study VAC52150EBL2004 (PREVAC), listed as a study 3 in the agreed PIP. This was a randomized, double-blind, placebo-controlled, parallel-group Phase 2 study conducted at multiple sites in West Africa to investigate the immunogenicity and safety of 3 Ebola vaccine regimens versus placebo in adults (aged ≥18 years), adolescents (aged 12-17 years), and children (2 age strata:	

5-11 years and 1-4 years) who never received a candidate Ebola vaccine (self-report) and had no history of Ebola virus disease (self-report). - Update of sections 4.2, 4.8 and 5.1 of the SmPC to add interim safety and immunogenicity data from study VAC52150EBL2005, a study conducted by the MAH in infants 4-11 months of age. - Update of sections 4.2, 4.8 and 5.1 of the SmPC to add final safety and immunogenicity data from study VAC52150EBL2011, a study in which an Ad26.ZEBOV booster dose was evaluated in children 1 to 11 years of age (at the time of first vaccination in EBL3001). The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce editorial changes and update the contact details of the local representatives in the Package Leaflet."	
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."	
WS2418 **Lyxumia-EMEA/H/C/002445/WS2418/0039** **Suliqua-EMEA/H/C/004243/WS2418/0030** Sanofi Winthrop Industrie, Lead Rapporteur: Kristina Dunder, "Update of section 4.4 of the SmPC in order to add a new special warning on acute gallbladder disease based on cumulative review of the pharmacovigilance databases, worldwide scientific literature, labelling documents of other GLP-1RAs, and biological plausibility. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."	
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."

B.6.10. CHMP-PRAC assessed procedures

Brukinsa - zanubrutinib - EMEA/H/C/004978/II/0009

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."

Carbaglu - carglumic acid - EMEA/H/C/000461/II/0045

Recordati Rare Diseases, Rapporteur: Fátima Ventura, PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to include a proposed dose adjustment for patients with impaired renal function based on final results from study RCD-P0-027; this is a Phase I, multicenter, open-label, parallel-group adaptive pharmacokinetic single dose study of oral Carbaglu in subjects with normal and varying degrees of impaired renal function. The Package Leaflet is updated accordingly. The RMP version 2.2 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in Annex II and Labelling, and to bring the PI in line with the latest QRD template version 10.3."

GAVRETO - pralsetinib - EMEA/H/C/005413/II/0012

Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.2, 4.4 and 4.5 of the SmPC in order to amend posology recommendations, warnings and drug-drug interaction information regarding the co-administration with CYP3A4 inhibitors, P-gp inhibitors and CYP3A4 inducers based on final results from the DDI study GP43162, listed as a category 3 study in the RMP, as well as results from the physiologically based pharmacokinetic (PBPK) analyses summarised in the PBPK Report 1120689. Study GP43162 is a phase 1, open-

label, fixed-sequence study to evaluate the effect of a single dose of cyclosporine on the single dose pharmacokinetics of pralsetinib in healthy subjects. The RMP version 1.6 has also been submitted."

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."

Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0095

Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Nathalie Gault, "Update of sections 4.4 and 5.2 of the SmPC in order to update 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."

Rydapt - midostaurin - EMEA/H/C/004095/II/0028, Orphan

Novartis Europharm Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Inês Ribeiro-Vaz, "Update of sections 4.2 and 5.2 of the SmPC in order to update efficacy and safety information in elderly patients based on final results from study CPKC412A2408 - An open-label, multi-center, Phase IIIb study to assess the safety and efficacy of midostaurin (PKC412) in patients 18 years of age or older with newly diagnosed FLT3-mutated Acute Myeloid Leukemia who are eligible for "7+3" or "5+2" chemotherapy, listed as a PAES in the Annex II. The RMP version 8.0 has also been submitted."

WS2409
Lixiana-EMEA/H/C/002629/WS2409/0042
Roteas-EMEA/H/C/004339/WS2409/0029

Daiichi Sankyo Europe GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Nathalie Gault, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC with available paediatric data based on final results from study DU176b-D-U312; this is a phase 3, open-label, randomised, multicentre, controlled trial to evaluate the pharmacokinetics and pharmacodynamics of edoxaban and to compare the efficacy and safety of edoxaban with standard-of-care anticoagulant therapy in paediatric subjects from birth to less than 18 years of age with confirmed venous thromboembolism (VTE). The Package Leaflet and Labelling are updated accordingly. The RMP version 15.0 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in the SmPC and to bring the PI in line with the latest QRD template version 10.3."

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."

B.6.11. 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."

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."

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."

B.6.12. CHMP-CAT assessed procedures

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0026, Orphan, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0027, Orphan,

ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Zolgensma - onasemnogene abeparvovec - EMEA/H/C/004750/II/0036/G, Orphan, ATMP
Novartis Europharm Limited, Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege

WS2426
Tecartus-
EMEA/H/C/005102/WS2426/0032
Yescarta-
EMEA/H/C/004480/WS2426/0061
Kite Pharma EU B.V., Lead Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

B.6.13. CHMP-PRAC-CAT assessed procedures

Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0014, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Concetta Quintarelli, CHMP Coordinator: Armando Genazzani, "Update of section 5.1 of the SmPC in order to update efficacy information based on final results from studies 017001 and JCAR-017-BCM-001 listed as obligations in the Annex II. These studies aimed to further characterise the long-term efficacy and safety of Breyanzi in patients treated with relapsed or refractory DLBCL, PMBCL, FL3B after two or more lines of systemic therapy. Study 017001 is a phase 1, open-label, single-arm, multicohort, multicentre, seamless design trial, while study JCAR-017-BCM-001 is a phase 2, open-label, single-arm, multicohort, multicentre trial. The Annex II is updated accordingly. The RMP version 3.0 has also been submitted."

B.6.14. PRAC assessed ATMP procedures

B.6.15. 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

WS2412
Hexacima-
EMEA/H/C/002702/WS2412/0144
Hexyon-
EMEA/H/C/002796/WS2412/0148
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

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

WS2423
Infanrix hexa-
EMEA/H/C/000296/WS2423/0324
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke

WS2424/G
Infanrix hexa-
EMEA/H/C/000296/WS2424/0323/G
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke

WS2425/G
Infanrix hexa-
EMEA/H/C/000296/WS2425/0325/G
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke

WS2428/G
Silodosin Recordati-
EMEA/H/C/004964/WS2428/0010/G
Silodyx-
EMEA/H/C/001209/WS2428/0050/G
Urorec-
EMEA/H/C/001092/WS2428/0053/G
Recordati Ireland Ltd, Generic, Generic of Urorec, Lead Rapporteur: Margareta Bego

WS2441/G
Exelon-
EMEA/H/C/000169/WS2441/0142/G
Prometax-
EMEA/H/C/000255/WS2441/0143/G
Novartis Europharm Limited, Lead Rapporteur:

Alexandre Moreau

WS2443
Ambirix-
EMEA/H/C/000426/WS2443/0126
Twinrix Adult-
EMEA/H/C/000112/WS2443/0161
Twinrix Paediatric-
EMEA/H/C/000129/WS2443/0162
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke

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

WS2448
Filgrastim Hexal-
EMEA/H/C/000918/WS2448/0069
Zarzio-EMEA/H/C/000917/WS2448/0070
Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege

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 20-23 February 2023 CHMP plenary:

G.2.2. List of procedures starting in February 2023 for March 2023 CHMP adoption of outcomes

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