24 January 2022
EMA/CHMP/778542/2021
Human Medicines Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 24-27 January 2022

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

24 January 2022, 09:00 – 19:30, virtual meeting/ room 1C

25 January 2022, 08:30 – 19:30, virtual meeting/ room 1C

26 January 2022, 08:30 – 19:30, virtual meeting/ room 1C

27 January 2022, 08:30 – 15:00, virtual meeting/ room 1C

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 24-27 January 2022. See January 2022 CHMP minutes (to be published post February 2022 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 24-27 January 2022.

1.3. Adoption of the minutes

CHMP minutes for 13-16 December 2021.

Minutes from PReparatory and Organisational Matters (PROM) meeting held on 17 January 2022.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. gefapixant - EMEA/H/C/005884

treatment of refractory or unexplained chronic cough

Scope: Oral explanation

Action: Oral explanation to be held on 26 January 2022 16:00

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

2.1.2. gefapixant - EMEA/H/C/005476

treatment of refractory or unexplained chronic cough

Scope: Oral explanation

Action: Oral explanation to be held on 26 January 2022 16:00

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

2.1.3. betulae cortex dry extract (5-10: 1); extraction solvent: n-heptane 95% (w/w) - Orphan - EMEA/H/C/005035

Amryt Pharmaceuticals DAC; Treatment to achieve accelerated healing of wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in patients from birth onwards.

Scope: Possible oral explanation

Action: Possible oral explanation to be held on 25 January 2022 14:00

List of Outstanding Issues adopted on 11.11.2021. List of Questions adopted on 22.07.2021.

2.1.4. PF-07321332/ritonavir – EMEA/H/C/005973

Treatment for adult patients with symptomatic COVID-19

Scope: Possible oral explanation/opinion

Action: Possible oral explanation to be held on 25 January 2022 16:00

See 3.1

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

No items

2.4. Referral procedure oral explanations

2.4.1. Stresam and generics – etifoxine (hydrochloride) - EMEA/H/A-31/1509

Biocodex

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

Scope: Oral explanation

Action: Oral explanation to be held on 24 January 2022 at 14:00

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

See 10.6

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

International Drug Development France

Re-examination Referral Rapporteur: Ewa Balkowiec Iskra, Re-examination Co-Rapporteur: Janet Koenig

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

Scope: Oral explanation

Action: Oral explanation to be held on 24 January 2022 at 16:00

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

See 10.7

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. lisocabtagene maraleucel / lisocabtagene maraleucel - PRIME - Orphan - ATMP - EMEA/H/C/004731

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 08.10.2021, 16.04.2021. List of Questions adopted on 06.11.2020.

3.1.2. dasatinib - EMEA/H/C/005446

treatment of leukaemia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 25.02.2021, 25.06.2020. List of Questions adopted on 17.10.2019.

3.1.3. dasatinib - EMEA/H/C/005317

treatment of leukaemia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 25.02.2021, 25.06.2020. List of Questions adopted on 17.10.2019.

3.1.4. trastuzumab - EMEA/H/C/005880

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

Scope: Opinion

Action: For adoption

3.1.5. tebentafusp - Orphan - EMEA/H/C/004929

Accelerated assessment

Immunocore Ireland Limited; treatment of uveal melanoma

Scope: Opinion

Action: For adoption

List of Questions adopted on 09.11.2021.

3.1.6. PF-07321332/ritonavir – EMEA/H/C/005973

Treatment for adult patients with symptomatic COVID-19

Scope: Opinion

Action: For adoption

See 2.1

3.1.7. doxorubicin - EMEA/H/C/005320

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.03.2020. List of Questions adopted on 17.10.2019.

3.1.8. teriparatide - EMEA/H/C/005827

treatment of osteoporosis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 16.12.2021. List of Questions adopted on 22.07.2021.

3.1.9. pegfilgrastim - EMEA/H/C/004780

treatment of neutropenia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 11.11.2021. List of Questions adopted on 17.09.2020.

3.1.10. trastuzumab - EMEA/H/C/005066

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 25.03.2021, 10.12.2020. List of Questions adopted on 19.09.2019.

3.1.11. vildagliptin / metformin hydrochloride - EMEA/H/C/005738

treatment of type 2 diabetes mellitus

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 16.12.2021, 16.09.2021. List of Questions adopted on 22.04.2021.

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

3.2.1. amifampridine - EMEA/H/C/005839

treatment of Lambert-Eaton Myasthenic Syndrome

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 16.09.2021.

3.2.2. leuprorelin - EMEA/H/C/005034

indicated for the treatment of hormone dependent advanced prostate cancer

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 23.07.2020.

3.2.3. dimethyl fumarate - EMEA/H/C/006039

treatment of multiple sclerosis

Scope: List of outstanding issues

Action: For adoption

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

treatment of multiple sclerosis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 14.10.2021.

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

treatment of multiple sclerosis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 14.10.2021.

3.2.6. dimethyl fumarate - EMEA/H/C/006042

treatment of multiple sclerosis

Scope: List of outstanding issues

Action: For adoption

3.2.7. budesonide, micronised - Orphan - EMEA/H/C/005653

Calliditas Therapeutics AB; treatment of primary immunoglobulin A (IgA) nephropathy

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 14.09.2021.

3.2.8. artesunate - Orphan - EMEA/H/C/005718

B And O Pharm; Treatment of severe malaria

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 16.09.2021, 22.07.2021. List of Questions adopted on 22.04.2021.

3.2.9. capmatinib - EMEA/H/C/004845

treatment of non-small cell lung cancer (NSCLC)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 16.09.2021.

3.2.10. insulin aspart - EMEA/H/C/005635

treatment of diabetes mellitus

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 16.09.2021.

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

3.3.1. vutrisiran - Orphan - EMEA/H/C/005852

Alnylam Netherlands B.V.; treatment of hereditary transthyretin-mediated amyloidosis

Scope: List of questions

Action: For adoption

3.3.2. mavacamten - EMEA/H/C/005457

treatment of symptomatic obstructive hypertrophic cardiomyopathy

Scope: List of questions

Action: For adoption

3.3.3. dimethyl fumarate - EMEA/H/C/005963

treatment of multiple sclerosis

Scope: List of questions

Action: For adoption

3.3.4. pegfilgrastim - EMEA/H/C/005810

Treatment of neutropenia

Scope: List of questions

Action: For adoption

3.3.5. maralixibat - Orphan - EMEA/H/C/005857

Mirum Pharmaceuticals International B.V.; Treatment of cholestatic liver disease in patients with Alagille syndrome (ALGS) 1 year of age and older

Scope: List of questions

Action: For adoption

3.3.6. mosunetuzumab - Orphan - EMEA/H/C/005680

Accelerated assessment

Roche Registration GmbH; refractory follicular lymphoma (FL)

Scope: List of questions

Action: For adoption

3.3.7. relatlimab / nivolumab - EMEA/H/C/005481

indicated for the first-line treatment of advanced (unresectable or metastatic) melanoma in adults and adolescents (12 years and older and weighing at least 40 kg).

Scope: List of questions

Action: For adoption

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

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

Scope: List of questions

Action: For adoption

3.3.9. teriflunomide - EMEA/H/C/005962

treatment of multiple sclerosis (MS)

Scope: List of questions

Action: For adoption

3.3.10. ranibizumab - EMEA/H/C/005617

treatment of neovascular age-related macular degeneration (AMD)

Scope: List of questions

Action: For adoption

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

Accelerated assessment

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

Scope: List of questions

Action: For adoption

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

3.4.1. eptacog alfa (activated) - EMEA/H/C/005547

treatment of bleeding episodes and for the prevention of bleeding

Scope: Letter from the applicant dated 20.12.2021 requesting an extension to the clock stop to respond to the list of questions adopted in November 2021.

List of Questions adopted on 11.11.2021

3.4.2. voclosporin - EMEA/H/C/005256

indicated in combination with background immunosuppressive therapies for the treatment of adult patients with class III, IV or V (including mixed class III/V and IV/V) lupus nephritis (LN).

Scope: Letter from the applicant dated 13.01.2022 requesting an extension to the clock stop to respond to the list of questions adopted in November 2021.

Action: For adoption

List of Questions adopted on 11.11.2021

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

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

Scope: List of experts for an ad-hoc expert group meeting.

Action: For adoption

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

3.4.4. adrenaline - EMEA/H/C/005584

For the emergency treatment of allergic reactions, including anaphylaxis

Scope: Update on the procedure.

Action: For discussion

List of Questions adopted on 25.03.2021.

3.4.5. autologous glioma tumor cells, inactivated / autologous glioma tumor cell lysates, inactivated / allogeneic glioma tumor cells, inactivated / allogeneic glioma tumor cell lysates, inactivated - Orphan - ATMP - EMEA/H/C/003693

Epitopoietic Research Corporation-Belgium (E.R.C.); treatment of glioma

Scope: Request from the company for an extension to the clock stop to respond to the list of outstanding issues adopted in July 2021.

Action: For information

List of Outstanding Issues adopted on 16.07.2021. List of Questions adopted on 22.01.2021.

3.4.6. palovarotene - Orphan - EMEA/H/C/004867

Ipsen Pharma; Treatment of fibrodysplasia ossificans progressiva

Scope: Letter from the applicant dated 14.01.2022 requesting an extension to the clock stop to respond to the list of questions adopted in September 2021.

Action: For adoption

List of Questions adopted on 16.09.2021

3.4.7. thalidomide - EMEA/H/C/005715

treatment of multiple myeloma

Scope: Letter from the applicant dated 14.01.2022 requesting an extension to the clock stop to respond to the list of questions adopted in September 2021.

Action: For adoption

List of Questions adopted on 16.09.2021

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

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

Scope: Letter from the applicant dated 18.01.2022 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in November 2021.

Action: For adoption

List of Outstanding Issues adopted on 16.12.2021, 16.09.2021, 25.02.2021. List of Questions adopted on 23.07.2020.

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

No items

3.6. Initial applications in the decision-making phase

3.6.1. Padcev - enfortumab vedotin - EMEA/H/C/005392

Astellas Pharma Europe B.V.; treatment of locally advanced (LA) or metastatic urothelial cancer (mUC)

Scope: Update on the status of this application.

Action: For adoption

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

Opinion adopted on 16.12.2021. List of Outstanding Issues adopted on 14.09.2021. List of Questions adopted on 22.06.2021.

3.6.2. Yselty - linzagolix choline - EMEA/H/C/005442

ObsEva Ireland Ltd; for the management of heavy menstrual bleeding (HMB) associated with uterine fibroids

Scope: Update on the status of this application.

Action: For adoption

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

Opinion adopted on 16.12.2021. List of Outstanding Issues adopted on 11.11.2021, 16.09.2021. List of Questions adopted on 22.04.2021.

3.7. Withdrawals of initial marketing authorisation application

3.7.1. arachis hypogaea extract - Article 28 - EMEA/H/C/004810

treatment of peanut allergy

Scope: Withdrawal of initial marketing authorisation application

Action: For information

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

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

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

Scope: Withdrawal of initial marketing authorisation application

Action: For information

List of Questions adopted on 14.10.2021.

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

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

4.1.1. Ayvakyt - avapritinib - Orphan - EMEA/H/C/005208/X/0004/G

Blueprint Medicines (Netherlands) B.V.

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

Scope: "Extension application to add two new strengths of film-coated tablets (25 mg and 50 mg), grouped with a type II variation (C.I.6.a) to introduce a new therapeutic indication for AyvakytYVAKYT. Extension of indication to include treatment of adult patients with advanced systemic mastocytosis (AdvSM), including aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated haematological neoplasm (SM-AHN), and mast cell leukaemia (MCL), after at least one systemic therapy for AyvakytYVAKYT based on the results of the BLU-285-2101 and BLU-285-2202 studies. The new indication is applicable to the new and existing presentations (25 mg, 50 mg, 100 mg and 200 mg film-coated tablets). As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.4, 4.5, 4.6, 4.8, 5.1, 5.2, 5.3, 6.1 and 8 of the SmPC are updated. The Labelling and Package Leaflet are updated in accordance. Version 1.1 of the RMP has also been submitted."

Action: For adoption

List of Outstanding Issues adopted on 11.11.2021. List of Questions adopted on 24.06.2021.

4.1.2. Dupixent - dupilumab - EMEA/H/C/004390/X/0045/G

sanofi-aventis groupe

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Kimmo Jaakkola

Scope: "1- Extension of a marketing authorisation for Dupixent to add a new strength, 100 mg solution for injection.
2- Type II (C.I.6) - Extension of indication to include treatment of paediatric patients with severe asthma with type 2 inflammation aged 6 to 11 years old.
Version 6.0 of the RMP has also been submitted."

Action: For adoption

List of Outstanding Issues adopted on 11.11.2021. List of Questions adopted on 22.07.2021.

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

Novo Nordisk A/S

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber

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

Action: For adoption

List of Questions adopted on 14.10.2021.

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

No items

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

4.3.1. Rinvoq - upadacitinib - EMEA/H/C/004760/X/0012/G

AbbVie Deutschland GmbH & Co. KG

Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension application to add a new strength (45 mg) of the prolonged-release tablets, grouped with a type II variation (C.I.6.a) to include the treatment of adults with moderately to severely active ulcerative colitis who had an inadequate response, lost response or were intolerant to either conventional therapy or a biologic agent; as a consequence of the EoI, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance.
The RMP (version 6.0) has also been submitted."

Action: For adoption

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

No items

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

No items

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

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

5.1.1. Briviact - brivaracetam - EMEA/H/C/003898/II/0032/G

UCB Pharma S.A.

Rapporteur: Filip Josephson, PRAC Rapporteur: Adam Przybylkowski

Scope: "- Extension of indication to include patients from 1 month to 4 years of age for the Briviact treatment. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The RMP version 8.0 has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.2 and the MAH took the opportunity to implement minor editorial updates. Procedure grouped with Quality Variation.
The Package Leaflet and Labelling are updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 11.11.2021, 16.09.2021, 24.06.2021.

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

Novartis Europharm Limited

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

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

Action: For adoption

Request for Supplementary Information adopted on 14.10.2021.

5.1.3. Enhertu - trastuzumab deruxtecan - EMEA/H/C/005124/II/0012

Daiichi Sankyo Europe GmbH

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of indication to include monotherapy treatment of adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior anti-HER2-based regimen for Enhertu based on

final results from studies DS8201 A J202 (DESTINY Gastric01) and DS8201-A-U205 (DESTINY Gastric02); as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, changes regarding the dosing recommendation for corticosteroid treatment and the protection of the infusion bag from light have been introduced. 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

5.1.4. Hemlibra - emicizumab - EMEA/H/C/004406/II/0027

Roche Registration GmbH

Rapporteur: Alexandre Moreau, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to include treatment of adult and paediatric patients with haemophilia A without factor VIII (FVIII) inhibitors who have mild or moderate disease for whom prophylaxis is clinically indicated. Consequently, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC and section 1 of the package leaflet are updated. In addition, section 4.2 is updated to make it clear that the maintenance dose for Hemlibra applies from week 5 of dosing. The PIL is updated accordingly. Version 4.0 of the RMP has also been submitted."

Action: For adoption

5.1.5. Imcivree - setmelanotide - Orphan - EMEA/H/C/005089/II/0002/G

Rhythm Pharmaceuticals Netherlands B.V.

Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Marek Juracka

Scope: "Group of variations consisting of:
C.I.6.a - To add the new therapeutic indication for the treatment of obesity and the control of hunger associated with genetically confirmed Bardet-Biedl syndrome (BBS). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC and sections 1, 3 and 4 of the PL are updated accordingly. The updated RMP version 1.0 has also been submitted.
C.I.6.a - To add the new therapeutic indication for the treatment of obesity and the control of hunger associated with genetically confirmed Alström syndrome (AS). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC and sections 1, 3 and 4 of the PL are updated accordingly. The updated RMP version 1.0 has also been submitted."

Action: For adoption

5.1.6. Jardiance - empagliflozin - EMEA/H/C/002677/II/0060

Boehringer Ingelheim International GmbH

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia

Scope: "Extension of indication to add the treatment of patients with Heart Failure with preserved ejection fraction based on the results from the clinical study 1245.110 EMPEROR-preserved. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC and sections 1 and 4 of the PIL are updated accordingly. Further, the MAH applied for an additional year of

market protection. The updated RMP v 16.0 has also been submitted.
In addition, the statement 'sodium free' was re-located from section 2 of the SmPC to section 4.4. to comply with EMA'S QRD guidance and minor linguistic changes to the national translations are included in this submission", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

5.1.7. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0117

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication to include a new indication for Keytruda, in combination with chemotherapy, with or without bevacizumab, for the treatment of persistent, recurrent, or metastatic cervical cancer in adults; as a consequence, sections 4.1 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 38.1 of the RMP has also been submitted."

Action: For adoption

5.1.8. Lynparza - olaparib - EMEA/H/C/003726/II/0051/G

AstraZeneca AB

Rapporteur: Alexandre Moreau, Co-Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to include adjuvant treatment of breast cancer for Lynparza (for tablets); as a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. In addition, sections 4.8 of the SmPC for Lynparza hard capsules are revised based on the updated safety data analysis. The Package Leaflet is updated in accordance. Version 23 of the RMP has also been submitted."

Action: For adoption

5.1.9. NovoSeven - eptacog alfa (activated) - EMEA/H/C/000074/II/0116

Novo Nordisk A/S

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include treatment of severe postpartum haemorrhage for NovoSeven. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is also updated in accordance. Version 8.0 of the RMP has also been submitted."

Action: For adoption

5.1.10. Reblozyl - luspatercept - Orphan - EMEA/H/C/004444/II/0009

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Daniela Philadelphy, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Laurence de Fays

Scope: "C.I.6 (Extension of indication)
Extension of indication in β-thalassaemia to include adult patients with non-transfusion dependent β-thalassaemia (NTDT) for Reblozyl; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

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

Shionogi B.V.

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

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

Action: For adoption

Request for Supplementary Information adopted on 16.12.2021, 14.10.2021.

5.1.12. Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0073

Biogen Netherlands B.V.

Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber

Scope: "C.I.6 (Extension of indication) type II Art.29 Extension of indication to include treatment of relapsing remitting multiple sclerosis (RRMS) in paediatrics patients from 10 years of age and over; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.3 are updated. The Package Leaflet is updated in accordance.
The MAH is requesting an extension of the market protection of one additional year in line with the guidance on elements required to support the significant clinical benefit in comparison with existing therapies of a new therapeutic indication in accordance with Article

14(11) of Regulation (EC) 726/2004.
Version 11.4 of the RMP has also been submitted to update the RMP (parts I-IV) based on study 109MS306 data supporting the request for a paediatric indication and the applicant took the opportunity to update the RMP with the most updated data (Part II modules SIV, SV and SVII). " Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 16.12.2021, 16.09.2021.

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

Eli Lilly Nederland B.V.

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

Scope: "Extension of indication to include Verzenios in combination with endocrine therapy for adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive early breast cancer at high risk of recurrence; as a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 5.1 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 14.10.2021, 24.06.2021, 25.02.2021.

5.1.14. WS2049/G
Lacosamide UCB - lacosamide - EMEA/H/C/005243/WS2049/0009/G
Vimpat - lacosamide - EMEA/H/C/000863/WS2049/0091/G

UCB Pharma S.A.

Lead Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include patients from 1 month to 4 years of age for treatment of partial-onset seizures with or without secondary generalisation as monotherapy and adjunctive therapy for Vimpat/Lacosamide USB. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. Version 16.0 of the RMP has also been submitted.
B.IV.1.a.1
B.II.f.1.b.
The Package Leaflet and labelling are updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 11.11.2021, 16.09.2021, 24.06.2021.

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

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

Shire Pharmaceuticals Ireland Limited

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark

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

Letter from the applicant dated 14 January 2022 requesting an extension to the clock stop to respond to the request for supplementary information adopted in November 2021.

Action: For adoption

Request for Supplementary Information adopted on 11.11.2021

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

No items

6. 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

No items

6.4. Companion diagnostics – follow-up consultation

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.2. Priority Medicines (PRIME)

Information related to priority medicines cannot be released at present time as these contain commercially confidential information

8.2.1. List of applications received

Action: For information

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Comirnaty - tozinameran - EMEA/H/C/005735/II/0093

BioNTech Manufacturing GmbH

Rapporteur: Filip Josephson

Scope: "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information after booster dose, based on interim results from study C4591031, this is a randomized, placebo-controlled, phase 3 booster efficacy study involving participants ≥ 16 years of age who completed the primary series of BNT162b2 30 µg in study C4591001. The Package Leaflet and Labelling are updated accordingly.
In addition, the MAH took the opportunity to make minor editorial changes throughout the product information."

Action: For adoption

9.1.2. Comirnaty - tozinameran - EMEA/H/C/005735/II/0102

BioNTech Manufacturing GmbH

Rapporteur: Filip Josephson

Scope: "Update of sections 4.8 and 5.1 of the SmPC in order to update safety and efficacy information 6 months post-dose 2 follow-up for adolescence 12 through 15 years of age based on updated interim results from study C4591001, listed as a specific obligation; this is a Phase 1/2/3, placebo-controlled, observer-blind, interventional, dose-finding, study to evaluate the safety, tolerability, immunogenicity and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals.
In addition, the MAH took the opportunity to implement minor editorial changes in section 6.3 of the SmPC and section 5 of the PIL of Comirnaty 30 micrograms/dose dispersion for injection."

Action: For adoption

9.1.3. Elzonris - tagraxofusp - EMEA/H/C/005031/II/0009

Stemline Therapeutics B.V.

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst

Scope: "Submission of the final report from study 20255431 (CRL-263114) 'Characterization of fixed choroid plexus samples from primate study MPI-2231-007 by Immunohistochemistry with DT, CD123, IL-3 and IgG' (MEA002) listed as a category 3 study in the RMP. This is a non-interventional, post-authorisation study on blood brain barrier (BBB) models in order to determine a potential toxicity biomarker to further investigate the risk of choroid plexus lesions. The RMP version 2.0 has also been submitted."

Action: For discussion

9.1.4. Naglazyme - galsulfase - EMEA/H/C/000640/II/0086

BioMarin International Limited

Rapporteur: Fátima Ventura, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "C.I.11.b variation to update the RMP to version 6.4 to remove gastrointestinal haemorrhage, hepatic impairment and thrombocytopenia from the list of important potential risks. This proposed update is supported by the submission of the final report from the MPS VI Clinical Surveillance Program (CSP) listed as a Specific Obligation (SOB002) in the Annex II of the Product Information for this MAA under exceptional circumstances. This observational CSP was undertaken to characterise the natural progression of MPS VI, to evaluate the long-term safety and efficacy data from Naglazyme treatment, to collect information on the effect of Naglazyme treatment on lactation, growth and development of infants of Naglazyme treated mothers and to evaluate the effects of Naglazyme treatment on children under 5 years of age."

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021.

9.1.5. COVID-19 vaccines use during pregnancy

Comirnaty; Rapporteur: Filip Josephson, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Menno van der Elst

COVID-19 Vaccine Janssen; Rapporteur: Christophe Focke, Co-Rapporteur: Sol Ruiz, PRAC Rapporteur: Ulla Wändel Liminga

Nuvaxovid; Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Brigitte Keller-Stanislawski

Spikevax; Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Hans Christian Siersted

Vaxzevria; Rapporteur: Sol Ruiz, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jean-Michel Dogné

Scope: The CHMP has discussed in its December 2021 meeting the COVID-19 vaccine use during pregnancy and lactation and agreed on the importance of reviewing the current label as soon as possible. In order to do that, the CHMP has decided to request to the MAH a review of all available evidence on vaccination in pregnant women and breastfeeding that has to be provided to the EMA as a LEG by 10 January 2022, at the latest.

The review should not be limited to data generated/owned by the company but needs to include relevant literature as well as a progress update and/or data coming from the RMP measures related to this topic. The MAH should, within this review, critically discuss the need to update the product information.

Action: For adoption

9.1.6. Imbruvica - ibrutinib - EMEA/H/C/003791/II/0069

Janssen-Cilag International NV

Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Update of the SmPC section 4.4 to include information on fatal and serious cardiac arrythmias and cardiac failure, relevant warnings and periodical monitoring of patients- following a safety assessment for increased risk of sudden death/cardiac death with the use of ibrutinib. Section 2 of the PL has been updated accordingly. Typographical errors have been corrected throughout the PI. The revised RMP version 11 has been submitted."

Action: For adoption

9.1.7. Bosulif - bosutinib - EMEA/H/C/002373/II/0050/G

Pfizer Europe MA EEIG

Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber

Scope: "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to reflect results from the studies B1871039 (SOB) and B1871040 (category 3); study B1871039 is a Phase 4 Safety and Efficacy Study of Bosutinib in Patients With Philadelphia Chromosome Positive Chronic Myeloid Leukaemia Previously Treated With One or More Tyrosine Kinase Inhibitors and study B1871040 is an Open-Label Bosutinib Treatment Extension Study for Subjects

With Chronic Myeloid Leukaemia (CML) who Have Previously Participated in Bosutinib Studies B1871006 or B1871008. The Package Leaflet is updated accordingly. The MAH requests deletion of the SOB from annex II of the PI and requests consideration for a switch of the Conditional Marketing Authorisation to a full Marketing Authorisation. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives for Belgium, Luxemburg, Germany and Northern Island in the Package Leaflet. The MAH is also asking the deletion of the product from the additional monitoring list."

Action: For adoption

Request for Supplementary Information adopted on 16.12.2021, 16.09.2021.

10. Referral procedures

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

No items

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

No items

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

No items

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

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

Tiofarma B.V

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Kristina Dunder

Scope: Opinion/LoOI

Action: For adoption

Decentralised procedure number: NL/H/5089/001-003/DC, notification by the Agency of the Netherlands dated 24 September 2021 notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC.

10.4.2. Daruph and Anafezyn - dasatinib (anhydrous) - EMEA/H/A-29(4)/1516

Zentiva k.s.

Rapporteur: TBC, Co-Rapporteur: TBC

Scope: Start of procedure, list of questions, timetable, appointment of rapporteurs

Action: For adoption

Decentralised Procedure number: SE/H/2098/01–06/DC; SE/H/2099/01–06/DC, notification by the Swedish Agency notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC. The objecting MSs are of the opinion that a positive benefit risk balance is not established under Article 10(3) of Directive 2001/83/EC, as applied, in the absence of bioequivalence and that additional justification is needed to support extrapolation of efficacy and safety to the reference product. Concerns are also raised on the different warning with the reference medicinal product regarding concomitant administration of PPI and /or H2-antagonist and the risk of medication error.

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

No items

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

10.6.1. Stresam and generics – etifoxine (hydrochloride) - EMEA/H/A-31/1509

Biocodex

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

Scope: Oral explanation/ list of outstanding issues/ opinion

Action: For adoption

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

See 2.4

10.6.2. Synchron Research Services – various – EMEA/H/A-31/1515

Various

Referral Rapporteur: TBC, Referral Co-Rapporteur: TBC

Scope: Start of procedure, list of questions, timetable, appointment of rapporteurs

Action: For adoption

Article 31 procedure triggered by the Federal Agency for Medicines and Health Products (FAMHP) in Belgium, the Danish Medicines Agency (DKMA), the Finnish Medicines Agency

(Fimea), the Medicines Evaluation Board (MEB) in the Netherlands and the Medical Products Agency (MPA) in Sweden concerning the contract research organisation (CRO) Synchron Research Services, located in Ahmedabad, Gujarat, India

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

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

International Drug Development France

Re-examination Referral Rapporteur: Ewa Balkowiec Iskra, Re-examination Co-Rapporteur: Janet Koenig

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

Scope: Oral explanation/ Opinion

Action: For adoption

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

See 2.4

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

January 2022 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

No items

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on 10-13 January 2022

Action: For information

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for January 2022

Action: For adoption

14.2.2. Paediatric Committee (PDCO)

PIPs reaching D30 at January 2022 PDCO

Action: For information

Report from the PDCO meeting held on 18-21 January 2022

Action: For information

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

14.3.1. Biologics Working Party (BWP)

Chair: Sol Ruiz

Reports from BWP January 2022 meeting to CHMP for adoption:

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

Action: For adoption

14.3.2. Scientific Advice Working Party (SAWP)

Chair: Anja Schiel

Report from the SAWP meeting held on 10-13 January 2022. Table of conclusions

Action: For information

Scientific advice letters:

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

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Update on COVID-19

Action: For information

15.1.2. Tixagevimab/Cilgavimab – EMEA/H/C/005837/0000

treatment of COVID-19

Scope: Rolling review 1st interim opinion

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)*

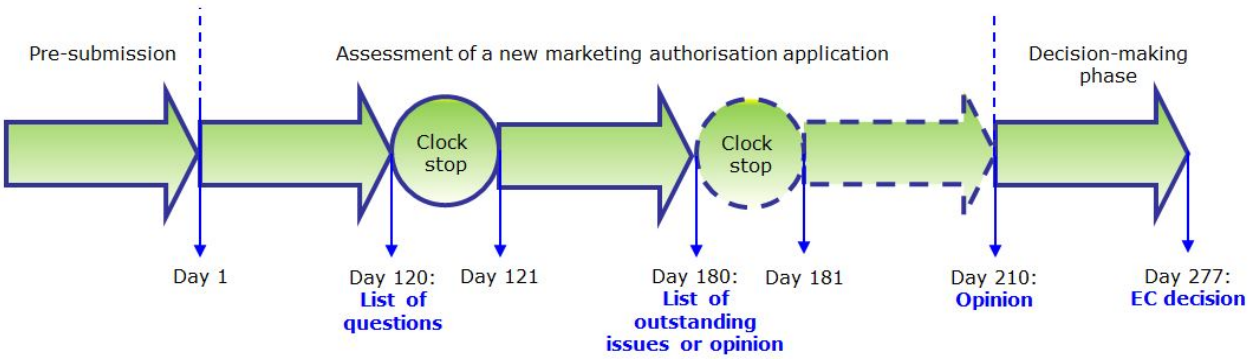
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

24 January 2022
EMA/CHMP/40429/2022

Annex to 24-27 January 2022 CHMP Agenda

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A. PRE-SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for January 2022: **For adoption**

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

Final Outcome of Rapporteurship allocation for January 2022: **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

Myalepta - metreleptin -
EMEA/H/C/004218/S/0023, Orphan
Amryt Pharmaceuticals DAC, Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Adam Przybylkowski

Raxone - idebenone -
EMEA/H/C/003834/S/0029, Orphan
Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

OXERVATE - cenegermin -
EMEA/H/C/004209/R/0037, Orphan
Dompe farmaceutici S.p.A., Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Jan Neuhauser

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Brineura - cerliponase alfa - EMEA/H/C/004065/R/0034, Orphan
BioMarin International Limited, Rapporteur: Martina Weise, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Ulla Wändel Liminga
Request for Supplementary Information adopted on 11.11.2021.

Dupixent - dupilumab - EMEA/H/C/004390/R/0053
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Kimmo Jaakkola

Efavirenz/Emtricitabine/Tenofovir disoproxil Zentiva - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/004250/R/0025
Zentiva k.s., Generic, Generic of Atripla (SRD), Rapporteur: Tomas Radimersky, PRAC Rapporteur: Martin Huber

Erelzi - etanercept - EMEA/H/C/004192/R/0037
Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Eva A. Segovia
Request for Supplementary Information adopted on 11.11.2021.

Insulin lispro Sanofi - insulin lispro - EMEA/H/C/004303/R/0013
sanofi-aventis groupe, Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Annika Folin

Kisqali - ribociclib - EMEA/H/C/004213/R/0034
Novartis Europharm Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Anette Kirstine Stark

Kyntheum - brodalumab - EMEA/H/C/003959/R/0019
LEO Pharma A/S, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Eva A. Segovia

Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/R/0048
AbbVie Deutschland GmbH & Co. KG,

Rapporteur: Jean-Michel Race, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins

Reagila - cariprazine - EMEA/H/C/002770/R/0026
Gedeon Richter Plc., Rapporteur: Kristina Dunder, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Ana Sofia Diniz Martins

TAGRISSO - osimertinib - EMEA/H/C/004124/R/0044
AstraZeneca AB, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 11.11.2021.

Trimbow - beclometasone / formoterol / glycopyrronium bromide - EMEA/H/C/004257/R/0025
Chiesi Farmaceutici S.p.A., Rapporteur: Janet Koenig, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Jan Neuhauser
Request for Supplementary Information adopted on 16.12.2021.

Ucedane - carglumic acid - EMEA/H/C/004019/R/0011
Eurocept International B.V., Generic, Generic of Carbaglu, Rapporteur: Anastasia Mountaki, PRAC Rapporteur: Ana Sofia Diniz Martins

Veltassa - patiromer - EMEA/H/C/004180/R/0028
Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Jayne Crowe, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Kirsti Villikka
Request for Supplementary Information adopted on 16.12.2021.

B.2.3. Renewals of Conditional Marketing Authorisations

Bosulif - bosutinib - EMEA/H/C/002373/R/0051
Pfizer Europe MA EEIG, Rapporteur: Janet Koenig, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Martin Huber
Request for Supplementary Information adopted on 16.12.2021.

Deltyba - delamanid - EMEA/H/C/002552/R/0052, Orphan

Otsuka Novel Products GmbH, Rapporteur: Christophe Focke, PRAC Rapporteur: Laurence de Fays
Request for Supplementary Information adopted on 16.12.2021.

Lorviqua - lorlatinib - EMEA/H/C/004646/R/0019
Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Nikica Mirošević Skvrce

Natpar - parathyroid hormone - EMEA/H/C/003861/R/0034, Orphan
Takeda Pharmaceuticals International AG, Rapporteur: Karin Janssen van Doorn, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Rhea Fitzgerald
Request for Supplementary Information adopted on 16.12.2021.

Ondexxya - andexanet alfa - EMEA/H/C/004108/R/0025
Alexion Europe SAS, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst

Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (h5n1) (live attenuated, nasal) - EMEA/H/C/003963/R/0047
AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sonja Hrabcik

Rubraca - rucaparib - EMEA/H/C/004272/R/0030
Clovis Oncology Ireland Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Annika Folin

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 10-13 January 2022
PRAC:

Signal of arthralgia

Imfinzi – durvalumab

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: David Olsen
PRAC recommendation on a variation
Action: For adoption

Signal of toxic epidermal necrolysis

Lyrica – pregabalin

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Liana Gross-Martirosyan
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 January 2022 meeting:

EMEA/H/C/PSUSA/00000274/202105
(azacitidine)
CAPS:
Vidaza (EMEA/H/C/000978) (azacitidine), Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "18/05/2018 To: 18/05/2021"

EMEA/H/C/PSUSA/00000935/202106
(dasatinib)
CAPS:
Sprycel (EMEA/H/C/000709) (dasatinib), Bristol-Myers Squibb Pharma EEIG, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, "27/06/2020 To: 27/06/2021"

EMEA/H/C/PSUSA/00001725/202105
(imatinib)
CAPS:
Glivec (EMEA/H/C/000406) (imatinib), Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa
NAPS:
NAP - EU
PRAC Rapporteur: Eva A. Segovia, "11/05/2018 To: 10/05/2021"

EMEA/H/C/PSUSA/00002700/202105 (sildenafil (indicated for pulmonary hypertension)) CAPS: **Revatio** (EMEA/H/C/000638) (sildenafil), Upjohn EESV, Rapporteur: Johann Lodewijk Hillege, "01/06/2018 To: 31/05/2021"	
EMEA/H/C/PSUSA/00010516/202106 (opicapone) CAPS: **Ongentys** (EMEA/H/C/002790) (opicapone), Bial - Portela & Cª, S.A., Rapporteur: Martina Weise, PRAC Rapporteur: Maria del Pilar Rayon, "25/06/2020 To: 24/06/2021"	
EMEA/H/C/PSUSA/00010761/202105 (pegvaliase) CAPS: **Palynziq** (EMEA/H/C/004744) (pegvaliase), BioMarin International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, "24/11/2020 To: 23/05/2021"	
EMEA/H/C/PSUSA/00010787/202106 (ravulizumab) CAPS: **Ultomiris** (EMEA/H/C/004954) (ravulizumab), Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa, "30/12/2020 To: 30/06/2021"	
EMEA/H/C/PSUSA/00010897/202106 (COVID-19 mRNA vaccine (nucleoside-modified) (Spikevax)) CAPS: **Spikevax** (EMEA/H/C/005791) (COVID-19 mRNA vaccine (nucleoside-modified)), Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Hans Christian Siersted, "18/12/2020 To: 30/06/2021"	

B.4. EPARs / WPARs

ABYLQIS (WD) - arachis hypogaea extract - EMEA/H/C/004810, Article 28 DBV Technologies, treatment of peanut allergy, Known active substance (Article 8(3) of Directive No 2001/83/EC) **WPAR**	For information only. Comments can be sent to the PL in case necessary.
Aduhelm - aducanumab - EMEA/H/C/005558 Biogen Netherlands B.V., Alzheimer's disease,	For information only. Comments can be sent to the PL in case necessary.

New active substance (Article 8(3) of Directive No 2001/83/EC)	
Aliqopa - copanlisib - EMEA/H/C/004334, Orphan Bayer AG, treatment of adult patients with relapsed marginal zone lymphoma, New active substance (Article 8(3) of Directive No 2001/83/EC) **WPAR**	For information only. Comments can be sent to the PL in case necessary.
Apexxnar - pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - EMEA/H/C/005451 Pfizer Europe MA EEIG, prevention of invasive disease and pneumonia caused by Streptococcus pneumoniae serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F, 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.
Kerendia - finerenone - EMEA/H/C/005200 Bayer AG, delay progression of kidney disease, reduce the risk of cardiovascular mortality and morbidity, 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.
NGENLA - somatrogon - EMEA/H/C/005633, Orphan Pfizer Europe MA EEIG, indicated for the long-term treatment of paediatric patients with growth disturbance due to insufficient secretion of growth hormone., 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.
Okedi - risperidone - EMEA/H/C/005406 Laboratorios Farmacéuticos Rovi, S.A., treatment of schizophrenia, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Ontilyv - opicapone - EMEA/H/C/005782 Bial Portela & Companhia S.A., treatment of Parkinson's disease and motor fluctuations, Informed Consent of Ongentys, Informed consent application (Article 10c of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Oxbryta - voxelotor - EMEA/H/C/004869, Orphan Global Blood Therapeutics Netherlands, Indicated for the treatment of haemolytic anaemia in adults and paediatric patients 12 years of age and older with sickle cell disease	For information only. Comments can be sent to the PL in case necessary.

(SCD)., New active substance (Article 8(3) of Directive No 2001/83/EC)	
Saphnelo - anifrolumab - EMEA/H/C/004975 AstraZeneca AB, indicated as an add-on therapy for the treatment of adult patients with moderate to severe systemic lupus erythematosus (SLE), despite standard 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.
Sapropterin Dipharma - sapropterin - EMEA/H/C/005646 Dipharma B.V., treatment of hyperphenylalaninemia (HPA), Generic, Generic of Kuvan, 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 Mylan - metformin hydrochloride / sitagliptin hydrochloride monohydrate - EMEA/H/C/005678 Mylan Ireland Limited, 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.
TEPMETKO - tepotinib - EMEA/H/C/005524 Merck Europe B.V., treatment of advanced non-small cell lung cancer Treatment of adult patients with advanced non-small cell lung cancer, 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.
Xevudy - sotrovimab - EMEA/H/C/005676 GlaxoSmithKline Trading Services Limited, Treatment of coronavirus disease 2019 (COVID-19), 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.

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

Abevmy - bevacizumab - EMEA/H/C/005327/II/0005/G Mylan IRE Healthcare Limited, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.

Request for Supplementary Information adopted on 11.11.2021.	
ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0027 Baxalta Innovations GmbH, Rapporteur: Andrea Laslop Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
Alymsys - bevacizumab - EMEA/H/C/005286/II/0005 Mabxience Research SL, Rapporteur: Christian Gartner Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0157/G Amgen Europe B.V., Rapporteur: Martina Weise Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0158 Amgen Europe B.V., Rapporteur: Martina Weise Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Bimzelx - bimekizumab - EMEA/H/C/005316/II/0003/G UCB Pharma S.A., Rapporteur: Peter Kiely Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Bimzelx - bimekizumab - EMEA/H/C/005316/II/0004 UCB Pharma S.A., Rapporteur: Peter Kiely Request for Supplementary Information adopted on 20.01.2022.	Request for supplementary information adopted with a specific timetable.
Cerezyme - imiglucerase - EMEA/H/C/000157/II/0123/G Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 13.01.2022, 14.10.2021.	Request for supplementary information adopted with a specific timetable.
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0075/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 11.11.2021.	Positive Opinion adopted by consensus on 13.01.2022.
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0090	

BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0097 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 21.12.2021.	Positive Opinion adopted by consensus on 21.12.2021.
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0101 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
Darzalex - daratumumab - EMEA/H/C/004077/II/0056/G, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac	
Dupixent - dupilumab - EMEA/H/C/004390/II/0050/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 14.10.2021.	Positive Opinion adopted by consensus on 13.01.2022.
Enhertu - trastuzumab deruxtecan - EMEA/H/C/005124/II/0009 Daiichi Sankyo Europe GmbH, Rapporteur: Sinan B. Sarac Opinion adopted on 20.01.2022. Request for Supplementary Information adopted on 28.10.2021.	Positive Opinion adopted by consensus on 20.01.2022.
Erbitux - cetuximab - EMEA/H/C/000558/II/0092 Merck Europe B.V., Rapporteur: Filip Josephson Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Erelzi - etanercept - EMEA/H/C/004192/II/0038/G Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 02.12.2021.	Positive Opinion adopted by consensus on 13.01.2022.
Fasenra - benralizumab - EMEA/H/C/004433/II/0038/G AstraZeneca AB, Rapporteur: Fátima Ventura Request for Supplementary Information adopted on 16.12.2021.	

Febuxostat Mylan - febuxostat - EMEA/H/C/004374/II/0012 Mylan Pharmaceuticals Limited, Generic, Generic of Adenuric, Rapporteur: Elita Poplavska	
Fluad Tetra - influenza vaccine (surface antigen, inactivated, adjuvanted) - EMEA/H/C/004993/II/0021 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Hepcludex - bulevirtide - EMEA/H/C/004854/II/0009/G, Orphan Gilead Sciences Ireland Unlimited Company, Rapporteur: Filip Josephson	
Hepsera - adefovir dipivoxil - EMEA/H/C/000485/II/0087 Gilead Sciences Ireland UC, Rapporteur: Jean-Michel Race Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
ILARIS - canakinumab - EMEA/H/C/001109/II/0078 Novartis Europharm Limited, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
Infanrix hexa - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/000296/II/0309/G GlaxoSmithkline Biologicals SA, Rapporteur: Christophe Focke Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Insulin lispro Sanofi - insulin lispro - EMEA/H/C/004303/II/0014/G sanofi-aventis groupe, Rapporteur: Outi Mäki-Ikola Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0061/G Roche Registration GmbH, Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 09.12.2021.	

Kirsty - insulin aspart - EMEA/H/C/004965/II/0003/G Mylan IRE Healthcare Limited, Rapporteur: Sinan B. Sarac Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 09.12.2021.	Positive Opinion adopted by consensus on 13.01.2022.
Leqvio - inclisiran - EMEA/H/C/005333/II/0008 Novartis Europharm Limited, Rapporteur: Martina Weise	
Lysodren - mitotane - EMEA/H/C/000521/II/0024 HRA Pharma Rare Diseases, Rapporteur: Blanca Garcia-Ochoa Request for Supplementary Information adopted on 13.01.2022, 02.09.2021.	Request for supplementary information adopted with a specific timetable.
Memantine Mylan - memantine / memantine hydrochloride - EMEA/H/C/002660/II/0018 Mylan Pharmaceuticals Limited, Generic, Generic of Ebixa, Rapporteur: Maria Concepcion Prieto Yerro Request for Supplementary Information adopted on 20.01.2022.	Request for supplementary information adopted with a specific timetable.
Menveo - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/001095/II/0106/G GSK Vaccines S.r.l, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0059/G GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 11.11.2021.	Positive Opinion adopted by consensus on 13.01.2022.
Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0023/G, Orphan Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac	
Natpar - parathyroid hormone - EMEA/H/C/003861/II/0035, Orphan	Request for supplementary information adopted with a specific timetable.

Takeda Pharmaceuticals International AG, Rapporteur: Karin Janssen van Doorn Request for Supplementary Information adopted on 13.01.2022.	
Nordimet - methotrexate - EMEA/H/C/003983/II/0021/G Nordic Group B.V., Rapporteur: Bruno Sepodes Request for Supplementary Information adopted on 13.01.2022. Letter from the applicant dated 17.01.2022 requesting a clock stop extension.	Request for supplementary information adopted with a specific timetable.
Nplate - romiplostim - EMEA/H/C/000942/II/0081/G Amgen Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
Onivyde pegylated liposomal - irinotecan hydrochloride trihydrate - EMEA/H/C/004125/II/0029/G, Orphan Les Laboratoires Servier, Rapporteur: Filip Josephson Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
Oyavas - bevacizumab - EMEA/H/C/005556/II/0004 STADA Arzneimittel AG, Duplicate, Duplicate of Alymsys, Rapporteur: Christian Gartner Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
Polivy - polatuzumab vedotin - EMEA/H/C/004870/II/0013/G, Orphan Roche Registration GmbH, Rapporteur: Alexandre Moreau	
POTELIGEO - mogamulizumab - EMEA/H/C/004232/II/0013/G, Orphan Kyowa Kirin Holdings B.V., Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
ProQuad - measles, mumps, rubella and varicella vaccine (live) - EMEA/H/C/000622/II/0154 MSD Vaccins, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 20.01.2022. Request for Supplementary Information adopted on 16.12.2021.	Positive Opinion adopted by consensus on 20.01.2022.
Qarziba - dinutuximab beta - EMEA/H/C/003918/II/0035/G, Orphan	

EUSA Pharma (Netherlands) B.V., Rapporteur: Paula Boudewina van Hennik	
Rekovelle - follitropin delta - EMEA/H/C/003994/II/0030 Ferring Pharmaceuticals A/S, Rapporteur: Jean-Michel Race Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Retacrit - epoetin zeta - EMEA/H/C/000872/II/0108 Pfizer Europe MA EEIG, Rapporteur: Martina Weise Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Rhokiinsa - netarsudil - EMEA/H/C/004583/II/0007/G Aerie Pharmaceuticals Ireland Limited, Rapporteur: Jayne Crowe Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 11.11.2021.	Positive Opinion adopted by consensus on 13.01.2022.
RoActemra - tocilizumab - EMEA/H/C/000955/II/0106/G Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
Rybelsus - semaglutide - EMEA/H/C/004953/II/0020 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege	
Tigecycline Accord - tigecycline - EMEA/H/C/005114/II/0002/G Accord Healthcare S.L.U., Generic, Generic of Tygacil, Rapporteur: Daniela Philadelphy Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Toviaz - fesoterodine - EMEA/H/C/000723/II/0065/G Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro Request for Supplementary Information adopted on 20.01.2022.	Request for supplementary information adopted with a specific timetable.
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0061/G AstraZeneca AB, Co-Rapporteur: Johann	Positive Opinion adopted by consensus on 20.01.2022.

Lodewijk Hillege Opinion adopted on 20.01.2022.	
Xolair - omalizumab - EMEA/H/C/000606/II/0114 Novartis Europharm Limited, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Yuflyma - adalimumab - EMEA/H/C/005188/II/0009/G Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola Opinion adopted on 20.01.2022. Request for Supplementary Information adopted on 16.12.2021.	Positive Opinion adopted by consensus on 20.01.2022.
Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/II/0027/G Pfizer Ireland Pharmaceuticals, Rapporteur: Ingrid Wang Request for Supplementary Information adopted on 13.01.2022, 02.12.2021, 28.10.2021, 09.09.2021.	Request for supplementary information adopted with a specific timetable.
Zercepac - trastuzumab - EMEA/H/C/005209/II/0015/G Accord Healthcare S.L.U., Rapporteur: Sol Ruiz Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
Zercepac - trastuzumab - EMEA/H/C/005209/II/0016 Accord Healthcare S.L.U., Rapporteur: Sol Ruiz Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Zutectra - human hepatitis B immunoglobulin - EMEA/H/C/001089/II/0051 Biotest Pharma GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
WS2164/G **Blitzima- EMEA/H/C/004723/WS2164/0047/G** **Truxima- EMEA/H/C/004112/WS2164/0051/G** Celltrion Healthcare Hungary Kft., Duplicate, Duplicate of Truxima, Lead Rapporteur: Sol Ruiz Opinion adopted on 20.01.2022. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 20.01.2022.

on 11.11.2021.	
WS2177/G **Nilemdo-** **EMEA/H/C/004958/WS2177/0018/G** **Nustendi-** **EMEA/H/C/004959/WS2177/0020/G** Daiichi Sankyo Europe GmbH, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
WS2188/G **Hexacima-** **EMEA/H/C/002702/WS2188/0124/G** **Hexyon-** **EMEA/H/C/002796/WS2188/0128/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
WS2189 **Advate-EMEA/H/C/000520/WS2189/0113** **ADYNOVI-** **EMEA/H/C/004195/WS2189/0026** Takeda Manufacturing Austria AG, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.

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

ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0028 Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, "Update of section 4.8 of the SmPC in order to add ''Urticaria'' to the list of adverse drug reactions (ADRs) with frequency ''common''. The Package Leaflet is updated accordingly." Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
Alunbrig - brigatinib / brigatinib - EMEA/H/C/004248/II/0033/G Takeda Pharma A/S, Rapporteur: Sinan B. Sarac, "Update of section 4.5 of the SmPC in order to add drug-drug interaction information about the effect of brigatinib on the pharmacokinetics of a sensitive cytochrome P450 3A substrate (midazolam) in patients with ALK-positive or ROS1-positive solid tumours based on a clinical study report (study 1001).	

Update of section 4.2 of the SmPC in order to clarify the existing renal impairment dosage adjustment recommendation based on results of previously submitted studies (clinical study AP26113-15-108, study 108). Update of section 4.2 of the SmPC in order to clarify the existing hepatic impairment dosage adjustment recommendation based on results of previously submitted studies (clinical study AP26113-15-107, study 107). Update of sections 4.4 and 4.5 of the SmPC in order to update drug-drug interaction information regarding concomitant treatment with moderate CYP3A inhibitors or inducers based on results of previously submitted studies (physiologically-based pharmacokinetic (PBPK) report and PBPK report addendum). Update of section 5.1 of the SmPC in order to amend the ATC code; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement a statement regarding the sodium content of Alunbrig in section 4.4 of the SmPC and Package Leaflet. The MAH also took the opportunity to bring the Product Information in line with the latest QRD template (version 10.2 rev.1) and to update the list of local representatives in the Package Leaflet. Moreover, the MAH took the opportunity to introduce minor editorial changes in the PI in different languages." Request for Supplementary Information adopted on 14.10.2021, 22.07.2021.	
Alunbrig - brigatinib / brigatinib - EMEA/H/C/004248/II/0034 Takeda Pharma A/S, Rapporteur: Sinan B. Sarac, "Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on photosensitivity based on a report of cumulative evidence for an association between exposure to brigatinib and subsequent development of photosensitivity reaction; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make a minor editorial change in section 4.8 of the SmPC." Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 14.10.2021, 22.07.2021.	Positive Opinion adopted by consensus on 13.01.2022.
Blenrep - belantamab mafodotin - EMEA/H/C/004935/II/0006/G, Orphan	

GlaxoSmithKline (Ireland) Limited, Rapporteur: Johanna Lähteenvuo, "C.I.4 Update of section 4.4 of the SmPC in order to add a new warning on pneumonitis based on reports from the GSK safety database and clinical trials. C.I.4 Update of section 4.8 of the SmPC in order to add albuminuria to the list of adverse drug reactions (ADRs) with frequency common based on a safety review by the MAH. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to perform minor editorial changes."	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0093 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information after booster dose, based on interim results from study C4591031, this is a randomized, placebo-controlled, phase 3 booster efficacy study involving participants ≥ 16 years of age who completed the primary series of BNT162b2 30 µg in study C4591001. The Package Leaflet and Labelling are updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes throughout the product information."	See 9.1
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0102 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC in order to update safety and efficacy information 6 months post-dose 2 follow-up for adolescence 12 through 15 years of age based on updated interim results from study C4591001, listed as a specific obligation; this is a Phase 1/2/3, placebo-controlled, observer-blind, interventional, dose-finding, study to evaluate the safety, tolerability, immunogenicity and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals. In addition, the MAH took the opportunity to implement minor editorial changes in section 6.3 of the SmPC and section 5 of the PIL of Comirnaty 30 micrograms/dose dispersion for injection."	See 9.1

Copiktra - duvelisib - EMEA/H/C/005381/II/0002 Secura Bio Limited, Rapporteur: Sinan B. Sarac, "Update of section 5.1 of the SmPC based on the final overall survival results from study IPI-145-07, an interventinal Phase 3 study of duvelisib (IPI-145) vs ofatumumab in patients with relapsed or refractory Chronic Lymphocytic leukaemia/Small Lymphocytic Lymphoma." Request for Supplementary Information adopted on 11.11.2021.	
Dapivirine Vaginal Ring 25 mg - dapivirine - EMEA/H/W/002168/II/0014/G International Partnership for Microbicides Belgium AISBL, Rapporteur: Paula Boudewina van Hennik, "C.I.13: Submission of the study report from study MTN-020 (Version 2.0). This is a multicentre, randomized, double-blind, placebo-controlled Phase III safety and effectiveness trial of a vaginal matrix ring containing dapivirine for the prevention of HIV-1 infection in women. C.I.13: Submission of the Clinical Virology Report (Version 4.0). This report describes virologic characterisation of virus from HIV-1 seroconversion events during double-blind, placebo-controlled, randomized, multicentre Phase III clinical trials evaluating the safety and efficacy of Dapivirine Vaginal Ring." Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Dovprela - pretomanid - EMEA/H/C/005167/II/0008, Orphan Mylan IRE Healthcare Limited, Rapporteur: Filip Josephson, "Submission of the final report from study Nix-TB-(B-L-Pa) listed as a Specific Obligation the Annex II of the Product Information. This is a phase 3 open-label trial assessing the safety and efficacy of bedaquiline plus pretomanid plus linezolid in subjects with pulmonary infection of either extensively drug-resistant tuberculosis (XDR-TB) or treatment intolerant/non-responsive multi-drug resistant tuberculosis (MDR-TB). The Annex II is updated accordingly." Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
Epidyolex - cannabidiol - EMEA/H/C/004675/II/0015, Orphan GW Pharma (International) B.V., Rapporteur:	

Thalia Marie Estrup Blicher, "Update of sections 4.5 and 5.1 of the SmPC to add drug-drug interaction information with everolimus and P-gp substrates following the assessment the study GWCP19195, a phase I open-label pharmacokinetic drug-drug interaction trial to investigate the effect of cannabidiol on the pharmacokinetics of everolimus in healthy subject. In addition, the MAH took the opportunity to introduce editorial updates in section 5.1 and section 4.9." Request for Supplementary Information adopted on 11.11.2021.	
Epidyolex - cannabidiol - EMEA/H/C/004675/II/0016, Orphan GW Pharma (International) B.V., Rapporteur: Thalia Marie Estrup Blicher, "Update of section 5.3 of the SmPC to reflect of the conclusions of the study GWTX1504, 104 week oral (gavage) administration carcinogenicity study in mouse." Request for Supplementary Information adopted on 11.11.2021.	
Eylea - aflibercept - EMEA/H/C/002392/II/0076 Bayer AG, Rapporteur: Alexandre Moreau, "Submission of the final report from study AZURE, a randomised PAES in patients with neovascular (wet) AMD with the primary objective of comparing the standard regime of injections every 8 weeks with a reactive regimen based on visual and anatomic outcomes, based on a CHMP approved protocol." Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Fasenra - benralizumab - EMEA/H/C/004433/II/0041 AstraZeneca AB, Rapporteur: Fátima Ventura, "Update of section 5.1 of the SmPC in order to update efficacy information based on the final results from study D3250C00065 (PONENTE); this is a multicentre, open-label, Phase IIIb efficacy and safety study of benralizumab 30 mg administered subcutaneously to reduce oral corticosteroid use in adult patients with severe eosinophilic asthma on high-dose inhaled corticosteroid plus long-acting β2 agonist and chronic oral corticosteroid therapy. In addition, the MAH took the opportunity to update the list	

of local representatives in the Package Leaflet."	
Fetcroja - cefiderocol - EMEA/H/C/004829/II/0006/G Shionogi B.V., Rapporteur: Filip Josephson, "Submission of the final report from the in vitro RIS correlation study S-649266-PF-415-N (REC 003), to address CYP3A4 induction by cefiderocol. In addition, the MAH submitted the final report of in vitro study S-649266-CPK-008-C to investigate the DDI between cefiderocol as a CYP3A4 inducer and Midazolam using physiologically-based pharmacokinetic model." Request for Supplementary Information adopted on 13.01.2022, 11.11.2021.	Request for supplementary information adopted with a specific timetable.
Iclusig - ponatinib - EMEA/H/C/002695/II/0061, Orphan Incyte Biosciences Distribution B.V., Rapporteur: Filip Josephson, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC based on results from the OPTIC study (AP24534-14-203) listed as a specific obligation in the Annex II. This is a randomised, open-label, Phase 2 trial of ponatinib in patients with chronic myeloid leukaemia to characterise the efficacy and safety of ponatibib over a range of doses; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 13.01.2022, 14.10.2021.	Request for supplementary information adopted with a specific timetable.
IMCIVREE - setmelanotide - EMEA/H/C/005089/II/0003, Orphan Rhythm Pharmaceuticals Netherlands B.V., Rapporteur: Karin Janssen van Doorn, "Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations in patients with renal impairment, based on final results from study RM-493-029, a Phase I, open-label, single-dose study to evaluate the pharmacokinetics of setmelanotide in subjects with varying degrees of renal impairment; with secondary objectives to evaluate the safety and tolerability of a single dose of setmelanotide administered subcutaneously in subjects with varying degrees of renal impairment. The Package Leaflet is updated accordingly."	
Imfinzi - durvalumab - EMEA/H/C/004771/II/0034 AstraZeneca AB, Rapporteur: Sinan B. Sarac,	

"Update of sections 4.4 and 4.8 of the SmPC in order to reflect the outcome of the re-defined process to identify and calculate immune-mediated Adverse Event (imAE) rates from clinical study and pooled datasets within the durvalumab development programmes. In addition, the MAH implemented minor editorial corrections to sections 4.4 and 5.1 of the SmPC." Request for Supplementary Information adopted on 21.10.2021.	
JEMPERLI - dostarlimab - EMEA/H/C/005204/II/0007 GlaxoSmithKline (Ireland) Limited, Rapporteur: Blanca Garcia-Ochoa, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update dose modifications recommendations in immune related adverse reactions, amend existing warnings, and add further immune-related ADRs to the list of adverse drug reactions (ADRs), with different frequencies, based on data from company sponsored trials and literature. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to remove information on Polysorbate 80 and update the list of local representatives in the Package Leaflet."	
Jyseleca - filgotinib - EMEA/H/C/005113/II/0008 Galapagos N.V., Rapporteur: Kristina Dunder, "C.I.4 - Update of section 4.8 of the SmPC in order to add Lymphopenia to the list of adverse drug reactions (ADRs) with frequency common and update the information on serum phosphate and the experience from the long-term extension studies based on interim results from study GS-US-417-0304 (FINCH 4); this is a Multicentre, Double-Blind, Long Term Extension Study to Assess the Safety and Efficacy of Filgotinib in Subjects with Rheumatoid Arthritis; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 13.01.2022, 09.09.2021.	Request for supplementary information adopted with a specific timetable.
Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0087 Genzyme Europe BV, Rapporteur: Alexandre Moreau, "Update of section 4.8 of the SmPC in order to add palpitations, asthenia, malaise, feeling cold and blood pressure decreased to the	Request for supplementary information adopted with a specific timetable.

list of adverse drug reactions (ADRs) with frequency "not-known" following the Final Assessment Report for the Post-Authorisation Measure MEAs 024.13 and 0.25.13 (the 2019 Pompe Disease Registry Annual Report) dated 15 October 2020; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update section 5.1 of the SmPC to update the internet website address of the Pompe Registry." Request for Supplementary Information adopted on 20.01.2022.	
Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0050 Orexigen Therapeutics Ireland Limited, Rapporteur: Sinan B. Sarac, "Submission of the final report of study 20077697; a Toxicity Study of Bupropion and Naltrexone by Twice Daily Oral (Gavage) in Juvenile Mice." Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 30.09.2021.	Positive Opinion adopted by consensus on 13.01.2022.
Oncaspar - pegaspargase - EMEA/H/C/003789/II/0038 Les Laboratoires Servier, Rapporteur: Alexandre Moreau, "Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on the risk of osteonecrosis and to include it as an adverse drug reaction associated with pegaspargase use with an unknown frequency, following review of all available non-clinical, epidemiological and clinical data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2." Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 25.11.2021, 28.05.2021.	Positive Opinion adopted by consensus on 13.01.2022.
Opsumit - macitentan - EMEA/H/C/002697/II/0044, Orphan Janssen-Cilag International N.V., Rapporteur: Maria Concepcion Prieto Yerro, "C.I.4: Update of SmPC sections 4.8 and 5.1, based on the long-term follow-up data from SERAPHIN open-label (OL) study. SERAPHIN OL study was a long-term single-arm open-label extension study of the SERAPHIN double-blind (DB) study, to assess the safety and tolerability of macitentan	Positive Opinion adopted by consensus on 13.01.2022.

in patients with symptomatic pulmonary arterial hypertension (PAH) that have completed the DB study or that experienced a morbidity event and for who a written approval to roll over into the OL study was obtained by the sponsor." Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 11.11.2021.	
Phesgo - pertuzumab / trastuzumab - EMEA/H/C/005386/II/0004 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update in section 4.8, Undesirable Effects, to present the pooled data from Perjeta and Phesgo studies. In addition to this, the MAH has taken the opportunity to introduce minor updates in the SmPC and the Package leaflet: • Update in section 9 of the SmPC to reflect the date of first authorisation • Editorial update in section 4 of the Package leaflet to add a space • Update in section 6 of the Package leaflet to adapt to the revised QRD Template v10.2" Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 21.10.2021, 22.07.2021.	Positive Opinion adopted by consensus on 13.01.2022.
Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0133 Boehringer Ingelheim International GmbH, Rapporteur: Thalia Marie Estrup Blicher, "- to remove rice cereal from the food compatibility list in the "Instructions for use"- "A) Administration of Pradaxa coated granules with soft foods" of the Package Leaflet for Pradaxa coated granules in sachets based on long-term stability results and in-use food compatibility study."	
Prialt - ziconotide - EMEA/H/C/000551/II/0068 ESTEVE Pharmaceuticals GmbH, Rapporteur: Christophe Focke, "Update of section 4.2 of the SmPC to introduce a new posology regimen. The Package Leaflet to be updated accordingly. In addition, the MAH took the opportunity to update QRD template to v.10.2 Rev.1 and implement editorial changes in SmPC, PL, and Labelling." Request for Supplementary Information adopted	

on 16.09.2021.	
REKAMBYS - rilpivirine - EMEA/H/C/005060/II/0010 Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, "Update of section 4.8 (Table 6) of the SmPC in order to update the adverse reactions section, adding information regarding the majority of pyrexia events having a close temporal association with injections (reported within one week of injections); based on the data analysis from clinical trials study 201585 FLAIR, 201585 ATLAS and 207966 ATLAS-2M. The Package Leaflet (Section 4) is updated accordingly." Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
RINVOQ - upadacitinib - EMEA/H/C/004760/II/0014 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, "C.I.4 - Update of section 5.1 of the SmPC in order to update efficacy information based on interim results (Week 156) from studies M14-465 and M13-545; these are randomized phase 3, double blind studies to evaluate the long-term safety, tolerability and efficacy of upadacitinib in subjects with Rheumatoid Arthritis. In addition, the MAH took the opportunity to introduce editorial changes in section 5.1 of the SmPC." Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Siklos - hydroxycarbamide - EMEA/H/C/000689/II/0051 Addmedica S.A.S., Rapporteur: Karin Janssen van Doorn, "C.I.3.b Update of section 5.1 of the SmPC with the available paediatric data from the studies NOHARM and Escort HU according to the PAM-Leg 34." Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0042 Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include information on heterologous boosting using a 50 ug dose of Spikevax to boost subjects that have	

previously completed a primary vaccination series with any authorised COVID-19 vaccine, based on data from the DMID Study 21-0012, a Phase 1/2 heterologous SARS-CoV-2 vaccine dosing (mRNA-1273 booster) study of the various vaccines authorized in the US under Emergency Use Authorisation in participants ≥ 18 years old (NCT04889209). In addition, the MAH took the opportunity to make minor editorial changes/corrections throughout the product information." Request for Supplementary Information adopted on 16.12.2021.	
TAGRISSO - osimertinib - EMEA/H/C/004124/II/0045 AstraZeneca AB, Rapporteur: Blanca Garcia-Ochoa, "Update of section 5.3 of the SmPC in order to reflect the outcome of the 104 Week Oral (Gavage) Carcinogenicity Study (507363) in the Rat submitted as recommended by the CHMP." Request for Supplementary Information adopted on 16.12.2021, 11.11.2021.	
Tyverb - lapatinib - EMEA/H/C/000795/II/0072/G Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to add skin fissures to the list of adverse drug reactions (ADRs) with frequency common, following recently analysed safety data regarding skin fissures. The Package Leaflet is updated accordingly. The ATC code is also updated." Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0088 MCM Vaccine B.V., Rapporteur: Christophe Focke, "Update of section 5.1 of the SmPC in order to include information about long-term durability of the immune protection against HBV infection based on study V419-013 A Hepatitis B Vaccine Challenge Study to Demonstrate the Durability of Protection Against Hepatitis B Virus Infection in Healthy Children Vaccinated Approximately 9 Years Previously With a 2- or 3-Dose Infant Series and Toddler Dose of	

Vaxelis (study report P013V419). In addition, the MAH is updating sections 4.7 and 4.8 of the SmPC to implement EMA proposed wording and a typo error. The MAH took the opportunity to update the list of local representatives in the PL and implement minor editorial changes in sections 4.8 and 6.6 of the SmPC and section 2 of the PL. Furthermore, the PI is brought in line with the latest QRD template version 10.2 rev. 1." Request for Supplementary Information adopted on 11.11.2021.	
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0031 AstraZeneca AB, Rapporteur: Sol Ruiz, "Submission of the final study report for MS1222-0002 "In Vitro Assay to Determine Release of Spike Protein From Transduced Cells" to fulfil the imposed study as reflected in Annex II of the product information and the RMP. As a result, Annex II of the product information is being updated to remove this study. The MAH is taking the opportunity to provide two additional studies linked to support the investigation on the platelet activation: the final study report for MS1222-0001 "Computational Prediction of Spike Protein Interaction with Platelet Factor 4 (PF4)" which is the first report requested within the required studies for "in vitro interaction of AZD1222 or spike protein with PF4 and/or platelets" as reflected in the RMP; and the study report for 520447 "Investigative Vaccine Study in the Mouse" to evaluate spike protein levels and haematology parameters." Request for Supplementary Information adopted on 13.01.2022, 23.09.2021.	Request for supplementary information adopted with a specific timetable.
Verzenios - abemaciclib - EMEA/H/C/004302/II/0021 Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to include second OS interim results from study MONARCH 3; this is a randomised, double blind, placebo-controlled phase 3 study of Nonsteroidal Aromatase Inhibitors (Anastrozole or Letrozole) plus LY2835219, a CDK4/6 Inhibitor, or Placebo in Postmenopausal Women with Hormone Receptor-Positive, HER2-	

Negative Locoregionally Recurrent or Metastatic Breast Cancer with No Prior Systemic Therapy in this Disease Setting."

Xagrid - anagrelide -
EMEA/H/C/000480/II/0091
Takeda Pharmaceuticals International AG, Rapporteur: Alexandre Moreau, "C.I.4 Update of section 4.4 of the SmPC in order to add a new warning on the risks of fatal thrombotic complications associated with abrupt treatment discontinuation based on New Pharmacovigilance data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to perform a minor editorial change in section 4.2."
Request for Supplementary Information adopted on 09.12.2021, 02.09.2021.

WS2048
Kalydeco-
EMEA/H/C/002494/WS2048/0101
Symkevi-
EMEA/H/C/004682/WS2048/0030
Vertex Pharmaceuticals (Ireland) Limited, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Rhea Fitzgerald, "Update of the Product information to provide the final clinical study report (CSR) Part A of Study VX17-661-116 (A Phase 3, Open-label, Rollover Study to Evaluate the Safety and Efficacy of Long-term
Treatment With Tezacaftor in Combination With Ivacaftor in Subjects With Cystic Fibrosis Aged 6 Years and Older, Homozygous or Heterozygous for the F508del-CFTR Mutation).
Consequently, the SmPC sections 4.2, 4.5, 4.8 and 5.1 and the package leaflet are updated accordingly. The RMP is also updated."
Request for Supplementary Information adopted on 14.10.2021, 24.06.2021.

WS2156
Nuwiq-EMEA/H/C/002813/WS2156/0047
Vihuma-
EMEA/H/C/004459/WS2156/0029
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus, "Submission of the final report from study GENA-99 including the integrated analysis report of studies GENA-99, GENA-13, GENA-15, GENA-21, GENA-21b and GENA-100. GENA-99 is a Prospective, multinational, non-

interventional post-authorisation study to document the long-term immunogenicity, safety, and efficacy of Human-cl rhFVIII (simoctocog alfa) in patients with haemophilia A treated in routine clinical practice." Request for Supplementary Information adopted on 28.10.2021.	
WS2170 **OPDIVO-** **EMEA/H/C/003985/WS2170/0114** **Yervoy-EMEA/H/C/002213/WS2170/0094** Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy information based on 5 years follow-up OS data from study CA209214; this is a phase 3, randomised, open-label study in previously untreated, intermediate/poor risk advanced RCC." Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
WS2174 **Hexacima-** **EMEA/H/C/002702/WS2174/0123** **Hexyon-** **EMEA/H/C/002796/WS2174/0127** Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus, "Update of section 4.5 of the SmPC in order to add drug-drug interaction information regarding the co-administration of Hexyon / Hexacima with varicella vaccines based on a re-analysis of the A3L15 clinical trial varicella serological data, submitted in the initial CTD dossier. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to correct some typo errors in the SmPC and PL." Request for Supplementary Information adopted on 20.01.2022.	Request for supplementary information adopted with a specific timetable.

B.5.3. CHMP-PRAC assessed procedures

Alecensa - alectinib - **EMEA/H/C/004164/II/0037/G** Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Jana Lukacisinova, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add a new warning,	

dose modification advice and description of the known ADR haemolytic anaemia based on an updated Drug Safety Report; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce editorial updates in the Maltese and Romanian product information. Moreover, the ATC code for alectinib is being updated from L01XE36 to L01ED03."	
Alunbrig - brigatinib / brigatinib - EMEA/H/C/004248/II/0037 Takeda Pharma A/S, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of section 5.1 of the SmPC in order to update efficacy information based on final results from study AP26113-13-301 listed as a PAES in the Annex II; this is a randomised, open-label, multicentre phase III study comparing brigatinib versus crizotinib in patients with advanced ALK-positive NSCLC who have not previously received ALK-directed therapy; The RMP version 5.4 has also been submitted." Request for Supplementary Information adopted on 13.01.2022, 30.09.2021.	Request for supplementary information adopted with a specific timetable.
Bosulif - bosutinib - EMEA/H/C/002373/II/0050/G Pfizer Europe MA EEIG, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to reflect results from the studies B1871039 (SOB) and B1871040 (category 3); study B1871039 is A Phase 4 Safety and Efficacy Study of Bosutinib in Patients With Philadelphia Chromosome Positive Chronic Myeloid Leukaemia Previously Treated With One or More Tyrosine Kinase Inhibitors and study B1871040 is An Open-Label Bosutinib Treatment Extension Study for Subjects With Chronic Myeloid Leukaemia (CML) who Have Previously Participated in Bosutinib Studies B1871006 or B1871008. The Package Leaflet is updated accordingly. The MAH request deletion of the SOB from annex II of the PI and request consideration for switch of the Conditional Marketing Authorisation to a full Marketing Authorisation. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local	See 9.1

representatives for Belgium, Luxemburg, Germany and Northern Island in the Package Leaflet. The MAH is also asking the deletion of the product from the additional monitoring list.” Request for Supplementary Information adopted on 16.12.2021, 16.09.2021.	
Cablivi - caplacizumab - EMEA/H/C/004426/II/0035, Orphan Ablynx NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Jan Neuhauser, “Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning on increased risk of bleeding and add blood and lymphatic system disorders to the list of adverse drug reactions (ADRs) with frequency not known based on a safety evaluation report; the Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted.” Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Deltyba - delamanid - EMEA/H/C/002552/II/0053, Orphan Otsuka Novel Products GmbH, Rapporteur: Christophe Focke, PRAC Rapporteur: Laurence de Fays, “Update of section 4.8 of the SmPC in order to update the list of adverse drug reactions (ADRs table) following the development of an improved methodology to identify relevant ADRs likely attributable to delamanid. The section 4 of the Package Leaflet is updated accordingly. The RMP version 3.6 has also been submitted.” Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
ELZONRIS - tagraxofusp - EMEA/H/C/005031/II/0009, Orphan Stemline Therapeutics B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst, “Submission of the final report from study 20255431 (CRL-263114) 'Characterization of fixed choroid plexus samples from primate study MPI-2231-007 by Immunohistochemistry with DT, CD123, IL-3 and IgG' (MEA002) listed as a category 3 study in the RMP. This is a non-interventional, post-authorisation study on blood brain barrier (BBB) models in order to determine a potential toxicity biomarker to further investigate the risk of choroid plexus lesions. The RMP version 2.0 has	Request for supplementary information adopted with a specific timetable. See 9.1

also been submitted." Request for Supplementary Information adopted on 13.01.2022.	
Enbrel - etanercept - EMEA/H/C/000262/II/0246 Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "Update of section 5.1 of the SmPC in order to update clinical information based on final results obtained from the clinical paediatric study B1801023 (CLIPPER 2). The RMP version 7.5 has also been submitted." Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
Galafold - migalastat - EMEA/H/C/004059/II/0034, Orphan Amicus Therapeutics Europe Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ulla Wändel Liminga, "To update sections 4.8, 5.1 and 5.2 of the SmPC based on final results from study AT1001-020 listed as category 3 in the RMP. Study AT1001-020-is a Phase 3b, 2-stage, open-label, uncontrolled, multicentre study to evaluate the safety, pharmacokinetic, pharmacodynamic and efficacy of migalastat treatment in paediatric subjects 12 to < 18 years of age and weighing ≥ 45 kg with Fabry disease and with amenable GLA variants. The updated RMP version 7.0 has also been submitted. The final results of study AT1001-020, which is involving paediatric patients are submitted in fulfilment of Article 46 of Regulation 1901/2006, as amended. In addition, the MAH took the opportunity to introduce some minor editorial changes to the SmPC and Package Leaflet and bring the PI in line with the latest QRD template v. 10.2." Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 30.09.2021.	Positive Opinion adopted by consensus on 13.01.2022.
GIVLAARI - givosiran - EMEA/H/C/004775/II/0006, Orphan Alnylam Netherlands B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Martin Huber, "Type II C.I.4 : Update of SmPC section 4.8 to add 'blood homocysteine increase' as a new ADR and update to SmPC section 4.4 to add a related warning. The package leaflet is	Request for supplementary information adopted with a specific timetable.

being updated accordingly. RMPv1.1 is also being submitted: consequences of blood homocysteine increase is being added as a new important potential risk, the clinical and post-marketing exposure is being updated and the due dates for ALN-AS1-002 and ALN-AS1-003 final study reports are being postponed. In addition, the MAH took the opportunity to make editorial changes to the Product Information in other EU languages and to update the contact number of the local representatives for Malta and Cyprus." Request for Supplementary Information adopted on 13.01.2022, 28.10.2021, 02.09.2021.	
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0069 Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of the SmPC section 4.4 to include information on fatal and serious cardiac arrythmias and cardiac failure, relevant warnings and periodical monitoring of patients-following a safety assessment for increased risk of sudden death/cardiac death with the use of ibrutinib. Section 2 of the PL has been updated accordingly. Typographical errors have been corrected throughout the PI. The revised RMP version 11 has been submitted."	See 9.1
Lemtrada - alemtuzumab - EMEA/H/C/003718/II/0038 Sanofi Belgium, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, "Update of sections 4.4 and 4.8 of the SmPC to add Adult Onset Still's Disease (AOSD) to the list of adverse drug reactions (ADRs) with frequency not known, based on a signal validated during a routine pharmacovigilance surveillance; the Package Leaflet is updated accordingly. The MAH took the opportunity to update the list of local representatives in the Package Leaflet. The RMP v.9.0 submitted to include AOSD; and to remove the PASS study OBS13436 (Pregnancy Registry)." Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
Mavenclad - cladribine - EMEA/H/C/004230/II/0020 Merck Europe B.V., Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Marcia Sofia	Positive Opinion adopted by consensus on 13.01.2022.

Sanches de Castro Lopes Silva, "C.I.4 Type II Update of sections 4.2 and 4.4 of the SmPC in order to change posology recommendations by adding an advice on preventive measures to avoid liver injury and to add a new warning on liver function and liver injury based on a review of post-approval data in MAH's safety database, non-clinical and clinical trial data and scientific literature (cladribine and liver injury and epidemiological data on hepatic injury in MS). The Package Leaflet is updated accordingly. The RMP version 1.6 has also been submitted." Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 02.09.2021, 10.06.2021.	
Naglazyme - galsulfase - EMEA/H/C/000640/II/0086 BioMarin International Limited, Rapporteur: Fátima Ventura, PRAC Rapporteur: Ana Sofia Diniz Martins, "C.I.11.b variation to update the RMP to version 6.4 to remove gastrointestinal haemorrhage, hepatic impairment and thrombocytopenia from the list of important potential risks. This proposed update is supported by the submission of the final report from the MPS VI Clinical Surveillance Program (CSP) listed as a Specific Obligation (SOB002) in the Annex II of the Product Information for this MAA under exceptional circumstances. This observational CSP was undertaken to characterise the natural progression of MPS VI, to evaluate the long-term safety and efficacy data from Naglazyme treatment, to collect information on the effect of Naglazyme treatment on lactation, growth and development of infants of Naglazyme treated mothers, and to evaluate the effects of Naglazyme treatment on children under 5 years of age." Request for Supplementary Information adopted on 16.09.2021.	See 9.1
Ontruzant - trastuzumab - EMEA/H/C/004323/II/0036 Samsung Bioepis NL B.V., Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Submission of the final report from clinical study (SB3-G31-BC-E) listed as a category 3 study in the RMP. This is an observational cohort study assessing the long-term cardiac safety (for Cardiac Safety and	Positive Opinion adopted by consensus on 13.01.2022.

Survival Cohort) and survival (Survival Only Cohort and Cardiac Safety and Survival Cohort) in patients who received treatment in study SB3-G31-BC. The RMP version 5.0 is also provided."
Opinion adopted on 13.01.2022.
Request for Supplementary Information adopted on 02.09.2021.

Rydapt - midostaurin - EMEA/H/C/004095/II/0018/G, Orphan
Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "A.6 - Administrative change - Change in ATC Code/ATC Vet Code
C.I.4, Update of the SmPC in section 4.5 in order to add drug-drug interaction information with P-gp, BCRP, CYP2D6, substrates (digoxin, rosuvastatin, and dextromethorphan), based on final results from study CPKC412A2121, a Phase 1, open-label, drug-drug interaction study, listed as category 3 study in the RMP; section 5.2 of the SmPC and the Package Leaflet is updated accordingly. (MEA 005.3)C.I.4, Update of the SmPC in section 4.5 in order to add drug-drug interaction information with CYP2B6, CYP2C8, CYP3A4 substrates, based on final results from study CPKC412A2122, a Phase 1, open-label, drug-drug interaction study, listed as category 3 study in the RMP; section 5.2 of the SmPC and the Package Leaflet is updated accordingly. (MEA 007.2)
C.I.4 Update of the SmPC in section 4.5 in order to add drug-drug interaction information with oral contraceptives, and section 4.6 to update information on pregnancy and contraception based on final results from study CPKC412A2123, a Phase 1, open-label, drug-drug interaction study, listed as category 3 study in the RMP; the Package Leaflet is updated accordingly. (MEA 008.2)
C.I.4 Update of the SmPC in section 5.2 in order to update pharmacokinetic information on OATP1B1 transporters based on final results from PBPK modelling study DMPK R2000528 listed as category 3 studies in the RMP (MEA 009);
C.I.4 Update of the SmPC in section 4.2 in order to amend posology instructions, section 4.4 to amend an existing warning and section 5.2 to

update pharmacokinetic information for patients with severe hepatic impairment, based on final results from study CPKC412A2116 listed as category 3 study in the RMP. This is an open label, multiple dose study to evaluate the PK of midostaurin in subjects with mild, moderate and severe hepatic impairment compared to matched healthy subjects; (MEA010) The RMP version 6.0 has also been submitted. In addition, MAH takes this opportunity to introduce minor changes to edit the wording related to the ethanol excipient in the Package Leaflet, according the Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (SANTE-2017-11668), by rounding the volume of alcohol to the next integer number, i.e. from 16.9 to 17 ml. The requested group of variations proposed amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP)." Request for Supplementary Information adopted on 11.11.2021, 24.06.2021.	
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0069/G Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "C.I.4 type II variation: Update of section 4.8 of the SmPC in order to add rhinorrhoea to the list of adverse drug reactions (ADRs) with frequency unknown based on a systematic review of information from clinical and non-clinical studies, post-marketing data and scientific literature. The Package Leaflet has been updated accordingly. C.I.4 type II variation: Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study 109MS303 (ENDORSE) listed as a category 3 study in the RMP. This is a dose-blind, multicentre, extension study to determine the long-term safety and efficacy of two doses of BG00012 monotherapy in subjects with Relapsing-Remitting Multiple Sclerosis. The RMP version 11.1 has also been submitted." Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 28.10.2021, 02.09.2021, 08.07.2021,	Positive Opinion adopted by consensus on 13.01.2022.

06.05.2021, 14.01.2021.	
Tremfya - guselkumab - EMEA/H/C/004271/II/0031 Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, "C.I.4 Update the sections 4.8 and 5.1 of the SmPC based on the 2-year data from the psoriatic arthritis Phase 3 clinical study CNTO1959PSA3002 and to remove this study as an additional PV activity from the EU RMP. The RMP version 8.2 has also been submitted." Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 28.10.2021.	Positive Opinion adopted by consensus on 13.01.2022.
Tresiba - insulin degludec - EMEA/H/C/002498/II/0054 Novo Nordisk A/S, Rapporteur: Kristina Dunder, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Annika Folin, "Update of sections 4.6 and 5.1 of the Summary of product characteristics in order to include new clinical data from the pregnancy trial EXPECT conducted for Tresiba. This was a multi-centre, randomised, active controlled trial comparing the efficacy and safety of Tresiba once daily with insulin detemir once or twice daily both in combination with insulin aspart 2-4 times daily with meals in pregnant women or women who intended to become pregnant, all with type 1 diabetes. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to introduce minor administrative changes. The RMP version 9.0 is also submitted." Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 02.12.2021.	Positive Opinion adopted by consensus on 13.01.2022.
WS2141 **Ozempic-** **EMEA/H/C/004174/WS2141/0024** **Rybelsus-** **EMEA/H/C/004953/WS2141/0018** Novo Nordisk A/S, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Annika Folin, "Submission of the final report from study NN9535-4386 (SUSTAIN-11), listed as a category 3 study in the RMP. This is a 52-week, multi-centre, multinational, open-label, active	Request for supplementary information adopted with a specific timetable.

controlled, two armed, parallel, randomised trial undertaken to investigate the effect on glycaemic control, body weight, safety and health-related quality of life of once-weekly semaglutide s.c. vs insulin aspart three times daily, both as add-on to metformin and optimised insulin glargine U100 treatment in subjects with inadequately controlled T2DM. The RMP version 7.0 has also been submitted." Request for Supplementary Information adopted on 13.01.2022.	

B.5.4. PRAC assessed procedures

PRAC Led **AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0038** sanofi-aventis groupe, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the final PASS OBS12753 study report listed as a category 3 study in the RMP. This is a prospective cohort study of long-term safety of teriflunomide in multiple sclerosis patients in Europe. The updated RMP v 7.3 is agreed." Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 02.12.2021, 30.09.2021.	Positive Opinion adopted by consensus on 13.01.2022.
PRAC Led **Calquence - acalabrutinib - EMEA/H/C/005299/II/0011** AstraZeneca AB, Rapporteur: Filip Josephson, PRAC Rapporteur: Željana Margan Koletić, PRAC-CHMP liaison: Selma Arapovic Dzakula, "Submission of an updated RMP version 3 in order to add hepatotoxicity as an important potential risk to the safety concerns." Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
PRAC Led **COMIRNATY - tozinameran - EMEA/H/C/005735/II/0080** BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC in order to amend an existing warning on anxiety-related reactions to add hypoaesthesia and paraesthesia and remove tingling sensations	Positive Opinion adopted by consensus on 13.01.2022.

following the outcome of the Post-Authorisation Measure MEA-002.8 (EMEA/H/C/005735/MEA/002.8, dated 30 September 2021). Update of section 4.8 of the SmPC in order to add hypoaesthesia and paraesthesia to the list of adverse drug reactions (ADRs) with frequency 'not known' following the outcome of the Post-Authorisation Measure MEA-002.8 (EMEA/H/C/005735/MEA/002.8, dated 30 September 2021). The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes throughout the product information." Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 02.12.2021.	
PRAC Led **COMIRNATY - tozinameran - EMEA/H/C/005735/II/0087** BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 2.6 to include data from the booster/third dose, including data in patients who have undergone a solid organ transplantation, following the outcomes of procedures EMEA/H/C/005735/II/0062 (third dose in immunocompromise as part of the primary vaccination) and EMEA/H/C/005735/II/0067 (booster dose). The MAH takes the opportunity to update the RMP regarding the discontinuation of enrolment in study C4591015 (phase 2/3 study to evaluate the safety, tolerability, and immunogenicity in healthy pregnant women 18 years of age and older) and the CSR milestones." Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **COVID-19 Vaccine Janssen - adenovirus type 26 encoding the sars-cov-2 spike glycoprotein - EMEA/H/C/005737/II/0029** Janssen-Cilag International N.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version	Positive Opinion adopted by consensus on 13.01.2022.

3.1 in order to upgrade the important potential risk of venous thromboembolism (VTE) to an important identified risk as an outcome of the procedure MEA-32, addition of the clinical trial VAC31518COV3003 and update of study VAC18193RSV2008 as additional pharmacovigilance activities to further characterize the important identified risks of Thrombosis with thrombocytopenia syndrome (TTS), thrombocytopenia (including immune thrombocytopenia) and VTE as an outcome of MEA 14.4. The MAH took the opportunity to include other minor updates in the RMP. In addition, the MAH consolidated in RMP version 3.1 the updates made in the RMP as part of the approved procedure EMEA/H/C/005737/II/0018 and procedure EMEA/H/C/005737/II/0029." Opinion adopted on 13.01.2022.	
PRAC Led **COVID-19 Vaccine Janssen - adenovirus type 26 encoding the sars-cov-2 spike glycoprotein - EMEA/H/C/005737/II/0035** Janssen-Cilag International N.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Update of sections 4.4 and 4.8 of the SmPC in order to add transverse myelitis to the list of warnings and precautions and to the list of adverse drug reactions (ADRs) with frequency 'not known' based on the PRAC request from the post-authorisation measures MEA 14.5 and MEA 14.6 (6th and 7th Monthly Summary Safety Report covering the months of August 2021 and September 2021, respectively). The Package Leaflet is updated accordingly. Update of section 4.4 of the SmPC in order to amend the wording on Thrombosis and thrombocytopenia syndrome (TTS) following the PRAC request from the post-authorisation measure MEA 14.5. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement an editorial Quality review document (QRD) comment in the labelling following procedure EMEA/H/C/005737/II/014." Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
PRAC Led **Cystadrops - mercaptamine - EMEA/H/C/003769/II/0023, Orphan**	Request for supplementary information adopted with a specific timetable.

Recordati Rare Diseases, Rapporteur: Kristina Dunder, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "C.I.11 for RMP: Submission of an updated RMP version 1.4 in order to align with the new RMP format according to GVP Rev.2 and to remove a missing information from the list of safety concerns." Request for Supplementary Information adopted on 13.01.2022.	
PRAC Led **Evoltra - clofarabine - EMEA/H/C/000613/II/0075** Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "Update of section 4.6 of the SmPC following a request during EMEA/H/C/PSUSA/00000805/202012 to revise section 4.6 of the SmPC and corresponding sections in the PIL considering the recommendations of the Safety Working Party as reflected in the 'SWP recommendations on the duration of contraception following the end of treatment with a genotoxic drug' and available data. The proposed update of the product information should be based on a detailed scientific rationale from all available data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.2" Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
PRAC Led **Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0023** Seqirus Netherlands B.V., Rapporteur: Sol Ruiz, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of section 4.6 of the SmPC in order to update information on Pregnancy Registry 130_110B, listed as a category 3 study in the RMP. The PL is updated accordingly. The RMP version 3.1 has also been submitted in order to update information related to the pregnancy study, clinical and post-marketing exposure." Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.

Request for Supplementary Information adopted on 02.12.2021.	
PRAC Led **Hemlibra - emicizumab - EMEA/H/C/004406/II/0025** Roche Registration GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Armando Genazzani, "Update of sections 4.4, 4.8 and 5.1 of the Product information concerning immunogenicity and loss of efficacy due to anti-emicizumab antibodies. The RMP (v.3.0) is proposed to be updated accordingly." Request for Supplementary Information adopted on 13.01.2022, 02.12.2021, 02.09.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Hemlibra - emicizumab - EMEA/H/C/004406/II/0028** Roche Registration GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Armando Genazzani, "Submission of the final study report for BO40853 (Hemlibra Survey to Prescribers and Patients/Carers to Evaluate Awareness, Knowledge, and Compliance to Additional Risk Minimization Measures, listed as a category 3 study in the RMP). An updated RMP (version 4.0) is presented in support of this application," Request for Supplementary Information adopted on 13.01.2022, 02.12.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Moventig - naloxegol - EMEA/H/C/002810/II/0034** Kyowa Kirin Holdings B.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Submission of the final report from the observational Post Authorisation Safety Study (PASS)- Drug Utilisation in Selected European Populations (D3820R00006), listed as a category 3 study in the Risk Management Plan (RMP). The RMP version 7.1 is accepted." Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 28.10.2021.	Positive Opinion adopted by consensus on 13.01.2022.
PRAC Led **Obizur - susoctocog alfa - EMEA/H/C/002792/II/0043**	Positive Opinion adopted by consensus on 13.01.2022.

Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from US PASS 241302 study, EUPAS register Number EUPAS36659, listed as a category 3 study in the RMP. This is a post-marketing non-interventional safety evaluation of Obizur in the treatment of bleeding episodes for patients with acquired haemophilia A (AHA). The primary objective is to determine the incidence of therapy-related serious adverse events (SAEs) in patients with AHA who are prescribed and treated with OBIZUR in routine clinical practice. The RMP version 5.0 has also been submitted and endorsed." Opinion adopted on 13.01.2022.	
PRAC Led **OFEV - nintedanib - EMEA/H/C/003821/II/0046** Boehringer Ingelheim International GmbH, Rapporteur: Peter Kiely, PRAC Rapporteur: Nikica Mirošević Skvrce, PRAC-CHMP liaison: Selma Arapovic Dzakula, "C.I.11 for RMP: Submission of an updated RMP version 11.0 in order to fulfil a request made in the renewal (EMEA/H/C/003821/R/0025) to remove the following safety concerns (Modules SIV, SVII, SVIII; Parts III, V, VI; Appendices 4, 8) : 1-Important identified risks: Diarrhoea, Liver enzyme and bilirubin elevations including DIL, Bleeding, Myocardial infarction); 2-Important potential risks: Venous thromboembolism, Arterial thromboembolism excluding myocardial infarction, Perforation, Hepatic failure, Treatment of pregnant women and teratogenicity, Cardiac failure; 3- Missing information: Treatment of patients with moderate or severe hepatic impairment (Child Pugh B/C), Treatment of Black patients, Treatment of patients with healing wounds, Treatment of patients with severe renal impairment or end-stage renal disease, Treatment of patients receiving full-dose therapeutic anticoagulation, Treatment of breastfeeding women. Moreover, it is updated ATC code (Part I) and post-marketing exposure (Module SV)." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 13.01.2022.	
PRAC Led **Olumiant - baricitinib - EMEA/H/C/004085/II/0031** Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski, PRAC-CHMP liaison: Ewa Balkowiec Iskra, "C.I.4 - Update of section 4.4 of the SmPC in order to add new warnings on Major Adverse Cardiac Events (MACE) and amend existing warning on Malignancy and Venous thromboembolism (VTE) following the request made in PSUSA (EMEA/H/C/PSUSA/00010578/202102) and based on interim results from study I4V-MC-B023; this is a retrospective observational study to compare baricitinib relative to the standard of care. The Package Leaflet is updated accordingly. The RMP version 13.1 has also been submitted. In addition, the MAH has submitted a proposal for a DHPC and communication plan." Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Otezla - apremilast - EMEA/H/C/003746/II/0039** Amgen Europe B.V., Rapporteur: Peter Kiely, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "C.I.13-Submission of the final study report (CSR) from UK Clinical Practice Research Database (CPRD), listed as a category 3 study in the RMP. This is an observational study to assess the long-term data of apremilast in patients with psoriasis and psoriatic arthritis. The RMP version 14.0 has also been submitted." Request for Supplementary Information adopted on 13.01.2022, 30.09.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Remicade - infliximab - EMEA/H/C/000240/II/0231** Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report of the Remicade AntiRheumatic Therapy in Sweden (ARTIS) registry study. The ARTIS registry study was performed to fulfil a post-authorisation measure	Request for supplementary information adopted with a specific timetable.

in the RMP for Remicade. The updated RMP v20.1. has also been submitted, including revisions agreed in previous procedures." Request for Supplementary Information adopted on 13.01.2022.	
PRAC Led **Suliqua - insulin glargine / lixisenatide - EMEA/H/C/004243/II/0024** sanofi-aventis groupe, Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final Clinical Study Report of the category 3 PASS INSLIC08571, a 'Survey to evaluate the knowledge and understanding of the key safety messages in the healthcare professional guide and the patient guide'. The provision of the final survey results addresses post-authorisation measure (PAM) MEA 002. The updated RMP version 6.1 was agreed during the procedure." Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 30.09.2021.	Positive Opinion adopted by consensus on 13.01.2022.
PRAC Led **Tegsedi - inotersen - EMEA/H/C/004782/II/0026, Orphan** Akcea Therapeutics Ireland Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Submission of an updated RMP version 3.0 to remove carcinogenicity in rats as missing information, add a targeted questionnaire as routine pharmacovigilance measure and a patient alert card as additional risk minimisation for liver transplant rejection. To add 'injection site reactions' and 'immunogenicity' as risks not considered important for inclusion in the summary of safety cencers, and to update the patient alert card with additional warnings on hepatic monitoring and ocular toxicity. Further sections of the RMP are updated." Request for Supplementary Information adopted on 13.01.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Temodal - temozolomide - EMEA/H/C/000229/II/0095** Merck Sharp & Dohme B.V., Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Update of the RMP	Positive Opinion adopted by consensus on 13.01.2022.

to version 6.1. to remove all the safety concerns (important identified risks, important potential risks and missing information). The deletion of the safety concerns is based on the guidance EU GVP Module V (Revision 2)." Opinion adopted on 13.01.2022.	
PRAC Led **TRISENOX - arsenic trioxide - EMEA/H/C/000388/II/0076** Teva B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "Update of section 4.6 of the SmPC in order to update information on pregnancy and contraception in male patients following the decision and discussion made for EMEA/H/C/PSUSA/00000235/202009 and to add an appropriate period of abstinence for breastfeeding during use of trisenox. The Package Leaflet is updated accordingly." Opinion adopted on 13.01.2022. Request for Supplementary Information adopted on 02.12.2021.	Positive Opinion adopted by consensus on 13.01.2022.
PRAC Led **Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0055** AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Christophe Focke, "Update of section 4.4 of the SmPC in order to update the warning on thrombosis with thrombocytopenia syndrome to indicate that the frequency after the second dose is lower than after the first dose based on the post-marketing data. The package leaflet is updated accordingly. The MAH took the opportunity to include editorial updates in the product information." Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
PRAC Led **Zessly - infliximab - EMEA/H/C/004647/II/0020** Sandoz GmbH, Rapporteur: Ingrid Wang, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the updated RMP version 3.0 to remove the RABBIT registry as an additional pharmacovigilance activity in alignment with the updated version of the reference product Remicade RMP (v19) and to remove the BADBIR registry as an additional	Request for supplementary information adopted with a specific timetable.

pharmacovigilance activity."
Request for Supplementary Information adopted on 13.01.2022.

PRAC Led
WS2185
Entresto-
EMEA/H/C/004062/WS2185/0041
Neparvis-
EMEA/H/C/004343/WS2185/0039
Novartis Europharm Limited, Lead PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "To provide an updated RMP in response to the assessment report for procedure EMEA/H/C/WS1830. In addition, the following changes have been introduced:
- change to the agreed milestone for study CLCZ696B2320 (EU PASS category 3), to update the date for the submission of the final report ;
- update of section 8.3.1 (Presentation of important identified risks and important potential risks);
- updated exposure and post-marketing data have been provided for the data lock point of PSUR 9 (31-Jul-21)."

B.5.5. CHMP-CAT assessed procedures

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0002, Orphan, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang
Request for Supplementary Information adopted on 05.11.2021.

Luxturna - voretigene neparvovec - EMEA/H/C/004451/II/0026/G, Orphan, ATMP
Novartis Europharm Limited, Rapporteur: Sol Ruiz, CHMP Coordinator: Maria Concepcion Prieto Yerro

Tecartus - autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - EMEA/H/C/005102/II/0016,

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

Zolgensma - onasemnogene abeparvovec - EMEA/H/C/004750/II/0019/G, Orphan, ATMP
Novartis Gene Therapies EU Limited, Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege
Request for Supplementary Information adopted on 05.11.2021.

WS2181
Tecartus- EMEA/H/C/005102/WS2181/0014
Yescarta- EMEA/H/C/004480/WS2181/0044
Kite Pharma EU B.V., Lead Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus
Request for Supplementary Information adopted on 16.12.2021.

B.5.6. CHMP-PRAC-CAT assessed procedures

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0010, Orphan, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang, PRAC Rapporteur: Annika Folin, "Update of section 5.1 of the SmPC in order to update efficacy information based on 24 month follow up data from the pivotal study submitted during initial (BB2121-MM-001: A Phase 2, Multicentre Study to determine the Efficacy and Safety of bb2121 in Subjects with Relapsed and Refractory Multiple Myeloma) listed as a specific obligation in the Annex II and in the RMP; The annex II is updated with the proposed deletion of the relevant SOB. The RMP version 1.1 has also been submitted."

B.5.7. PRAC assessed ATMP procedures

B.5.8. Unclassified procedures and work-sharing procedures of type I variations

WS2111/G **Eucreas-** **EMEA/H/C/000807/WS2111/0089/G** **Icandra-** **EMEA/H/C/001050/WS2111/0092/G** **Zomarist-** **EMEA/H/C/001049/WS2111/0091/G** Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
WS2140 **Infanrix hexa-** **EMEA/H/C/000296/WS2140/0307** GlaxoSmithKline Biologicals SA, Lead Rapporteur: Christophe Focke Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
WS2155 **Ambirix-** **EMEA/H/C/000426/WS2155/0118** **Fendrix-** **EMEA/H/C/000550/WS2155/0077** **Twinrix Adult-** **EMEA/H/C/000112/WS2155/0153** **Twinrix Paediatric-** **EMEA/H/C/000129/WS2155/0154** GlaxoSmithKline Biologicals SA, Lead Rapporteur: Christophe Focke, "To add the warning on sodium to sections 2, 4.4 of the SmPC; section 3 of Labelling and section 2 of Package leaflet to bring the annexes in line with the excipients guideline. In addition, the QRD template v10.2 update is implemented. Contact details of local representatives are updated as follows: - Ambirix in Belgium, Croatia, Cyprus, Estonia, Greece, Hungary, Latvia, Lithuania, Luxemburg, Malta, Netherlands, Romania, Slovenia, Slovakia, and United Kingdom (Northern Ireland); - Fendrix in Belgium, Croatia, Cyprus, Estonia, Finland, Greece, Hungary, Italy, Latvia, Lithuania, Luxemburg, Malta, Netherlands, Norway, Romania, Slovenia, Slovakia, Spain and United Kingdom (Northern Ireland); - Twinrix Adult in Belgium, Croatia, Cyprus, Estonia, Finland, Greece, Hungary, Italy, Latvia, Lithuania, Luxemburg, Malta, Netherlands,	Positive Opinion adopted by consensus on 13.01.2022.

Norway, Romania, Slovenia, Slovakia, Spain and United Kingdom (Northern Ireland); - Twinrix Adult in Belgium, Croatia, Cyprus, Estonia, Finland, Greece, Hungary, Italy, Latvia, Lithuania, Luxemburg, Malta, Netherlands, Norway, Romania, Slovenia, Slovakia, Spain and United Kingdom (Northern Ireland);" Opinion adopted on 13.01.2022.	
WS2162 **Prezista-** **EMEA/H/C/000707/WS2162/0113** **Rezolsta-** **EMEA/H/C/002819/WS2162/0044** **Symtuza-** **EMEA/H/C/004391/WS2162/0038** Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege, "To update for the 3 Darunavir products (PREZISTA, REZOLSTA and Symtuza), section 4.3, section 4.4 (PREZISTA 100 mg/ml, 400 mg and 800 mg) and section 4.5 of each SmPC to emphasise that the lists of medications in the Contraindications and in the Interactions sections are not comprehensive and are to be considered as examples. The Package Leaflets are updated accordingly. The MAH also has taken the opportunity to include several minor changes as follows: - an update in section 4.5 of the SmPC and section 2 of the Patient leaflet of Symtuza to include information about elbasvir and grazoprevir, in order to align with the info provided in the PREZISTA and REZOLSTA labels (as approved in Feb 2017 in procedure WS1107/G); - correcting the capitalisation of 'wort' in St. John's Wort; - adding the prefix for Belgian postcodes to the addresses in the respective Package Leaflets." Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
WS2173 **HBVAXPRO-** **EMEA/H/C/000373/WS2173/0073** **Vaxelis-EMEA/H/C/003982/WS2173/0091** MCM Vaccine B.V., Lead Rapporteur: Christophe Focke Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
WS2175 **Corbilta-**	

EMEA/H/C/002785/WS2175/0026 **Levodopa/Carbidopa/Entacapone Orion-** **EMEA/H/C/002441/WS2175/0034** **Stalevo-EMEA/H/C/000511/WS2175/0096** Orion Corporation, Lead Rapporteur: Outi Mäki-Ikola, "To add Sodium warning to sections 2, 4.4 of the SmPC; section 3 of Labelling and section 2 of Package leaflet to Stalevo and its duplicates Corbilta and Levodopa/Carbidopa/Entacapone Orion. QRD template v10.2 update is implemented for Stalevo and Levodopa/Carbidopa/Entacapone Orion. Contact details of local representatives are updated as follows: - Stalevo in France and United Kingdom (Northern Ireland); - Corbilta in France; - Levodopa/Carbidopa/Entacapone Orion in Lithuania, Estonia, Ireland, Latvia and United Kingdom (Northern Ireland). Additionally, missing non-breaking spaces added, wherever applicable according to EMA guidance 'Compilation of QRD decisions on stylistic matters in product information'. Minor linguistic and typographical corrections have been performed in several languages as follows: Stalevo: CS, DE, EL, EN, ES, ET, FR, HR, HU, IS, LT, LV, MT, NL, NO, PL, PT, RO, SK and SL. Corbilta: CS, DA, DE, EL, EN, ES, ET, FR, HR, HU, IS, LT, LV, MT, NL, NO, PL, PT, RO, SK, SL and SV. Levodopa/Carbidopa/Entacapone Orion: CS, DA, DE, EL, EN, ES, ET, FR, HR, HU, IS, LT, LV, MT, NL, PL, PT, RO, SK and SL."	
WS2186 **Blitzima-** **EMEA/H/C/004723/WS2186/0050** **Truxima-** **EMEA/H/C/004112/WS2186/0053** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz Opinion adopted on 13.01.2022.	Positive Opinion adopted by consensus on 13.01.2022.
WS2208 **Blitzima-** **EMEA/H/C/004723/WS2208/0051** **Truxima-** **EMEA/H/C/004112/WS2208/0054** Celltrion Healthcare Hungary Kft., Lead	Positive Opinion adopted by consensus on 13.01.2022.

Rapporteur: Sol Ruiz
Opinion adopted on 13.01.2022.

WS2209
Blitzima-
EMEA/H/C/004723/WS2209/0052
Truxima-
EMEA/H/C/004112/WS2209/0055
Celltrion Healthcare Hungary Kft., Lead
Rapporteur: Sol Ruiz

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

LEDAGA - chlormethine - EMEA/H/C/002826/II/0027, Orphan Helsinn Birex Pharmaceuticals Limited, Rapporteur: Sinan B. Sarac, "Update of section 4.2 of the SmPC in order to allow flexibility in the starting frequency of the treatment based on current clinical practice; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 20.05.2021. Withdrawal request submitted on 11.01.2022.	The MAH withdrew the procedure on 11.01.2022.

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

ublituximab - EMEA/H/C/005914
treatment of relapsing forms of multiple sclerosis (RMS)

dimethyl fumarate - EMEA/H/C/005950
treatment of multiple sclerosis,

follitropin delta - EMEA/H/D/006065
In vitro quantitative determination of anti-Müllerian hormone (AMH) in human serum and plasma

trastuzumab - EMEA/H/C/005769
treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)

sirolimus - EMEA/H/C/005896, Orphan
Plusultra pharma GmbH, Treatment of

angiofibroma associated with tuberous sclerosis complex
tremelimumab - EMEA/H/C/004650 treatment of adults with metastatic NSCLC with no sensitising epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) genomic tumour aberrations
paclitaxel - EMEA/H/C/005997 treatment of metastatic breast cancer
parsaclisib - EMEA/H/C/005893, Orphan Incyte Biosciences Distribution B.V., Treatment of adult patients with relapsed or refractory marginal zone lymphoma (MZL).
PF-07321332 / ritonavir - EMEA/H/C/005973 treatment of COVID-19
tolvaptan - EMEA/H/C/005961 treatment of hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH)

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

Adcirca - tadalafil - EMEA/H/C/001021/X/0035/G Eli Lilly Nederland B.V., Informed Consent of Cialis, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maria del Pilar Rayon, "Extension application to introduce a new pharmaceutical form associated with a new strength (2 mg/ml oral suspension) grouped with a type II variation (C.I.6.a) to include paediatric use (from 6 months to 17 years) based on study 4 (H6D-MC-LVHV [LVHV]) - A 24-week placebo-controlled efficacy and safety study with an open-label long-term extension phase. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The paediatric indication is applicable to the new and all existing presentations. The Package Leaflet and Labelling are updated accordingly. Furthermore, the PI is brought in line with the latest QRD template and editorial changes have been implemented. The RMP (version 9.1) is

updated in accordance."

Betmiga - mirabegron - EMEA/H/C/002388/X/0039/G

Astellas Pharma Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, "Extension application to introduce a new pharmaceutical form associated with new strength (8 mg/ml prolonged-release granules for oral suspension), grouped with a type II variation (C.I.6.a) to include treatment of neurogenic detrusor overactivity (NDO) in paediatric patients aged 3 to less than 18 years. The RMP (version 9.0) is updated in accordance."

Byfavo - remimazolam - EMEA/H/C/005246/X/0002

PAION Netherlands B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Selma Arapovic Dzakula, PRAC Rapporteur: Rhea Fitzgerald, "Extension application to introduce a new pharmaceutical form associated with new strength (50 mg powder for concentrate for solution for injection/infusion). The new presentation is indicated to include the intravenous induction and maintenance of general anaesthesia (GA) in adults for Byfavo 50 mg, based on final results from two pivotal trials: Study ONO-2745-05, a phase IIb/III, single-blind, randomised, parallel-group study assessing safety and efficacy in induction and maintenance of anaesthesia in ASA I/II patients (general surgery), and study CNS-7056-022, a phase III, randomized, propofol controlled, parallel group, confirmatory single-blind efficacy and safety trial during induction and maintenance of anaesthesia in ASA III/IV patients.
A new combined version of the SmPC, labelling and Package Leaflet solely for the 50 mg strength and the GA indication is provided accordingly.
Version 1.1 of the RMP 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)

Dupixent - dupilumab -

EMEA/H/C/004390/X/0057
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus

Skyrizi - risankizumab - EMEA/H/C/004759/X/0020
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Peter Kiely, PRAC Rapporteur: Liana Gross-Martirosyan, "Extension application to:
- introduce a new pharmaceutical form (concentrate for solution for infusion), a new strength (600 mg) and a new route of administration (intravenous use)
- add a new strength of 360 mg (150 mg/ml) for risankizumab solution for injection (in cartridge) for subcutaneous use
The above new presentations are indicated for the treatment of patients 16 years and older with moderately to severely active Crohn's disease who have had an inadequate response to, lost response to, or were intolerant to conventional therapy or a biologic therapy, or if such therapies are not advisable.
The RMP (version 4.0) is updated in accordance."

Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/X/0101/G
ViiV Healthcare B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber, "Extension application to introduce a new pharmaceutical form associated with new strength (5 mg/60 mg/30 mg dispersible tablet). The new presentation is indicated for the treatment of Human Immunodeficiency Virus (HIV) infected children weighing at least 14 kg to less than 25 kg.
This extension application is grouped with a type II variation (C.I.6.a) to include treatment of children weighing at least 25 kg for the already approved film-coated tablets for Triumeq (EU/1/14/940/001-002); as a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance.
The RMP (version 19) is updated in accordance."

Xofluza - baloxavir marboxil - EMEA/H/C/004974/X/0008/G
Roche Registration GmbH, Rapporteur: Thalia

Marie Estrup Blicher, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Sonja Hrabcik, "Extension application to introduce a new pharmaceutical form associated with new strength (2 mg/ml granules for oral suspension) grouped with a type II variation (C.I.6.a) to include paediatric use (from 1 year and above). The paediatric indication is applicable to the new presentation (2 mg/ml granules for oral suspension) as well as all approved presentations (EU/1/20/1500/001 and 002). The RMP (version 2.0) is updated in accordance."

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

insulin human - EMEA/H/W/005779, Article 58
treatment of diabetes mellitus
List of Questions adopted on 11.11.2021.

dabigatran etexilate - EMEA/H/C/005639
prevention of venous thromboembolic events
List of Questions adopted on 12.11.2020.

ganirelix - EMEA/H/C/005641
Prevention of premature luteinising hormone (LH) surges in women undergoing controlled ovarian hyperstimulation (COH) for assisted reproduction techniques (ART).
List of Questions adopted on 22.07.2021.

Ilumetri - tildrakizumab - EMEA/H/C/004514/X/0023
Almirall S.A, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Adam Przybylkowski, "Extension application to introduce a new strength (200 mg solution for injection)."
List of Questions adopted on 11.11.2021.

insulin human - EMEA/H/W/005780, Article 58
treatment of diabetes mellitus
List of Questions adopted on 11.11.2021.

tebentafusp - EMEA/H/C/004929, Orphan
Immunocore Ireland Limited, treatment of uveal melanoma
List of Questions adopted on 09.11.2021.

molnupiravir - EMEA/H/C/005789

Treatment of coronavirus disease 2019 (COVID-19)
List of Questions adopted on 16.12.2021.

melphalan flufenamide - EMEA/H/C/005681, Orphan
Oncopeptides AB, treatment of multiple myeloma
List of Questions adopted on 16.09.2021.

pirfenidone - EMEA/H/C/005873
indicated in adults for the treatment of mild to moderate idiopathic pulmonary fibrosis (IPF).
List of Questions adopted on 16.09.2021.

bevacizumab - EMEA/H/C/005574
Treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer.
First-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer.
First-line treatment of patients with advanced and/or metastatic renal cell cancer.
List of Questions adopted on 22.04.2021.

mitapivat - EMEA/H/C/005540, Orphan
Agios Netherlands B.V., treatment of pyruvate kinase deficiency
List of Questions adopted on 11.11.2021.

sitagliptin / metformin hydrochloride - EMEA/H/C/005850
treatment of type 2 diabetes mellitus
List of Questions adopted on 16.09.2021.

ranibizumab - EMEA/H/C/005610
treatment of neovascular age-related macular degeneration in adults
List of Questions adopted on 16.09.2021.

tezepelumab - EMEA/H/C/005588
add-on maintenance treatment in adults and adolescents 12 years and older with severe asthma
List of Questions adopted on 14.10.2021.

Xofluza - baloxavir marboxil - EMEA/H/C/004974/X/0003/G
Roche Registration GmbH, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Sonja Hrabcik, "Extension application to add a new

strength of 80 mg grouped with a type IB variation to add a new pack size for 40 mg strength.
The RMP (version 1.2) is updated in accordance.
Furthermore, the PI is being brought in line with the QRD template version 10.2 to update the local representatives with "United Kingdom (Northern Ireland) "."
List of Questions adopted on 16.09.2021.

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

Orphacol - cholic acid - EMEA/H/C/001250/S/0042, Orphan
Laboratoires CTRS, Rapporteur: Anastasia Mountaki, PRAC Rapporteur: Sofia Trantza

SCENESSE - afamelanotide - EMEA/H/C/002548/S/0041, 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

Efavirenz/Emtricitabine/Tenofovir disoproxil Mylan - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/004240/R/0019
Mylan Pharmaceuticals Limited, Generic, Generic of Atripla (SRD), Rapporteur: Bruno Sepodes, PRAC Rapporteur: Martin Huber

Entecavir Accord - entecavir - EMEA/H/C/004458/R/0011
Accord Healthcare S.L.U., Generic, Generic of Baraclude, Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Ulla Wändel Liminga

Entecavir Mylan - entecavir - EMEA/H/C/004377/R/0008
Mylan Pharmaceuticals Limited, Generic, Generic of Baraclude, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ulla Wändel Liminga

Fotivda - tivozanib - EMEA/H/C/004131/R/0021
EUSA Pharma (Netherlands) B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Romaldas

Mačiulaitis, PRAC Rapporteur: Rugile Pilviniene

Koselugo - selumetinib -
EMEA/H/C/005244/R/0003, Orphan
AstraZeneca AB, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Annika Folin

Lacosamide Accord - lacosamide -
EMEA/H/C/004443/R/0015
Accord Healthcare S.L.U., Generic, Generic of Vimpat, Rapporteur: John Joseph Borg, PRAC Rapporteur: Ulla Wändel Liminga

LIBTAYO - cemiplimab -
EMEA/H/C/004844/R/0029
Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Menno van der Elst

LUTATHERA - lutetium (177Lu) oxodotreotide -
EMEA/H/C/004123/R/0032, Orphan
Advanced Accelerator Applications, Rapporteur: Janet Koenig, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Adam Przybylkowski

Nitisinone MDK - nitisinone -
EMEA/H/C/004281/R/0013
MendeliKABS Europe Limited, Generic, Generic of Orfadin, Rapporteur: Alar Irs, PRAC Rapporteur: Ilaria Baldelli

Rozlytrek - entrectinib -
EMEA/H/C/004936/R/0007
Roche Registration GmbH, Rapporteur: Armando Genazzani, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst

Symtuza - darunavir / cobicistat / emtricitabine / tenofovir alafenamide -
EMEA/H/C/004391/R/0040
Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Ana Sofia Diniz Martins

Veklury - remdesivir -
EMEA/H/C/005622/R/0031
Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, PRAC Rapporteur: Eva Jirsová

Zolgensma - onasemnogene abeparvovec -
EMEA/H/C/004750/R/0021, Orphan, ATMP

Novartis Gene Therapies EU Limited, Rapporteur: Carla Herberts, Co-Rapporteur: Egbert Flory, CHMP Coordinators: Johann Lodewijk Hillege and Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

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

Adtralza - tralokinumab - EMEA/H/C/005255/II/0002 LEO Pharma A/S, Rapporteur: Jayne Crowe, PRAC Rapporteur: Kimmo Jaakkola, "Extension of indication to include treatment of adolescent patients (12-17 years) for Adtralza based on final study LP0162-1334 (ECZTRA 6): a multicentre, randomised, double-blind, placebo-controlled study in adolescent patients 12 to 17 years of age with moderate-to-severe atopic dermatitis to evaluate the efficacy and safety of tralokinumab monotherapy in this population group. 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."
Enhertu - trastuzumab deruxtecan - EMEA/H/C/005124/II/0014 Daiichi Sankyo Europe GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Extension of indication for Enhertu to include treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received one or more prior anti-HER2-based regimens; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.2 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)
Fintepla - fenfluramine - EMEA/H/C/003933/II/0012, Orphan Zogenix ROI Limited, Rapporteur: Thalia Marie

Estrup Blicher, PRAC Rapporteur: Martin Huber, "Extension of indication to include treatment of seizures associated with Lennox-Gastaut syndrome as an add on therapy to other anti-epileptic medicines for patients 2 years of age and older. 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 2.3 of the RMP has also been submitted."	
GAVRETO - pralsetinib - EMEA/H/C/005413/II/0002/G Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Annika Folin, "Extension of indication to include monotherapy treatment of adult and paediatric patients 12 years of age and older with locally advanced or metastatic RET-mutant medullary thyroid cancer for Gavreto; based on the efficacy and safety data obtained from the pivotal study BO42863 (ARROW). 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 1.1 of the RMP has also been submitted. Furthermore, some minor changes to the PI have been implemented in line with the latest Anticancer Guidelines Recommendations. Extension of indication to include monotherapy treatment of adult and paediatric patients 12 years of age and older with locally advanced or metastatic RET fusion-positive thyroid cancer for Gavreto; based on the efficacy and safety data obtained from the pivotal study BO42863 (ARROW). 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 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)	
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0070 Janssen-Cilag International NV, Rapporteur: Filip Josephson, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Nikica Mirošević Skvrce, "Extension of the existing CLL indication to include combination treatment with venetoclax	

for previously untreated patients based on efficacy and safety data from phase 3 study GLOW and phase 2 study CAPTIVATE. The SmPC is revised to reflect the information on the combination with venetoclax. The PL is updated accordingly. The RMP version 18.4 has been submitted. Justification to support one-year extension of the marketing protection period is included in the submission." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)	
Imfinzi - durvalumab - EMEA/H/C/004771/II/0041 AstraZeneca AB, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: David Olsen,"Extension of indication to include first-line treatment, with Imfinzi in combination with tremelimumab and platinum-based chemotherapy, of adults with metastatic NSCLC with no sensitizing epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) genomic tumour aberrations, based on final results from study D419MC00004 (POSEIDON); This was a Phase III, randomised, multicentre, open-label, comparative global study to determine the efficacy and safety of tremelimumab and durvalumab or durvalumab in combination with platinum based chemotherapy for first-line treatment in patients with metastatic NSCLC. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.2. Version 5.1 of the RMP has also been submitted."	
LIBTAYO - cemiplimab - EMEA/H/C/004844/II/0028 Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Menno van der Elst, "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."

Lynparza - olaparib - EMEA/H/C/003726/II/0053

AstraZeneca AB, Rapporteur: Alexandre Moreau, Co-Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Amelia Cupelli, "Extension of indication to include treatment of adults with metastatic castration resistant prostate cancer (mCRPC), with Lynparza in combination with abiraterone and prednisone or prednisolone, based on the results of the pivotal Phase III study PROpel (D081SC00001) and supportive evidence from study 8 (D081DC00008). PROpel is a Phase III, randomised, double-blind, placebo-controlled, multicentre study evaluating olaparib vs placebo in combination with abiraterone as first line treatment for men with mCRPC. Consequently, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC for Lynparza tablets are being updated. In addition, sections 4.4 and 4.8 of the SmPC for Lynparza hard capsules are revised based on the updated safety data analysis. The Package Leaflet is updated accordingly. The RMP version 24 has also been submitted."

RINVOQ - upadacitinib - EMEA/H/C/004760/II/0016

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce, "Extension of indication to include the treatment of active non-radiographic axial spondyloarthritis in adult patients with objective signs of inflammation who have responded inadequately to NSAIDs or other conventional therapy, based on the final clinical study report from the pivotal study M19-944 Study 2 (nr-axSpA); a randomized, double-blind, phase III study evaluating the long-term safety, tolerability, and efficacy of upadacitinib 15 mg QD in subjects with nr-axSpA who completed the Double-Blind Period on study drug. As a consequence, SmPC sections 4.1, 4.2, 4.8, 5.1 and 5.2 have been updated and the Package Leaflet has been updated in

accordance. A revised RMP version 8.0 was also submitted."

Ultomiris - ravulizumab - EMEA/H/C/004954/II/0026
Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Kimmo Jaakkola, "Extension of indication to include treatment of adult patients with generalized myasthenia gravis (gMG). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 and 6.6 of the SmPC and corresponding sections in the Package Leaflet are updated accordingly. The RMP has been updated to version 4.0 to align with the indication extension. Lastly, the minor editorial corrections are made throughout the SmPC and package leaflet."
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

WS2150 DuoPlavin- EMEA/H/C/001143/WS2150/0060 Iscover- EMEA/H/C/000175/WS2150/0146 Plavix-EMEA/H/C/000174/WS2150/0145
sanofi-aventis groupe, Lead Rapporteur: Bruno Sepodes, Lead PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Extension of indication to include clopidogrel in combination with acetylsalicylic acid in ST segment elevation acute myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI); as a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. Version 1.5 of the RMP has also been submitted. In addition, an editorial update has been made to the labelling."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0030/G
Baxalta Innovations GmbH, Rapporteur: Andrea Laslop

Alymsys - bevacizumab - EMEA/H/C/005286/II/0007/G
Mabxience Research SL, Rapporteur: Christian

Gartner	
Azacitidine Accord - azacitidine - EMEA/H/C/005147/II/0009 Accord Healthcare S.L.U., Generic, Generic of Vidaza, Rapporteur: Hrefna Gudmundsdottir	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0090 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	See B.5.1
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0092/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0101 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	See B.5.1
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0105 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COVID-19 Vaccine Janssen - adenovirus type 26 encoding the sars-cov-2 spike glycoprotein - EMEA/H/C/005737/II/0040 Janssen-Cilag International N.V., Rapporteur: Christophe Focke	
Elaprase - idursulfase - EMEA/H/C/000700/II/0095 Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege	
Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0024 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz	
Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0025/G Seqirus Netherlands B.V., Rapporteur: Sol Ruiz	
Fulphila - pegfilgrastim - EMEA/H/C/004915/II/0029 Viatris Limited, Rapporteur: Martina Weise	
Hemlibra - emicizumab - EMEA/H/C/004406/II/0029/G Roche Registration GmbH, Rapporteur:	

Alexandre Moreau

Ilumetri - tildrakizumab - EMEA/H/C/004514/II/0029/G
Almirall S.A, Rapporteur: Jan Mueller-Berghaus

Odomzo - sonidegib - EMEA/H/C/002839/II/0041
Sun Pharmaceutical Industries Europe B.V., Rapporteur: Paula Boudewina van Hennik

Ogivri - trastuzumab - EMEA/H/C/004916/II/0040
Viatris Limited, Rapporteur: Karin Janssen van Doorn

Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0027
Alexion Europe SAS, Rapporteur: Jan Mueller-Berghaus

Pedea - ibuprofen - EMEA/H/C/000549/II/0030
Recordati Rare Diseases, Rapporteur: Jayne Crowe

Perjeta - pertuzumab - EMEA/H/C/002547/II/0063
Roche Registration GmbH, Rapporteur: Sinan B. Sarac

Regkirona - regdanvimab - EMEA/H/C/005854/II/0002
Celltrion Healthcare Hungary Kft., Rapporteur: Filip Josephson

Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0055/G
CSL Behring GmbH, Rapporteur: Kristina Dunder

Ruconest - conestat alfa - EMEA/H/C/001223/II/0071
Pharming Group N.V, Rapporteur: Andrea Laslop

Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0038/G
Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus

Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0046
Moderna Biotech Spain, S.L., Rapporteur: Jan

Mueller-Berghaus	
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0050 Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus	
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0051/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus	
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0052/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus	
Supemtek - quadrivalent influenza vaccine (recombinant, prepared in cell culture) - EMEA/H/C/005159/II/0007/G Sanofi Pasteur, Rapporteur: Jan Mueller-Berghaus	
TRODELVY - sacituzumab govitecan - EMEA/H/C/005182/II/0002/G Gilead Sciences Ireland UC, Rapporteur: Jan Mueller-Berghaus	
TRODELVY - sacituzumab govitecan - EMEA/H/C/005182/II/0003 Gilead Sciences Ireland UC, Rapporteur: Jan Mueller-Berghaus	
Tysabri - natalizumab - EMEA/H/C/000603/II/0132 Biogen Netherlands B.V., Rapporteur: Jan Mueller-Berghaus	
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0095 MCM Vaccine B.V., Rapporteur: Christophe Focke	
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0061/G AstraZeneca AB, Co-Rapporteur: Johann Lodewijk Hillege	See B.5.1

Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0062
AstraZeneca AB, Rapporteur: Sol Ruiz

Votrient - pazopanib - EMEA/H/C/001141/II/0071/G
Novartis Europharm Limited, Rapporteur: Sinan B. Sarac

ZABDENO - ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005337/II/0009/G
Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege

WS2159/G
Prolia- EMEA/H/C/001120/WS2159/0095/G
XGEVA- EMEA/H/C/002173/WS2159/0079/G
Amgen Europe B.V., Lead Rapporteur: Kristina Dunder

WS2190
Lixiana-EMEA/H/C/002629/WS2190/0036
Roteas-EMEA/H/C/004339/WS2190/0023
Daiichi Sankyo Europe GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro

WS2199
Infanrix hexa- EMEA/H/C/000296/WS2199/0311
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke

WS2225/G
Abseamed- EMEA/H/C/000727/WS2225/0097/G
Binocrit- EMEA/H/C/000725/WS2225/0096/G
Epoetin alfa Hexal- EMEA/H/C/000726/WS2225/0096/G
Sandoz GmbH, Lead Rapporteur: Alexandre Moreau

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

Caprelsa - vandetanib - EMEA/H/C/002315/II/0052
Genzyme Europe BV, Rapporteur: Alexandre Moreau, "Update of section 4.4 of the SmPC in

order to amend an existing warning on renal failure based on safety signal evaluation report. In addition, the MAH took the opportunity to update the contact details for local representative in DE in the Package Leaflet."	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0093 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information after booster dose, based on interim results from study C4591031, this is a randomized, placebo-controlled, phase 3 booster efficacy study involving participants ≥ 16 years of age who completed the primary series of BNT162b2 30 µg in study C4591001. The Package Leaflet and Labelling are updated accordingly.In addition, the MAH took the opportunity to make minor editorial changes throughout the product information."	See B.5.2
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0102 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC in order to update safety and efficacy information 6 months post-dose 2 follow-up for adolescence 12 through 15 years of age based on updated interim results from study C4591001, listed as a specific obligation; this is a Phase 1/2/3, placebo-controlled, observer-blind, interventional, dose-finding, study to evaluate the safety, tolerability, immunogenicity and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals. In addition, the MAH took the opportunity to implement minor editorial changes in section 6.3 of the SmPC and section 5 of the PIL of Comirnaty 30 micrograms/dose dispersion for injection."	See B.5.2
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0104 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update immunogenicity, safety and efficacy information regarding heterologous vaccination (both in the primary series and for booster vaccinations)	

based on published literature data; the Package Leaflet is updated accordingly.
In addition, the MAH took the opportunity to make minor editorial changes throughout the product information."

Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0053

MSD Vaccins, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to update long-term effectiveness and immunogenicity data following the final results of the Gardasil 9 long-term follow-up (LTFU) study V503-002-20 listed as a category 3 study in the RMP. In addition, the applicant took the opportunity to make some minor editorial changes (spacings) and included the updated long-term follow-up data received for the qHPV vaccine following V501-167 extension study. The Package Leaflet is updated accordingly."

Glivec - imatinib - EMEA/H/C/000406/II/0129

Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa, "C.I.4,
Update of section 4.8 of the SmPC in order to add pemphigus with frequency rare and osteonecrosis with frequency uncommon to the list of adverse drug reactions based on an analysis of pre-clinical data, scientific literature, clinical trial datasets, Novartis pharmacovigilance database, EVDAS and other safety databases. The Package Leaflet is updated accordingly. The MAH is also taking the opportunity to align section 4 of the PL with the already approved ADR section of the SmPC as a number of ADRs is not reflected accurately."

Imfinzi - durvalumab - EMEA/H/C/004771/II/0039/G

AstraZeneca AB, Rapporteur: Sinan B. Sarac, "Update of section 4.2 of the SmPC in order to update the recommendation for dose modification for the adverse reaction myocarditis based on NCCN guideline recommendations (2021) and findings in a Global Patient Safety Database, and update of section 4.8 of the SmPC to further clarify the medical concept of the adverse reaction encephalitis, by revising the footnote of the ADR

table for encephalitis."

Imfinzi - durvalumab - EMEA/H/C/004771/II/0040

AstraZeneca AB, Rapporteur: Sinan B. Sarac, "Update of section 5.1 of the SmPC in order to update efficacy data based on the results of the 5-year follow-up analysis of the PACIFIC study (a randomised, double blind, placebo controlled, multicentre study in patients with locally advanced, unresectable NSCLC). In addition, the MAH took the opportunity to include analyses of the exploratory endpoints to meet the commitment (recommendation) to submit exploratory analyses from the PACIFIC study."

MenQuadfi - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/005084/II/0013

Sanofi Pasteur, Rapporteur: Andrea Laslop, "Update of section 5.1 of the SmPC in order to add data on the immunogenicity of serogroup C based on the final results from study MEQ00065; this is a study to compare the immunogenicity and safety of serogroup C of a single dose of Menquadfi to Nimenrix or NeisVac in meningococcal naïve toddlers 12-23 months of age."

Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0060

GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus, "Submission of the final study report from study Malaria-073, a Phase III, randomized, open-label, controlled and multicentre study that addressed two safety concerns listed in the RMP: immunogenicity when coadministered with yellow fever and measles vaccines, and cross-immunisation against human catalase. The submission of the study addresses MEA 004."

Orphacol - cholic acid - EMEA/H/C/001250/II/0044, Orphan

Laboratoires CTRS, Rapporteur: Anastasia Mountaki, "Update of sections 4.3 and 4.5 of the SmPC in order to extend the currently existing contra-indication with phenobarbital in order to include primidone based on scientific literature. The Package Leaflet is updated accordingly.

In addition, the MAH is also taking this opportunity to submit a combined SmPC for both dosages, 50 mg and 250 mg and to introduce editorial changes and update the contact details of the local representatives in the Package Leaflet.”	
Orphacol - cholic acid - EMEA/H/C/001250/II/0045, Orphan Laboratoires CTRS, Rapporteur: Anastasia Mountaki, “Update of section 4.5 of the SmPC in order update the existing information regarding concomitant use of cholic acid (the active substance of Orphacol) and ursodeoxycholic acid based on scientific literature. The Package Leaflet is updated accordingly.”	
QINLOCK - ripretinib - EMEA/H/C/005614/II/0002, Orphan Deciphera Pharmaceuticals (Netherlands) B.V., Rapporteur: Filip Josephson, “Submission of the final report from study XT218029 (DP-4851: ABC Transporter Substrate Potential in Cells). This submission fulfils the PAM commitment “New in vitro experiment to study whether ripretinib is a substrate of BCRP, which follows the design outlined in appendix 3 of the DDI GL - October 2021-REC.”	
Repatha - evolocumab - EMEA/H/C/003766/II/0058 Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, “C.I.4 Update to section 5.1 of the SmPC following the results of interventional study 20160184. It was a double-blind, placebo-controlled, randomized study evaluating the effect of evolocumab on coronary atherosclerotic plaques as assessed by optical coherence tomography (OCT) following 50 weeks of treatment in subjects with non-ST-elevation acute coronary syndrome (NSTE-ACS) who take maximally tolerated statin therapy.”	
Roclanda - latanoprost / netarsudil - EMEA/H/C/005107/II/0002 Aerie Pharmaceuticals Ireland Limited, Rapporteur: Jayne Crowe, “C.I.4, Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study PG324-CS303; this is a prospective, double-masked, randomized,	

multicentre, active-controlled, parallel-group, 6-month study assessing the safety and ocular hypotensive efficacy of Roclanda compared to bimatoprost + timolol in subjects with elevated intraocular pressure that was insufficiently controlled and/or deemed to be in need of combination IOP-lowering therapy. The Package Leaflet is updated accordingly."

Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0047

Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, "Update of section 5.1 of the SmPC in order to introduce data on the immunogenicity of Spikevax against the B.1.617.2 (Delta) variant in adults and children, based on cross-neutralisation data from studies mRNA-1273-P301 (an ongoing Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older - NCT04470427), mRNA-1273-P201B (Part B of an ongoing Phase 2a, Randomized, Observer-Blind, Placebo-Controlled, Dose-Confirmation Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older - NCT04405076), and mRNA-1273-P204 (an ongoing Phase 2/3, 2-part, open-label, dose-escalation, age de-escalation and subsequent randomized, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of mRNA-1273 in healthy children - NCT04796896)."

Tivicay - dolutegravir - EMEA/H/C/002753/II/0077

ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Following the recommendation (REC) requested during the procedure EMA/H/C/2753/X/58G, the MAH submits the manuscript of the ODYSSEY study which contains efficacy and long-term safety results to 96 weeks for Tivicay tablets. This study an open-label, multicentre, randomized (1:1), non-inferiority, Phase II/III, 96-week, 2-arm clinical trial to compare the efficacy and toxicity of dolutrgravir (DTG) plus 2 NRTIs vs. standard of

care in HIV infected children aged less than 18 years who are starting first-line ART (ODYSSEY A) or switching to second-line ART (ODYSSEY B). Based on the results no amendments to the product information for DTG (Tivicay) are considered warranted and therefore, no updated SmPC is provided as part of this application.”	
Trogarzo - ibalizumab - EMEA/H/C/004961/II/0018 Theratechnologies Europe Limited, Rapporteur: Johann Lodewijk Hillege, “Update of section 5.1 of the SmPC in order to add additional efficacy data based on results from study TMB-311, a multicentre, expanded access phase 3 study providing post-hoc long-term data on patients from study TMB-301.”	
Trumenba - meningococcal group b vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0037 Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.8 and 5.1 of the SmPC in order to include immunopersistence and booster data based on final results from study B1971035 listed as a part of the paediatric investigation plan; this is a phase 2, randomized, controlled, observer-blinded study conducted to describe the immunogenicity, safety, and tolerability of Bivalent rLP2086 when administered to healthy toddlers aged 12 to <18 Months or 18 to <24 months, and the safety and immunogenicity of a booster dose of Bivalent rLP2086.”	
Xarelto - rivaroxaban - EMEA/H/C/000944/II/0093 Bayer AG, Rapporteur: Kristina Dunder, “Update of section 5.1 and subsequent changes in sections 4.2 and 4.8 based on final results from study 18226 (UNIVERSE); this is a prospective, open-label, active controlled, multicentre, 2-part study, designed to evaluate the single- and multiple-dose pharmacokinetic properties of rivaroxaban (Part A), and to evaluate the safety and efficacy of rivaroxaban when used for thromboprophylaxis for 12 months compared with acetylsalicylic acid (Part B) in children 2 to 8 years of age with single ventricle physiology who had the Fontan procedure. In addition, the MAH took the opportunity to	

introduce editorial changes to sections 4.8 and 4.9 of the SmPC."

Xtandi - enzalutamide - EMEA/H/C/002639/II/0058
Astellas Pharma Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 4.5 in order to add information regarding drug-drug interaction based on final results from study 9785-CL-0018 - A Phase 1 Open-label Study to Evaluate the Effect of Multiple Doses of Enzalutamide on the Pharmacokinetics of Substrates of P-glycoprotein (Digoxin) and Breast Cancer Resistant Protein (Rosuvastatin) in Male Subjects with Prostate Cancer. Additionally, MAH has taken the opportunity to make an update to the information about the excipients in section 4.4 of the SmPC, to introduce editorial changes in the SmPC and in the Package Leaflet, and to update the list of local representatives in the Package Leaflet."

WS2224
Eucreas-EMEA/H/C/000807/WS2224/0094
Galvus-EMEA/H/C/000771/WS2224/0075
Icandra-EMEA/H/C/001050/WS2224/0097
Jalra-EMEA/H/C/001048/WS2224/0077
Xiliarx-EMEA/H/C/001051/WS2224/0075
Zomarist-EMEA/H/C/001049/WS2224/0096
Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to update the list of ADRs and update the ADR table in line with the EC SmPC guideline (2009). The Package Leaflet is updated accordingly."

B.6.10. CHMP-PRAC assessed procedures

ADCETRIS - brentuximab vedotin - EMEA/H/C/002455/II/0099, Orphan
Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.8 and 5.1 of the SmPC, based on final results from study C25006, a multicentre open-label, phase 4 study of 50 patients with r/r sALCL undertaken to further evaluate the efficacy and

safety of brentuximab vedotin as a single agent in adult patients who had previously received at least 1 multiagent chemotherapy regimen. This study is listed as an interventional cat 2 PASS in the RMP (SOB 010). In addition, the MAH took the opportunity to delete SOB 010 from the annex II and to delete the mention of conditional approval from annex II and the package leaflet. The RMP version 16.1 has also been submitted."

Afstyla - lonoctocog alfa - EMEA/H/C/004075/II/0042

CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sonja Hrabcik, "Update of section 5.1 of the SmPC in order to update efficacy and safety information based on final results from study 3001 listed as a category 3 study in the RMP; this is an open label, multicentre extension study to assess the Safety and Efficacy of Afstyla in subjects with severe Haemophilia A. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 6.0 has also been submitted."

ASPAVELI - pegcetacoplan - EMEA/H/C/005553/II/0002, Orphan

Swedish Orphan Biovitrum AB (publ), Rapporteur: Alexandre Moreau, PRAC Rapporteur: Kimmo Jaakkola, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC based on final results from study APL2-302 (Pegasus) listed as a category 3 study in the RMP; this is a global, Phase 3, prospective, randomised, multicentre, open-label, active-comparator–controlled study in 80 subjects. The objective was to confirm treatment efficacy and safety of pegcetacoplan monotherapy for the treatment of Paroxysmal Nocturnal Hemoglobinuria (PNH). The submission of this study addresses MEA 001.The Package Leaflet is updated accordingly. The RMP version 0.5 has also been submitted."

Dexdor - dexmedetomidine - EMEA/H/C/002268/II/0035

Orion Corporation, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.4 of the SmPC in order to add a new warning on Mortality in ICU patients ≤ 65 years old, based on results from study SPICE III

(randomised controlled trial) and following the assessment of the post-authorisation measure LEG 16.4. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.
The RMP version 9, a proposed DHPC and communication plan have also been submitted."

Esperoct - turoctocog alfa pegol - EMEA/H/C/004883/II/0010, Orphan
Novo Nordisk A/S, Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski,
"Update of sections 4.4 and 4.8 of the SmPC to add a new warning and update the list of ADRs based on a validated safety signal concerning a lack of factor VIII activity in patients switching from a similar factor VIII product to Esperoct. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and to align it with the latest QRD template version 10.2. The RMP version 2.0 has also been submitted."

Fintepla - fenfluramine - EMEA/H/C/003933/II/0010/G, Orphan
Zogenix ROI Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber,
"- Update of section 5.3 of the SmPC in order to update the non-clinical information following the study 20147822 (A 6-month Carcinogenicity Study of Fenfluramine Hydrochloride in Mice).
- Update of section 5.3 of the in order to update the non-clinical information following the study 8001993 (A 2-year Oral Gavage Carcinogenicity Study of Fenfluramine Hydrochloride in Rats).
- Submission of the final report of study 20147821 (Dose range finding study for 20147822).
- Submission of the final report of study 20166554 (Dose range finding study for 20147822).
- Submission of the final report of study 2021006-Z001-01 (In-vitro Evaluation of Potential Melanin Binding by Fenfluramine and Norfenfluramine).
An RMP version 3.1 has also been submitted."

Fintepla - fenfluramine - EMEA/H/C/003933/II/0011/G, Orphan
Zogenix ROI Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber,

"- Update of sections 4.2 and 5.2 of the SmPC to include the relevant information regarding patients with renal impairment following the study 1902 (Pharmacokinetic study of fenfluramine hydrochloride in subjects with varying degrees of impaired and normal renal function). - Update of sections 4.4 and 4.5 of the SmPC in order to reflect the relevant information on CYP1A2 or CYP2B6 or CYP2D6 inducers following the study 1904 (Pharmacokinetic drug-drug interaction study of fenfluramine hydrochloride with and without fluvoxamine (CYP1A2 inhibitor), paroxetine (CYP2D6 inhibitor) and rifampin (CYP2B6 inducer) in healthy subjects). An RMP version 2.2 has also been submitted."	
Myalepta - metreleptin - EMEA/H/C/004218/II/0025, Orphan Amryt Pharmaceuticals DAC, Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Adam Przybylkowski, "Submission of an updated RPM version 2.1. The applicant is proposing an alternative study to the currently agreed protocol for Specific Obligation SOB002 (AEGR-734-002) due to the challenges of implementing the existing protocol. Annex II is being updated accordingly. MAH took the opportunity to update the RMP in line with the outcome of previous procedures and to include editorial changes."	
Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0056 Orexigen Therapeutics Ireland Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, "Submission of updated study design and protocol synopsis for CVOT-2 study, a category 1 study listed in Annex II.D (ANX/001.7) undertaken to assess the effect of naltrexone extended release (ER) / bupropion ER on the occurrence of major adverse cardiovascular events (MACE), as requested in the CHMP AR for ANX/001.6. The Annex II and the RMP version 13 are updated accordingly."	
Oxlumo - lumasiran - EMEA/H/C/005040/II/0008, Orphan Alnylam Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga,	

"Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to clarify administration instructions, remove an existing warning on metabolic acidosis in patients with severe or end stage renal impairment, update the description of adverse reactions injection site reactions, abdominal pain and immunogenicity, update efficacy, pharmacokinetic information based on interim results from a category 3 study in the RMP ILLUMINATE-C (ALN-GO1-005): A single arm study to evaluate efficacy, safety, pharmacokinetics, and pharmacodynamics of lumasiran in patients with advanced primary hyperoxaluria type 1 (PH1) and, in addition, based on available long-term efficacy and safety data from ongoing phase 3 studies ALN-GO1-003 in PH1 patients >6 years old and ALN-GO1-004 in PH1 patients <6 years old, and open-label extension study ALN-GO1-002. The Package Leaflet is updated accordingly. The RMP version 1.1 has also been submitted."

Pemazyre - pemigatinib - EMEA/H/C/005266/II/0005, Orphan

Incyte Biosciences Distribution B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4, 4.8 and 5.1 of the SmPC based on the final results from study INCB054828 (FIGHT-202) listed as a specific obligation in the Annex II (SOB/002); this is a phase 2 study investigating the efficacy and safety of pemigatinib in adults with advanced/metastatic or surgically unresectable cholangiocarcinoma including FGFR2 translocations who failed previous therapy. The Annex II has been updated accordingly. RMP version 2.0 has also been submitted."

Prolia - denosumab - EMEA/H/C/001120/II/0093

Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.2 and 4.4 of the SmPC in order to change the posology recommendation for paediatric population and add a new warning on hypercalcaemia in paediatric patients with osteogenesis imperfecta following an urgent safety measure regarding the risk of hypercalcaemia reported very commonly in ongoing clinical trials in paediatric patients with

osteogenesis imperfecta (OI) treated with denosumab; the Package Leaflet is updated accordingly. The RMP version 29.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to implement minor editorial changes in the Labelling."	
Raxone - idebenone - EMEA/H/C/003834/II/0031, Orphan Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli, "Update of sections 4.2, 4.4, 4.9 and 5.1 of the SmPC based on the final study report from the PAROS study SNT-IV-003 (SOB003; listed as a cat 2 study in the RMP): "A non-interventional study of clinical experience in patients prescribed Raxone for the treatment of Leber's Hereditary Optic Neuropathy (LHON)". Annex II is updated in accordance. A revised RMP version 1.14 was also submitted."	
RINVOQ - upadacitinib - EMEA/H/C/004760/II/0015/G AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce, "Grouping of 2 variations: C.I.4 - Update of sections 4.8 to add neutropenia and 5.1 of the SmPC in order to update efficacy information of Rinvoq in Ankylosing Spondylitis (AS) patients who are biologic DMARD inadequate responders (bDMARD-IR) based on interim results from study M19-944 Study 1; this is a Phase 3, randomized, double-blind, study evaluating the long-term safety, tolerability, and efficacy of upadacitinib 15 mg QD in subjects with active AS who have an inadequate response (IR) to bDMARD. C.I.4 - Update of section 5.1 of the SmPC in order to include long term (through week 104) data in AS patients who are naïve to previous treatment with a bDMARD based on interim results from study M16-098; this is a Multicentre, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Safety and Efficacy of Upadacitinib in Subjects with Active Ankylosing Spondylitis;	

The RMP version 7.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes in the product information."	
Rydapt - midostaurin - EMEA/H/C/004095/II/0024, Orphan Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "C.I.11.b Submission of the final report from study CPKC412E2301 listed as an obligation in the Annex II of the Product Information. This is a Phase III study to investigate the efficacy in elderly patients. A final pharmacogenomic report is also provided to fulfil MEA004. The Annex II and the RMP (submitted version 7.0) are updated accordingly."	
Ryeqo - relugolix / estradiol / norethisterone acetate - EMEA/H/C/005267/II/0006 Gedeon Richter Plc., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Martin Huber, "Submission of the final report from study MVT-601-035 listed as a category 3 study in the RMP. This is an international phase III double-blind, placebo-controlled, randomised withdrawal study of relugolix co-administered with estradiol and norethisterone in women with heavy menstrual bleeding associated with uterine fibroids to evaluate the efficacy and safety of long-term use of this medicinal product. The RMP version 1.0 has also been submitted."	
WAYLIVRA - volanesorsen - EMEA/H/C/004538/II/0017/G, Orphan Akcea Therapeutics Ireland Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber, "C.I.4: Update of sections 4.8 and 5.1 of the SmPC based on the final results from study (ISIS 304801 CS7), a multicentre open label extension study of Volanesorsen administered subcutaneously to patients with Familial Chylomicronemia Syndrome. The Package Leaflet has been updated accordingly. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI in order to align with the QRD template and to introduce minor linguistic update to Annex III of the	

product information to support product launch.
C.I.11b. for RMP: Submission of an updated RMP version 2.1 based on the clinical study report addendum: A randomized, double blind, placebo-controlled Phase 3 study of ISIS 304801 administered subcutaneously to patients with Familial Chylomicronemia Syndrome (ISIS 304801 CS6 (APPROACH).
C.I.11b. for RMP: Submission of an updated RMP version 2.1 in order to update section V.2 Additional Risk Minimisation Measures in the RMP to reflect a change in the distribution methodology of the educational materials (from a centralised model to a localised model of distribution) and to clarify what is meant by the prescriber kit.
C.I.13: Submission of the final report from study ISIS 304801 (CS17). This is a Phase 2/3 double blind, randomized, placebo-controlled study, with an open label extension of ISIS 304801 administered subcutaneously to patients with familial partial lipodystrophy. The RMP version 2.1 has also been submitted."

Xtandi - enzalutamide - EMEA/H/C/002639/II/0057

Astellas Pharma Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "C.I.4
Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to reflect the updated safety and efficacy data from the final analysis of the 9785-CCL-0335 (ARCHES) study, a phase 3 randomized, double-blind, placebo-controlled study that evaluated the safety and efficacy of enzalutamide plus androgen deprivation therapy (ADT) vs placebo plus ADT in men with mHSPC; the Package Leaflet is updated accordingly. The RMP version 17.0 has also been submitted. In addition, the MAH took the opportunity to make minor editorial changes to section 4.8 and section 5.1 of the SmPC."

B.6.11. PRAC assessed procedures

PRAC Led

Cyramza - ramucirumab - EMEA/H/C/002829/II/0047

Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison:

Jan Mueller-Berghaus, "Submission of the final report from study I4T-MC-JVDD listed as a category 3 study in the RMP for Cyramza, entitled 'Safety and Effectiveness of Ramucirumab in Patients with Advanced Gastric Cancer in the European Union and North America: A Prospective Observational Registry (Study I4T-MC-JVDD)' (Related to MEA 001.1). The RMP version 10.1 has also been submitted. "

PRAC Led

Inflectra - infliximab -

EMEA/H/C/002778/II/0105

Pfizer Europe MA EEIG, Duplicate, Duplicate of Remsima, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of the final report from study CT-P13 4.2; An Observational, Prospective Cohort Study to Evaluate Safety and Efficacy of Inflectra in Patients with Rheumatoid Arthritis (study report excluding the joint analysis of patients in the PERSIST study). The submission of the study report addresses MEA 007.6."

PRAC Led

Kuvan - sapropterin -

EMEA/H/C/000943/II/0073

BioMarin International Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Submission of the final report from study BMN 162-501 KAMPER (formerly EMR700773-001) listed as a category 3 study in the RMP. This is an observational drug registry to assess the long-term safety in subjects treated with Kuvan. The submission of this study addresses the PAM MEA 020. The RMP version 15.1 has also been submitted."

PRAC Led

Latuda - lurasidone -

EMEA/H/C/002713/II/0037

Aziende Chimiche Riunite Angelini Francesco A.C.R.A.F. S.p.A., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "Submission of an updated RMP version 9.0, based on the implementation of the PASS outcome (EMEA/H/C/002713/II/0033), to remove from the list of safety concerns of important identified

risks and important potential risks; and to discontinue the use of targeted adverse event follow-up questionnaire for angioedema."

PRAC Led

Moventig - naloxegol -

EMEA/H/C/002810/II/0038

Kyowa Kirin Holdings B.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Submission of an updated RMP version 7.2 proposing the cancellation of the cat. 3 study (D3820R00009: An Observational Drug Utilisation PASS of Moventig in selected European populations), following the assessment of MEA 006.11"

PRAC Led

Praluent - alirocumab -

EMEA/H/C/003882/II/0068

sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC, based on the final results from category 3 study OBS14697; a non-interventional, retrospective drug utilisation study that was designed to assess in Europe the effectiveness of the dosing recommendation and to describe patterns of alirocumab utilization in real world clinical practice. In addition, the MAH took the opportunity to implement editorial changes in SmPC and package leaflet. The submission of the study report addresses the Post-Authorisation Measure MEA/FSR 019.8."

PRAC Led

Remsima - infliximab -

EMEA/H/C/002576/II/0111

Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of the final report from study CT-P13 4.2; An Observational, Prospective Cohort Study to Evaluate Safety and Efficacy of Remsima in Patients with Rheumatoid Arthritis (study report excluding the joint analysis of patients in the PERSIST study). The submission of the study report addresses MEA 007.6."

PRAC Led

XALKORI - crizotinib -

EMEA/H/C/002489/II/0075
Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final report for non-interventional PASS cat 3 study A8081062, a descriptive study of potential sight threatening event and severe visual loss following exposure to crizotinib (related to MEA 024)."

PRAC Led
Zepatier - elbasvir / grazoprevir - EMEA/H/C/004126/II/0033
Merck Sharp & Dohme B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "Submission of the final report from study B20-146 listed as a category 3 study in the RMP. This is a non-imposed joint post-authorisation safety study to evaluate the risk of de novo hepatocellular carcinoma in patients with compensated cirrhosis treated with direct-acting antivirals for chronic hepatitis C (HCC De Novo PASS)."

PRAC Led
WS2210
Dovato-EMEA/H/C/004909/WS2210/0028
Juluca-EMEA/H/C/004427/WS2210/0041
Tivicay-EMEA/H/C/002753/WS2210/0076
Triumeq-EMEA/H/C/002754/WS2210/0100
ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Ingrid Wang, "Following the finalisation of procedure EMEA/H/C/WS1810 concerning submission of EUROSIDA (category 3 PASS) study, this Type II work-sharing variation is now proposed to address the removal of 3 identified risks (Dolutegravir Hypersensitivity reactions, Hepatobiliary reactions and Serious rash) from all 4 dolutegravir-containing product EU-RMPs; Tivicay (dolutegravir), Triumeq (dolutegravir/abacavir/lamivudine), Dovato (dolutegravir/lamivudine) and Juluca (dolutegravir/rilpivirine) - i.e. deletion of safety concerns.
In addition, the MAH takes the opportunity to propose a harmonisation of the risks across all 4 dolutegravir-containing product EU-RMPs and

other minor updates (including study details and epidemiology data), which the MAH considers can be included as part of an RMP update without the need for an additional variation scope as per EMA post-authorisation guidelines."

PRAC Led

WS2212

Effentora-

EMEA/H/C/000833/WS2212/0060

Teva B.V., Lead Rapporteur: Janet Koenig, Lead PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of an updated RMP version 5.1 in order to reformat the RMP according to the revised guidance on GVP Module V (revision 2) and to implement PRAC comments arising from previous assessments as follows:
- Revision of the list of safety concerns;
- Implementation of key messages in educational materials adopted by PRAC for Instanyl;
- Revision of Annex 6 to include verbatim the text adopted by PRAC for Instanyl as presented in Annex 2 of the PRAC PSUSA AR;
- Revision of the use of digital access to educational material;
- Explanation of the role of the Health Products Regulatory Authority (HPRA)'s CAPA being no longer found to be a trigger of the current RMP update.
The 'additional risk minimisation measures' in the Annex II of the product information have been updated accordingly."

PRAC Led

WS2214

Duloxetine Mylan-

EMEA/H/C/003981/WS2214/0029

Mylan Pharmaceuticals Limited, Generic, Generic of Cymbalta, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "To update the RMP in order to align with the originator.
The MAH has taken the opportunity to amend the RMP template GVP Module V Rev.2, where required, and to achieve one RMP covering multiple different marketing authorisations procedures containing the same active substance for which Mylan has an approved

RMP.
The RMP is also updated with the results of a follow-up up questionnaire pertaining to suicidality as recommended in the Renewal EMEA/H/C/003981/R/0021."

PRAC Led
WS2216
Exviera-EMEA/H/C/003837/WS2216/0052
Maviret-
EMEA/H/C/004430/WS2216/0049
Viekirax-
EMEA/H/C/003839/WS2216/0064
AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "Submission of the final report from study B20-146 listed as a category 3 study in the RMP. This is a non-imposed joint post-authorisation safety study to evaluate the risk of de novo hepatocellular carcinoma in patients with compensated cirrhosis treated with direct-acting antivirals for chronic hepatitis C (HCC De Novo PASS)."

PRAC Led
WS2222
Epclusa-
EMEA/H/C/004210/WS2222/0064
Harvoni-
EMEA/H/C/003850/WS2222/0104
Sovaldi-EMEA/H/C/002798/WS2222/0077
Vosevi-EMEA/H/C/004350/WS2222/0054
Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "Submission of the final report from study B20-146 listed as a category 3 study in the RMP. This is a non-imposed joint post-authorisation safety study to evaluate the risk of de novo hepatocellular carcinoma in patients with compensated cirrhosis treated with direct-acting antivirals for chronic hepatitis C (HCC De Novo PASS)."

B.6.12. CHMP-CAT assessed procedures

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0048, ATMP
Amgen Europe B.V., Rapporteur: Heli Suila,

CHMP Coordinator: Johanna Lähteenvuo, , "Update of section 4.4 of the SmPC in order to add a new warning about the potential risk of hepatic hemorrhage with the transcutaneous intrahepatic route of administration of talimogene laherparepvec. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."
Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0049/G, Orphan, ATMP Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang
Zolgensma - onasemnogene abeparvovec - EMEA/H/C/004750/II/0024, Orphan, ATMP Novartis Gene Therapies EU LimitedRapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege
WS2197 **Tecartus-** **EMEA/H/C/005102/WS2197/0017** **Yescarta-** **EMEA/H/C/004480/WS2197/0047** Kite Pharma EU B.V., Lead Rapporteur: Jan Mueller-Berghaus, , CHMP Coordinator: Jan Mueller-Berghaus

B.6.13. CHMP-PRAC-CAT assessed procedures

Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - EMEA/H/C/003854/II/0033, Orphan, ATMP Orchard Therapeutics (Netherlands) BV, Rapporteur: Sol Ruiz, CHMP Coordinator: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst, "Submission of the final report from study STRIM-001 "Evaluation of referring healthcare providers' and parents'/carers' understanding of specific risks associated with Strimvelis treatment" listed as a category 3 study in the RMP. The RMP version 6.1 has also been submitted."

B.6.14. PRAC assessed ATMP procedures

B.6.15. Unclassified procedures and work-sharing procedures of type I variations

WS2168 **Lyrica-EMEA/H/C/000546/WS2168/0114** **Pregabalin Pfizer-** **EMEA/H/C/003880/WS2168/0043** Upjohn EESV, Lead Rapporteur: Johann Lodewijk Hillege, "To update SmPC sections 4.4 and 4.8 to reflect new data on suicidal ideation following the review of the data provided in LEG 007 and 054. The package leaflet has been updated accordingly."
WS2213/G **Aprovel-** **EMEA/H/C/000141/WS2213/0189/G** **Karvea-** **EMEA/H/C/000142/WS2213/0191/G** sanofi-aventis groupe, Lead Rapporteur: Maria Concepcion Prieto Yerro
WS2220/G **Cymbalta-** **EMEA/H/C/000572/WS2220/0088/G** **Duloxetine Lilly-** **EMEA/H/C/004000/WS2220/0025/G** **Yentreve-** **EMEA/H/C/000545/WS2220/0073/G** Eli Lilly Nederland B.V., Duplicate, Duplicate of Ariclaim (SRD), Yentreve, Lead Rapporteur: Maria Concepcion Prieto Yerro
WS2221/G **Eucreas-** **EMEA/H/C/000807/WS2221/0093/G** **Galvus-** **EMEA/H/C/000771/WS2221/0074/G** **Icandra-** **EMEA/H/C/001050/WS2221/0096/G** **Jalra-** **EMEA/H/C/001048/WS2221/0076/G** **Xiliarx-** **EMEA/H/C/001051/WS2221/0074/G** **Zomarist-** **EMEA/H/C/001049/WS2221/0095/G** Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder

WS2228
Eucreas-
EMEA/H/C/000807/WS2228/0095
Icandra-
EMEA/H/C/001050/WS2228/0098
Zomarist-
EMEA/H/C/001049/WS2228/0097
Novartis Europharm Limited, Lead Rapporteur:
Kristina Dunder

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. 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.1.1. List of procedures concluding at 24-27 January 2022 CHMP plenary:

G.1.2. List of procedures starting in January 2022 for February 2022 CHMP adoption of outcomes

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