23 November 2022
EMA/CHMP/851047/2022
Human Medicines Division

Committee for medicinal products for human use (CHMP)

Minutes for the meeting on 10-13 October 2022

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

Disclaimers

Some of the information contained in this set of minutes 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, these minutes are a working document primarily designed for CHMP members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the minutes 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

The Chairperson opened the meeting by welcoming all participants. Due to the current coronavirus (COVID-19) outbreak, and the associated EMA Business Continuity Plan (BCP), the meeting was held remotely.

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced the restricted involvement of some meeting participants in upcoming discussions as included in the pre-meeting list of participants and restrictions. See October 2022 CHMP minutes for the list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session held 10 – 13 October 2022.

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 17 or more members were present remotely). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

1.2. Adoption of agenda

CHMP agenda for 10-13 October 2022.

The CHMP adopted the agenda.

1.3. Adoption of the minutes

CHMP minutes for 12-15 September 2022.

Minutes from Preparatory and Organisational Matters (PROM) meeting held on 03 October 2022.

The CHMP adopted the CHMP minutes for 12-15 September 2022.

The CHMP adopted the minutes from the PROM meeting held on 03 October 2022.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. iodine (131I) omburtamab - Orphan - EMEA/H/C/005499

Y-Mabs Therapeutics A/S; treatment of neuroblastoma

Scope: Possible oral explanation

Action: Possible oral explanation to be held on 11 October 2022 at 14:00

List of Outstanding Issues adopted on 23.06.2022. List of Questions adopted on 16.09.2021.

The CHMP agreed that an oral explanation was not needed at this time.

See 3.2

2.1.2. Pluvicto - lutetium (177Lu) vipivotide tetraxetan - EMEA/H/C/005483

Novartis Europharm Limited; treatment of prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC)

Scope: Oral explanation

Action: Oral explanation to be held on 12 October 2022 at 16:00

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

List of Outstanding Issues adopted on 21.07.2022. List of Questions adopted on 24.02.2022.

The CHMP agreed that an oral explanation was not needed at this time.

See 3.1

2.1.3. Spevigo - spesolimab - EMEA/H/C/005874

Boehringer Ingelheim International GmbH; treatment of flares in adult patients with generalised pustular psoriasis

Scope: Oral explanation

Action: Oral explanation to be held on 11 October 2022 at 16:00.

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

List of Outstanding Issues adopted on 21.07.2022. List of Questions adopted on 24.02.2022.

An oral explanation was held on 11 October 2022. The presentation by the applicant focused on the clinical data in support of the application.

See 3.1

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

2.3.1. Libtayo - cemiplimab - EMEA/H/C/004844/II/0026

Regeneron Ireland Designated Activity Company (DAC)

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

Scope: "Extension of indication to include monotherapy treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy for Libtayo; sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3 of the RMP has also been submitted."

Oral explanation

Action: Oral explanation to be held on 12 October 2022 at 11:00

Request for Supplementary Information adopted on 23.06.2022, 24.02.2022.

An oral explanation was held on 12 October 2022. The presentation by the applicant focused on the clinical data in support of the application.

See 5.1

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. Dengue quadrivalent vaccine (Art.58) - dengue tetravalent vaccine (live, attenuated) - Article 58 - EMEA/H/W/005362

Takeda GmbH; prevention of dengue disease

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 23.06.2022, 11.11.2021. List of Questions adopted on 24.06.2021.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus recommending the adoption of the

scientific opinion for the above-mentioned medicinal product.

Furthermore, the CHMP considered Dengue virus serotype 1 (live, attenuated), TDV-2: Dengue virus serotype 2 (live, attenuated), TDV-3: Dengue virus serotype 3 (live, attenuated) and TDV-4: Dengue virus serotype 4 (live, attenuated) are new active substances, as claimed by the applicant.

The legal status was agreed as medicinal product subject to medical prescription.

The CHMP noted the letter of recommendation dated 11 October 2022.

The summary of opinion was circulated for information.

3.1.2. Dimethylfumarate Teva - dimethyl fumarate - EMEA/H/C/005963

TEVA GmbH; treatment of multiple sclerosis

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 21.07.2022, 22.04.2022. List of Questions adopted on 27.01.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

3.1.3. Ebvallo - tabelecleucel - PRIME - Orphan - ATMP - EMEA/H/C/004577

Atara Biotherapeutics Ireland Limited; treatment of Epstein-Barr virus positive post-transplant lymphoproliferative disease (EBV^+ PTLD)

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 09.09.2022. List of Questions adopted on 18.03.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

Based on the draft opinion prepared by the CAT, the Committee adopted a positive opinion recommending the granting of a marketing authorisation under exceptional circumstances by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that tabelecleucel is a new active substance, as claimed by the applicant.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

3.1.4. Eladynos - abaloparatide - EMEA/H/C/005928

Radius Health Ireland Ltd; treatment of osteoporosis

Scope: Opinion

Action: For adoption

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

List of Questions adopted on 24.03.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus, together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that abaloparatide is a new active substance, as claimed by the applicant.

The legal status was agreed as medicinal product subject to medical prescription.

The summary of opinion was circulated for information.

3.1.5. Livmarli - maralixibat - Orphan - EMEA/H/C/005857

Mirum Pharmaceuticals International B.V.; Treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) 2 months of age and older.

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 15.09.2022, 23.06.2022. List of Questions adopted on 27.01.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation under exceptional circumstances by consensus, together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that maralixibat is a new active substance, as claimed by the applicant.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The CHMP noted the letter of recommendation dated 13 October 2022.

The summary of opinion was circulated for information.

3.1.6. Locametz - gozetotide - EMEA/H/C/005488

Novartis Europharm Limited; indicated for the identification of prostate-specific membrane antigen (PSMA)-positive lesions after radiolabelling with gallium-68

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 21.07.2022. List of Questions adopted on 24.02.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (28 positive out of 29 votes) together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that gozetotide is a new active substance, as claimed by the applicant.

The divergent position (Alexandre Moreau) was appended to the opinion.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

3.1.7. Pemetrexed Baxter - pemetrexed - EMEA/H/C/005848

Baxter Holding B.V.; treatment of malignant pleural mesothelioma and non-small cell lung cancer

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 15.09.2022, 19.05.2022. List of Questions adopted on 16.12.2021.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The CHMP noted the letter of recommendation dated 07 October 2022.

The summary of opinion was circulated for information.

3.1.8. Plerixafor Accord - plerixafor - EMEA/H/C/005943

Accord Healthcare S.L.U.; treatment of lymphoma and multiple myeloma

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 21.07.2022. List of Questions adopted on 24.02.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

3.1.9. Pluvicto - lutetium (177Lu) vipivotide tetraxetan - EMEA/H/C/005483

Novartis Europharm Limited; treatment of prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC)

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 21.07.2022. List of Questions adopted on 24.02.2022.

See 2.1

The CHMP agreed that an oral explanation was not needed at this time.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that lutetium (177Lu) vipivotide tetraxetan is a new active substance, as claimed by the applicant.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The CHMP noted the letter of recommendation dated 12 October 2022.

The summary of opinion was circulated for information.

3.1.10. Qdenga - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/005155

Takeda GmbH; prevention of dengue disease

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 23.06.2022, 11.11.2021. List of Questions adopted on 24.06.2021.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered Dengue virus serotype 1 (live, attenuated), TDV-2: Dengue virus serotype 2 (live, attenuated), TDV-3: Dengue virus serotype 3 (live, attenuated) and TDV-4: Dengue virus serotype 4 (live, attenuated) are new active substances, as claimed by the applicant.

The legal status was agreed as medicinal product subject to medical prescription.

The summary of opinion was circulated for information.

3.1.11. Spevigo - spesolimab - EMEA/H/C/005874

Boehringer Ingelheim International GmbH; treatment of flares in adult patients with generalised pustular psoriasis

Scope: Opinion

Action: For adoption

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

List of Outstanding Issues adopted on 15.09.2022, 21.07.2022. List of Questions adopted on 24.02.2022.

See 2.1

An oral explanation was held on 11 October 2022. The presentation by the applicant focused on the clinical data in support of the application.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a conditional marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that spesolimab is a new active substance, as claimed by the applicant.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

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

3.2.1. dimethyl fumarate - EMEA/H/C/005950

treatment of multiple sclerosis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.04.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.2. pegfilgrastim - EMEA/H/C/005810

Treatment of neutropenia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 27.01.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.3. etranacogene dezaparvovec - PRIME - Orphan - ATMP - EMEA/H/C/004827

CSL Behring GmbH; treatment of adults with Haemophilia B

Scope: List of outstanding issues

Action: For information

List of Questions adopted on 15.07.2022.

The CHMP was updated on discussions at the CAT. The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee endorsed the list of outstanding issues with a specific timetable as adopted by the CAT.

3.2.4. iodine (131I) omburtamab - Orphan - EMEA/H/C/005499

Y-Mabs Therapeutics A/S; treatment of neuroblastoma

Scope: List of outstanding issues

Action: For adoption

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

16.09.2021.

See 2.1

The CHMP agreed that an oral explanation was not needed at this time.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a 2nd list of outstanding issues with a specific timetable.

3.2.5. 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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.04.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.6. paclitaxel - EMEA/H/C/005997

treatment of metastatic breast cancer

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 19.05.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues.

3.2.7. sodium thiosulfate - PUMA - EMEA/H/C/005130

for the prevention of ototoxicity induced by cisplatin (CIS) chemotherapy in patients 1 month to < 18 years of age with localized, non-metastatic, solid tumours.

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 16.12.2021, 24.06.2021. List of Questions adopted on 25.06.2020.

The Committee was reminded of the status of this application and its remaining outstanding

issues.

The Committee adopted a 3rd list of outstanding issues with a specific timetable.

3.2.8. ruxolitinib - EMEA/H/C/005843

treatment of non-segmental vitiligo

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 24.02.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues.

3.2.9. tolvaptan - EMEA/H/C/005961

treatment of hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.04.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

3.2.10. SARS-CoV-2 prefusion Spike delta TM protein, recombinant - EMEA/H/C/005754

Active immunisation to prevent COVID-19 caused by SARS-CoV-2, in individuals 18 years of age and older.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.06.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

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

3.3.1. aripiprazole - EMEA/H/C/005929

Maintenance treatment of schizophrenia

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

3.3.2. crisantaspase - EMEA/H/C/005917

Indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukaemia (ALL) and lymphoblastic lymphoma (LBL).

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

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

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

3.4.1. molnupiravir - EMEA/H/C/005789

Treatment of coronavirus disease 2019 (COVID-19)

Scope: Update on the status of the procedure

Action: For information

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

The CHMP noted the update on the procedure.

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

prevention of venous thromboembolic events

Scope: Letter by the applicant dated 26.09.2022 requesting an extension to the clock stop to respond to the list of questions adopted in June 2022.

Action: For adoption

List of Questions adopted on 23.06.2022.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted in June 2022.

3.4.3. dabigatran etexilate - EMEA/H/C/005639

prevention of venous thromboembolic events

Scope: Letter by the applicant dated 15.09.2022 requesting an extension to the clock stop to respond to the 3rd list of outstanding issues adopted in September 2022.

Action: For adoption

List of Outstanding Issues adopted on 15.09.2022, 23.06.2022, 24.02.2022. List of Questions adopted on 12.11.2020.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the 3rd list of outstanding issues adopted in September 2022.

3.4.4. ferumoxytol - EMEA/H/C/005974

intravenous treatment of iron deficiency anaemia (IDA)

Scope: Letter by the applicant dated 11.10.2022 requesting an extension to the clock stop to respond to the list of questions adopted in September 2022.

Action: For adoption

List of Questions adopted on 15.09.2022.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted in September 2022.

3.4.5. vadadustat - EMEA/H/C/005131

Treatment of anaemia

Scope: Request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted in September 2022.

Action: For information

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

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted in September 2022 at its PROM meeting held on 03.10.2022.

3.4.6. tislelizumab - Orphan - EMEA/H/C/005919

Novartis Europharm Limited; treatment of adult patients with unresectable, recurrent, locally advanced or metastatic oesophageal squamous cell carcinoma after prior chemotherapy

Scope: Letter by the applicant dated 23.09.2022 requesting an extension to the clock stop to respond to the list of questions adopted in July 2022.

Action: For adoption

List of Questions adopted on 21.07.2022.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted in July 2022.

3.4.7. tislelizumab - EMEA/H/C/005542

treatment of locally advanced or metastatic non-squamous non-small cell lung cancer in adults, treatment of locally advanced or metastatic squamous non-small cell lung cancer in adults, locally advanced or metastatic non-small cell lung cancer after prior chemotherapy in adults.

Scope: Letter by the applicant dated 23.09.2022 requesting an extension to the clock stop to respond to the list of questions adopted in July 2022.

Action: For adoption

List of Questions adopted on 21.07.2022.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted in July 2022.

3.4.8. mavacamten - EMEA/H/C/005457

treatment of symptomatic obstructive hypertrophic cardiomyopathy

Scope: Request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted in July 2022.

Action: For information

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

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted in July 2022 at its PROM meeting held on 03.10.2022.

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

No items

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. treprostinil diolamine - Orphan - EMEA/H/C/005990

Ferrer Internacional S.A.; Treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to delay disease progression and to improve exercise capacity.

The studies that established effectiveness included predominantly patients with WHO functional class II-III symptoms and aetiologies of idiopathic or heritable PAH or PAH associated with connective tissue disease (see section 5.1).

Scope: Withdrawal of marketing authorisation application

Action: For information

The CHMP noted the withdrawal of the marketing authorisation application.

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. Refixia - nonacog beta pegol - EMEA/H/C/004178/X/0027/G

Novo Nordisk A/S

Rapporteur: Andrea Laslop

Scope: "Extension application to introduce a new strength (3000 IU Powder and solvent for solution for injection). The extension application is grouped with a type II variation (B.II.d.1.e). Sections 1, 2, 5.3, 6.3, 6.6 and 8 of the SmPC, the Labelling and Package Leaflet are updated."

Action: For adoption

List of Questions adopted on 21.07.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

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

4.2.1. Adcirca - tadalafil - EMEA/H/C/001021/X/0035/G

Eli Lilly Nederland B.V.

Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maria del Pilar Rayon

Scope: "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."

Action: For adoption

List of Questions adopted on 19.05.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues, concerning clinical aspects.

The Committee adopted a list of outstanding issues with a specific timetable.

4.2.2. Ultomiris - ravulizumab - EMEA/H/C/004954/X/0027/G

Alexion Europe SAS

Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension application to introduce a new pharmaceutical form (solution for injection) associated with new strength (245 mg) and route of administration (subcutaneous use), grouped with a type II variation (C.I.4) to align the summary of product characteristics and labelling of Ultomiris intravenous formulation (IV) with the proposed Ultomiris subcutaneous formulation (SC). The RMP (version 5.0) is updated in accordance."

Action: For adoption

List of Questions adopted on 21.07.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues, concerning clinical aspects.

The Committee adopted a list of outstanding issues with a specific timetable.

4.2.3. Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/X/0101/G

ViiV Healthcare B.V.

Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber

Scope: "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."

Action: For adoption

List of Questions adopted on 19.05.2022.

The Committee was reminded of the status of this application and its remaining outstanding issues, concerning quality and clinical aspects.

The Committee adopted a list of outstanding issues with a specific timetable.

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. Comirnaty - tozinameran - EMEA/H/C/005735/X/0138

BioNTech Manufacturing GmbH

Rapporteur: Filip Josephson

Scope: "Extension application to add a new strength of 3 µg for individuals 6 months to 4 years of age. In addition, the applicant took the opportunity to introduce editorial changes in Annex I, IIIA and IIIB of the PI. The RMP (version 5.1) is updated in accordance."

Action: For adoption

The Committee discussed the issues identified in this application, concerning quality and clinical aspects.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

4.3.2. Hefiya - adalimumab - EMEA/H/C/004865/X/0036/G

Sandoz GmbH

Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add a new strength (80 mg/0.8 ml) of the solution for injection grouped with quality variations. The Package Leaflet and Labelling are updated in accordance.
The RMP (version 9.0) has also been submitted.
Additionally, the applicant takes the opportunity to include editorial changes in the pack sizes (approved (001-003) and new presentations) in the List of All Authorised

Presentations (Annex A) to differentiate packs of pre-filled syringes with or without needle safety device."

Action: For adoption

The Committee discussed the issues identified in this application, concerning quality aspects.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

4.3.3. Hyrimoz - adalimumab - EMEA/H/C/004320/X/0036/G

Sandoz GmbH

Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to add a new strength (80 mg/0.8 ml) of the solution for injection grouped with quality variations. The Package Leaflet and Labelling are updated in accordance.
The RMP (version 9.0) has also been submitted.
Additionally, the applicant takes the opportunity to include editorial changes in the pack sizes (approved (001-003) and new presentations) in the List of All Authorised Presentations (Annex A) to differentiate packs of pre-filled syringes with or without needle safety device."

Action: For adoption

The Committee discussed the issues identified in this application, concerning quality aspects.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

Vertex Pharmaceuticals (Ireland) Limited

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

Scope: "Extension application to add a new strength of 75 mg of lumacaftor and 94 mg of ivacaftor fixed dose combination granules, grouped with a type II variation (C.I.6.a).
C.I.6: Extension of indication to include treatment of cystic fibrosis for children aged 1 to less than 2 years old of age who are homozygous for the F508del mutation in the CFTR gene, based on final results from study 122, a 2-part study of CF subjects 1 to <2 years of age homozygous for F508del. As a consequence, sections 4.1, 4.2, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 11.2 of the RMP has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application, concerning clinical aspects.

The Committee adopted the CHMP recommendation and scientific discussion together with

the list of questions.

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

4.4.1. 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

Scope: "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."

Letter by the applicant dated 22.09.2022 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in September 2022.

Action: For adoption

List of Outstanding Issues adopted on 15.09.2022. List of Questions adopted on 22.04.2022.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted in September 2022.

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

Menarini International Operations Luxembourg S.A

Rapporteur: Janet Koenig, PRAC Rapporteur: Adam Przybylkowski

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

Letter by the applicant dated 12.10.2022 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in September 2022.

Action: For adoption

List of Questions adopted on 21.07.2022.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted in July 2022.

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. Brukinsa - zanubrutinib - EMEA/H/C/004978/II/0003

BeiGene Ireland Ltd

Rapporteur: Aaron Sosa Mejia, Co-Rapporteur: Johanna Lähteenvuo, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include treatment of adult patients with chronic lymphocytic leukaemia (CLL) or small lymphocytic leukaemia (SLL) based on results from study BGB-3111-304; an ongoing, international, Phase 3, open-label, multiple-cohort, randomized study designed to evaluate the efficacy of zanubrutinib versus B+R in patients with previously untreated CLL/SLL, and study BGB-3111-305; an ongoing, international Phase 3, open-label, randomized study of zanubrutinib versus ibrutinib with R/R CLL/SLL. As a consequence, sections 4.1, 4.2, 4.4, 4,5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are being updated. The Package Leaflet is updated in accordance.
An updated RMP version 1.1 (specific for the proposed indication CLL/SLL) was also submitted. In addition, as part of the application the MAH requested a 1-year extension of the market protection."

Action: For adoption

Request for Supplementary Information adopted on 19.05.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The summary of opinion was circulated for information.

5.1.2. Dupixent - dupilumab - EMEA/H/C/004390/II/0060

sanofi-aventis groupe

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Finbarr Leacy, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension of indication to include treatment of atopic dermatitis in paediatric patients from 6 months to <6 years of age based on final results from study R668-AD-1539; this is a phase 2/3 study investigating the pharmacokinetics, safety and efficacy of dupilumab in patients aged ≥6 months to <6 years with moderate-to-severe atopic dermatitis. 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 7.0 of the RMP has also been

submitted."

Action: For adoption

Request for Supplementary Information adopted on 23.06.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects and the RMP.

The Committee adopted a 2nd request for a supplementary information with a specific timetable.

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

Roche Registration GmbH

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

Scope: "Extension of indication to include treatment of 'advanced' idiopathic pulmonary fibrosis (IPF) by the deletion of the current qualifier 'mild to moderate', based on the results from study MA29957; this is a 52-week Phase IIb, multicentre, randomised, double-blind, placebo-controlled clinical trial in IPF patients with advanced lung function impairment (DLco < 40% of predicted) and at high risk of grade 3 pulmonary hypertension, and additional analyses performed on the original pivotal trials for pirfenidone in IPF.
As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. In addition, the MAH took the opportunity to include information in section 4.4 of the SmPC related to the content of sodium per Esbriet capsule and tablet. The Package Leaflet is updated in accordance. Version 12.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 19.05.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects.

The Committee adopted a 2nd request for a supplementary information with a specific timetable.

5.1.4. Evrysdi - risdiplam - Orphan - EMEA/H/C/005145/II/0005/G

Roche Registration GmbH

Rapporteur: Bruno Sepodes, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Jan Neuhauser

Scope: "Grouping of three variations as follows:
Extension of indication to include treatment of patients below 2 months of age based on interim results from study BN40703 (RAINBOWFISH). The pivotal study RAINBOWFISH is an ongoing phase II multicentre, open-label, and single-arm study designed to evaluate the efficacy, safety, tolerability, and PK/PD of risdiplam in pre-symptomatic infants below 2 months of age who were genetically diagnosed with SMA. 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. In addition, the MAH took the opportunity to make some editorial improvements in the product information. A revised RMP version 1.1 was also submitted as

part of the application.
Type IAIN, B.IV.1.a.1 variation to update Evrysdi pack configuration with the addition of a new 1 mL oral syringe into the product carton allowing precise dosing of infants below 2 months of age. As a consequence, section 6.5 of the SmPC has been updated and the labelling and Package Leaflet have been updated in accordance.
Type IAIN, B.IV.1.b variation to remove the spare unit of 12 mL oral syringe out of the two units currently provided in the product carton. As a consequence, section 6.5 of the SmPC has been updated and the labelling and Package Leaflet have been updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 21.07.2022, 22.04.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects.

The Committee adopted a 3rd request for a supplementary information with a specific timetable.

5.1.5. Eylea - aflibercept - EMEA/H/C/002392/II/0077/G

Bayer AG

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Nathalie Gault

Scope: "C.I.6 (Extension of indication) Extension of indication to include the paediatric indication retinopathy of prematurity (ROP) for Eylea; as a consequence, sections 2, 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Separate Package Leaflet is proposed for the guardians of preterm babies. Version 32.1 of the RMP has also been submitted. B.IV.1.a.3."

Action: For adoption

Request for Supplementary Information adopted on 24.02.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects.

The Committee adopted a 2nd request for a supplementary information with a specific timetable.

5.1.6. Fintepla - fenfluramine - Orphan - EMEA/H/C/003933/II/0012

Zogenix ROI Limited

Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber

Scope: "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."

Action: For adoption

Request for Supplementary Information adopted on 22.04.2022.

The Committee discussed the issues identified in this application, concerning clinical

aspects.

The Committee adopted a 2nd request for a supplementary information with a specific timetable.

5.1.7. 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

Request for Supplementary Information adopted on 19.05.2022, 27.01.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects and the RMP.

The Committee adopted a 3rd request for a supplementary information with a specific timetable.

5.1.8. Imbruvica - ibrutinib - EMEA/H/C/003791/II/0073

Janssen-Cilag International N.V.

Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication to include treatment with Imbruvica in combination with bendamustine and rituximab (BR) of adult patients with previously untreated mantle cell lymphoma (MCL) who are unsuitable for autologous stem cell transplantation, based on final results from the category 3 study PCI-32765MCL3002 (SHINE); this is a randomized, double-blind, placebo-controlled phase 3 study of ibrutinib in combination with BR in subjects with newly diagnosed MCL. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 19.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 23.06.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects.

The Committee adopted a 2nd request for a supplementary information with a specific timetable.

The CHMP agreed to consult a SAG and adopted a list of questions to this group.

5.1.9. Imfinzi - durvalumab - EMEA/H/C/004771/II/0041

AstraZeneca AB

Rapporteur: Aaron Sosa Mejia, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: David Olsen

Scope: "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."

Action: For adoption

Request for Supplementary Information adopted on 22.04.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.10. Imfinzi - durvalumab - EMEA/H/C/004771/II/0046

AstraZeneca AB

Rapporteur: Aaron Sosa Mejia, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: David Olsen

Scope: "Extension of indication to include Imfinzi in combination with chemotherapy for the treatment of adults with locally advanced or metastatic biliary tract cancer (BTC), based on the second interim analysis from the ongoing pivotal study D933AC00001 (TOPAZ-1); a phase III randomized, double-blind, placebo-controlled, multi-regional, international study conducted to assess the efficacy and safety of durvalumab in combination with the current standard of care Gemcitabine/Cisplatin for the first-line treatment of patients with locally advanced or metastatic BTC. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package Leaflet has been updated accordingly. Version 7.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 21.07.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects and the RMP.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.11. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0121

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication to include Keytruda as monotherapy for the adjuvant treatment of adults with Stage IB (T2a ⩾ 4 cm), II or IIIA non-small cell lung carcinoma (NSCLC) who have undergone complete resection, based on study KEYNOTE-091; an ongoing Phase 3, randomized, triple-blinded, placebo-controlled, multicenter study of pembrolizumab versus placebo in patients with early-stage NSCLC after resection and completion of standard adjuvant therapy. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are being updated and the Package Leaflet is updated in accordance. An updated RMP version 39.1 was also submitted."

Action: For adoption

Request for Supplementary Information adopted on 21.07.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects and the RMP.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.12. Libtayo - cemiplimab - EMEA/H/C/004844/II/0026

Regeneron Ireland Designated Activity Company (DAC)

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

Scope: "Extension of indication to include monotherapy treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy for Libtayo; sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 23.06.2022, 24.02.2022.

See 2.3

An oral explanation was held on 12 October 2022. The presentation by the applicant focused on the clinical data in support of the application.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by majority (29 out of 30 votes) together with the CHMP Assessment Report and translation timetable.

The divergent position (Armando Genazzani) was appended to the opinion.

The summary of opinion was circulated for information.

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

AstraZeneca AB

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

Scope: "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."

Action: For adoption

Request for Supplementary Information adopted on 21.07.2022, 22.04.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects and the RMP.

The Committee adopted a 3rd request for supplementary information with a specific timetable.

5.1.14. Lyumjev - insulin lispro - EMEA/H/C/005037/II/0014

Eli Lilly Nederland B.V.

Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Mari Thorn

Scope: "Extension of indication to include the treatment of diabetes mellitus in adolescents and children aged 1 year and above, based on final results from study I8B-MC-ITSB; this is a pivotal Phase 3 study designed to evaluate the safety and efficacy of Lyumjev compared to Humalog in combination with basal insulin in children and adolescent patients with T1D. The study was designed to compare change in HbA1c as the primary endpoint. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement update minor editorial and linguistic changes in the SmPC and Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2022, 21.07.2022, 22.04.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The summary of opinion was circulated for information.

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

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include Opdivo in combination with platinum-based chemotherapy for neoadjuvant treatment of adult patients with resectable Stage IB-IIIA non-small cell lung cancer (NSCLC), based on results from study CA209816; a randomised, open-label, phase 3 trial of nivolumab plus ipilimumab or nivolumab plus platinum-doublet chemotherapy versus platinum-doublet chemotherapy in early-stage NSCLC. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 27.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 23.06.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

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

Roche Registration GmbH

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

Scope: "Extension of indication to include treatment of COVID-19 in hospitalised patients in adults and adolescents aged 12 years and older weighing at least 40 kg for Ronapreve; as a consequence, sections 4.2, 4.4, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 1.1 of the RMP has also been submitted.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 19.05.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.17. Spikevax - elasomeran - EMEA/H/C/005791/II/0067

Moderna Biotech Spain, S.L.

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

Scope: "Extension of indication to include immunisation of paediatric individuals from 6 months through 5 years of age based on results from the study P204 (KidCove); this is a phase 2/3, two-part, open-label, dose-escalation, age de-escalation and randomized, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of mRNA-1273 SARS-CoV-2 vaccine in healthy children 6 months to less than 12 years of age. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated and the Package Leaflet is updated in accordance. The MAH also

took the opportunity to implement minor editorial changes in the product information. The submission includes a revised RMP version 4.1."

Action: For adoption

Request for Supplementary Information adopted on 23.06.2022.

The Committee discussed the issues identified in this application, concerning clinical aspects and the RMP.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

5.1.18. Trulicity - dulaglutide - EMEA/H/C/002825/II/0065

Eli Lilly Nederland B.V.

Rapporteur: Martina Weise, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to include treatment of type 2 diabetes mellitus (T2DM) in children and adolescents aged 10 to less than 18 years based on final results from study H9X-MC-GBGC; this is a phase 3, double-blind, randomised, multi-centre, placebo-controlled superiority trial to evaluate PK, PD, safety and efficacy of dulaglutide in children from 10 to less than 18 years of age, with an open label extension to evaluate safety. 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 7.1 of the RMP has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application, concerning clinical aspects and the RMP.

The Committee adopted a request for supplementary information with a specific timetable.

5.1.19. Xydalba - dalbavancin - EMEA/H/C/002840/II/0043

AbbVie Deutschland GmbH & Co. KG

Rapporteur: Filip Josephson, PRAC Rapporteur: Rugile Pilviniene

Scope: "Extension of indication to the paediatric population (aged 3 months to < 18 years) for the treatment of ABSSSI based on the interim results from the safety and efficacy Phase 3 study DUR001-306, together with data from 3 Phase 1 PK studies (A8841004, DUR001-106 and DAL-PK-02). Consequently, the sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC were updated. The Package Leaflet has been updated accordingly.
In addition, the applicant has taken the opportunity to make minor editorial amendments and QRD updates (v10.2) to the SmPC/PIL. Version 7.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 23.06.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP

Assessment Report and translation timetable.

The summary of opinion was circulated for information.

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. Gavreto - pralsetinib - EMEA/H/C/005413/II/0002/G

Roche Registration GmbH

Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Ulla Wändel Liminga

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

Letter by the applicant dated 22.09.2022 requesting an extension to the clock stop to respond to the request for supplementary information adopted in September 2022.

Action: For adoption

Request for Supplementary Information adopted on 15.09.2022, 23.06.2022, 24.03.2022.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the request of supplementary information adopted in September 2022.

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

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Daniela Philadelphy, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Jean-Michel Dogné

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)

List of experts to the Ad-Hoc Expert Group (AHEG).

Action: For adoption

Request for Supplementary Information adopted on 23.06.2022, 27.01.2022.

The CHMP adopted the list of experts to the AHEG.

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

No items

6. Medical devices

6.1. Ancillary medicinal substances - initial consultation

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

human assisted reproductive techniques including in-vitro fertilisation procedures

Scope: List of questions

Action: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

6.2. Ancillary medicinal substances – post-consultation update

No items

6.3. Companion diagnostics - initial consultation

6.3.1. in vitro diagnostic medical device - EMEA/H/D/006107

In vitro qualitative immunohistochemical detection of programmed death-ligand 1 (PD-L1)

Scope: Opinion

Action: For adoption

Request for Supplementary Information adopted on 15.09.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report.

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

No topics

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

The CHMP noted the information.

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 1 recommendation for eligibility to PRIME: 1 was accepted.

The individual outcomes are listed in PRIME Monthly Report on EMA website.

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Evusheld - tixagevimab / cilgavimab - EMEA/H/C/005788/II/0003

AstraZeneca AB

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

"Update of sections 4.2, 4.8, 4.9, 5.1 and 5.2 of the SmPC in order to change the posology recommendations in the pre-exposure prophylaxis indication based on study TACKLE (D8851C00001). The Package Leaflet is updated accordingly. The RMP version 2 has also been submitted."

Action: For adoption

The Committee discussed the issues identified in this application, concerning clinical aspects.

The Committee adopted a request for supplementary information with a specific timetable.

9.1.2. Spikevax - elasomeran - EMEA/H/C/005791/II/84/G

Moderna Biotech Spain, S.L.

Rapporteur: Jan Mueller-Berghaus

Scope: "B.I.a.6.a (Type II): Addition of a new strain (Omicron BA.4-5) resulting in a new Spikevax bivalent Original/Omicron BA.4-5 (50 µg elasomeran/50 µg davesomeran)/mL 0.1 mg/mL dispersion for injection presentation. The Annex A, the SmPC, the Annex II, the labelling and the Package Leaflet are updated accordingly."

Action: For adoption

The Committee discussed the issues identified in this application, concerning clinical aspects.

The Committee adopted a request for supplementary information with a specific timetable.

9.1.3. Ronapreve - casirivimab / imdevimab - EMEA/H/C/005814/II/0007

Roche Registration GmbH

Rapporteur: Jan Mueller-Berghaus

Scope: "Update of sections 4.2, 4.4, 5.1 and 5.2 of the SmPC in order to introduce the proposed dose for SARS-CoV-2 Omicron BA.2, BA.2.12.1, BA.4 and BA.5 subvariants along with dose preparation and infusion instructions for treatment of outpatients and post-exposure prophylaxis as well as to update efficacy and pharmacokinetic information based on pharmacokinetic (PK) modelling data from R10933-PK-21187-SR-01V2 and R10933-R10987-4800mgIV-KRM and in vitro viral neutralisation data from the updated virus neutralisation report R10933-PH-20091-SR-01V7 and its addendum; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial

changes to the PI."

Action: For adoption

The Committee discussed the issues identified in this application, concerning clinical aspects.

The Committee adopted a request for supplementary information with a specific timetable.

9.1.4. Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/R/0079

AstraZeneca AB

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

Scope: Renewal of conditional marketing authorisation; proposal to switch to standard marketing authorisation

Action: For adoption

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

Based on the review of the available information, the CHMP was of the opinion that the risk-benefit balance remains favourable and that all specific obligations have been fulfilled, therefore the CHMP recommended granting of a Marketing Authorisation not subject to specific obligations.

9.1.5. Natpar - Parathyroid hormone – EMEA/H/C/003861

Takeda Pharmaceuticals International AG

Rapporteur: Karin Janssen van Doorn, Co-Rapporteur: Agnes Gyurasics

Scope: DHPC; the DHPC has been adopted via written procedure on 26 September 2022.

Action: For information

The CHMP noted the DHPC and communication plan.

9.1.6. Comirnaty - tozinameran - EMEA/H/C/005735/II/0139

BioNTech Manufacturing GmbH

Rapporteur: Filip Josephson

Scope: "Update of sections 4.8 and 5.1 of the SmPC of Comirnaty 30 µg concentrate for dispersion for injection and Comirnaty 30 µg dispersion for injection as well as section 4.8 of the SmPC of Comirnaty 10 µg concentrate for dispersion for injection in order to update information based on six-month post (booster) dose three interim report data in patients aged 16 years of age and above from studies C4591001 and C4591031. Study C4591001 is a phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals, while study C4591031 is a phase 3 master protocol to evaluate additional dose(s) of BNT162b2 in healthy individuals previously vaccinated with BNT162b2."

Action: For adoption

The Committee discussed the issues identified in this application, concerning clinical aspects.

The Committee adopted a request for supplementary information with a specific timetable.

9.1.7. WS2244 - Nuwiq-EMEA/H/C/002813/WS2244/0048 Vihuma-EMEA/H/C/004459/WS2244/0030

Octapharma AB

Lead Rapporteur: Jan Mueller-Berghaus

Scope: "Update of sections 4.8 and 5.1 of the SmPC in order to add safety and efficacy data based on the final CSR from the category 3 study GENA-21b; a prospective, open-label, multicentre phase 3b study to assess the efficacy and safety of personalized prophylaxis with Human-cl rhFVIII in previously treated adult patients with severe haemophilia A. Further, upon request by the CHMP following the assessment of study GENA-05 (P46 013 and P46 014), the MAH is updating the numbers of evaluated subjects in SmPC section 4.8 and is removing of the sentence "A prospective open-label clinical study in PUPs with severe haemophilia A (<1% FVIII:C) is ongoing" in section 5.1 of the SmPC. The Package Leaflet is updated accordingly."

Action: For adoption

Request for Supplementary Information adopted on 01.09.2022, 16.06.2022, 05.05.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

9.1.8. Imbruvica - ibrutinib - EMEA/H/C/003791/II/0075

Janssen-Cilag International N.V.

Rapporteur: Filip Josephson

Scope: "Update of section 4.2 of the SmPC to incorporate information specific for dose modifications for non-cardiac events and events of cardiac failure or cardiac arrhythmias events based on data pool from clinical studies which included 4 Phase II (PCYC-1102-CA, PCYC-1104-CA, PCYC-1118E, PCYC-1142-CA) and 8 Phase III studies (PCYC-1112-CA, PCYC-1115-CA, CLL3001, PCYC-1130-CA, MCL3001, PCYC-1127-CA, CLL3011, and MCL3002)."

Action: For adoption

Request for Supplementary Information adopted on 21.07.2022.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The CHMP noted the DHPC and communication plan.

9.1.9. Kymriah - tisagenlecleucel – Orphan, ATMP - EMEA/H/C/004090/II/0053

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: "Submission of the final report from study CCTL019H2301 (BELINDA) listed as an obligation in the Annex II of the Product Information. This is a randomized open-label parallel-group multicenter Phase III trial to evaluate the efficacy and safety of tisagenlecleucel in adult patients with relapsed or refractory B-cell aggressive NHL after failure of rituximab and anthracycline containing first-line immune-chemotherapy. The Annex II is updated accordingly."

Action: For adoption

Request for Supplementary Information adopted on 13.05.2022.

The CHMP was updated on discussions at the CAT.

The CHMP, after having considered the CAT assessment, concluded that the Annex II condition has not been fulfilled, pending the delivery of final OS results of study CCTL019H2301.

The CHMP, based on the draft opinion prepared by the CAT, adopted a positive opinion by consensus with scientific grounds for the differences with the CAT draft opinion.

The CHMP adopted the CHMP Assessment Report and translation timetable.

The summary of opinion was circulated for information.

9.1.10. Kymriah - tisagenlecleucel - Orphan, ATMP - EMEA/H/C/004090/II/0059

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Scope: "Update of section 5.1 of the SmPC based on a subgroup analysis from CCTL019B2401 (B2401) disease registry listed as a PAES (ANX006) in the Annex II; this is a non-interventional study to evaluate the efficacy and safety of Kymriah in ALL patients below the age of 3 years. In addition, the MAH took the opportunity to update Annex II.D of the SmPC to reflect the fulfilment of the PAES."

Action: For adoption

Request for Supplementary Information adopted on 15.07.2022.

The CHMP was updated on discussions at the CAT.

The CHMP, after having considered the CAT assessment, concurred with the CAT that the current variation application fulfilled the PAES commitment (ANX006) but concluded that OS data from study B2401 do not isolate a treatment effect of Kymriah and therefore should not be included in section 5.1 of the SmPC.

The CHMP, based on the draft opinion prepared by the CAT, adopted a positive opinion by consensus with scientific grounds for the differences with the CAT draft opinion.

The CHMP adopted the CHMP Assessment Report and translation timetable.

The summary of opinion was circulated for information.

9.1.11. Zejula - niraparib - EMEA/H/C/004249/II/0033, Orphan

GlaxoSmithKline (Ireland) Limited

Rapporteur: Ingrid Wang, PRAC Rapporteur: Jan Neuhauser

Scope: Update on the status of this application. "Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning and add MDS/AML to the list of adverse drug reactions (ADRs) with frequency common and update of section 5.1 based on final results from NOVA study (213356); this is a Phase 3 Randomized Double-Blind Trial of Maintenance with Niraparib Versus Placebo in Patients with Platinum Sensitive Ovarian Cancer. In addition, the MAH also took this opportunity to update sections 4.4 and 4.6 to update information on contraception based on EMA and CTFG recommendations. The Package Leaflet is updated accordingly. The RMP version 6 has also been submitted."

Action: For information

Request for Supplementary Information adopted on 19.05.2022, 10.02.2022.

The CHMP noted the status of this application.

10. Referral procedures

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

October 2022 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

The CHMP noted the information.

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

No items

13.2. Innovation Task Force briefing meetings

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Vote by proxy

None

14.1.2. CHMP membership

The CHMP chair welcomed Finbarr Leacy, as new alternate for Ireland.

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

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

Action: For adoption

The CHMP adopted the EURD list.

14.2.2. Paediatric Committee (PDCO)

PIPs reaching D30 at October 2022 PDCO

Action: For information

Report from the PDCO meeting held on 26-29 September 2022

Action: For information

The CHMP noted the information.

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

14.3.1. Biologics Working Party (BWP)

Chair: Sol Ruiz/Sean Barry

Reports from BWP October 2022 meeting to CHMP for adoption:

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

Action: For adoption

The CHMP adopted the BWP reports.

14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 20-21 September 2022.

Action: For adoption

The CHMP adopted table of decisions.

14.3.3. Scientific Advice Working Party (SAWP)

Chair: Paolo Foggi

Report from the SAWP meeting held on 26-29 September 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.

The CHMP noted the update.

14.3.4. Vice-Chair election of the Central Nervous System Working Party (CNSWP)

Election of vice-chair of the Central Nervous System Working Party.

Application(s) received

Action: For adoption

The CHMP elected Ewa Balkowiec Iskra as Vice-Chair of the CNSWP.

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

The CHMP noted the information.

15.1.2. Regulatory & scientific conference on RNA based medicines

This conference aims to facilitate the dialogue between industry/academia and regulators, to discuss scientific and regulatory opportunities and challenges to promote the development of RNA-based innovative medicines

Action: For information

This topic was postponed to the next CHMP meeting.

Lists of participants

List of participants including any restrictions with respect to involvement of members/alternates/experts following evaluation of declared interests for the 10-13 October 2022 CHMP meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Harald Enzmann	Chair	Germany	No interests declared	
Andrea Laslop	Member	Austria	No interests declared	
Daniela Philadelphy	Alternate	Austria	No interests declared	
Christophe Focke	Member	Belgium	No restrictions applicable to this meeting	
Karin Janssen van Doorn	Alternate	Belgium	No interests declared	
Ilko Getov	Member	Bulgaria	No interests declared	
Velislava Todorova	Alternate	Bulgaria	No interests declared	
Margareta Bego	Member	Croatia	No interests declared	
Selma Arapovic Dzakula	Alternate	Croatia	No interests declared	
Helena Panayiotopoulou	Member	Cyprus	No interests declared	
Emilia Mavrokordatou	Alternate	Cyprus	No participation in final deliberations and voting on:	COVID-19 vaccines
Ondřej Slanař	Member	Czechia	No restrictions applicable to this meeting	
Tomas Radimersky	Alternate	Czechia	No interests declared	
Thalia Marie Estrup Blicher	Member	Denmark	No restrictions applicable to this meeting	
Aaron Sosa Mejia	Alternate	Denmark	No participation in final deliberations and voting on:	Refixia - nonacog beta pegol - EMEA/H/C/004178/X/0027/G
Alar Irs	Member	Estonia	No restrictions applicable to this meeting	
Edward Laane	Alternate	Estonia	No restrictions applicable to this meeting	
Outi Mäki-Ikola	Member	Finland	No restrictions applicable to this meeting	
Johanna Lähteenvuo	Alternate	Finland	No interests declared	
Alexandre Moreau	Member	France	No interests declared	
Jean-Michel Race	Alternate	France	No interests declared	
Martina Weise	Member	Germany	No restrictions applicable to this meeting	
Janet Koenig	Alternate	Germany	No interests declared	
Konstantina Alexopoulou	Member	Greece	No interests declared	
Anastasia Mountaki	Alternate	Greece	No interests declared	
Robert Porszasz	Member	Hungary	No interests declared	
Agnes Gyurasics	Alternate	Hungary	No interests declared	
Hrefna Gudmundsdottir	Member	Iceland	No interests declared	
Hjalti Kristinsson	Alternate	Iceland	No interests declared	
Jayne Crowe	Member	Ireland	No interests declared	
Finbarr Leacy	Alternate	Ireland	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Armando Genazzani	Member	Italy	No interests declared	
Maria Grazia Evandri	Alternate	Italy	No interests declared	
Elita Poplavska	Member	Latvia	No interests declared	
Silvijus Abramavicius	Alternate	Lithuania	No restrictions applicable to this meeting	
Martine Trauffler	Member	Luxembourg	No interests declared	
Alexandra Branchu	Alternate	Luxembourg	No participation in final deliberations and voting on:	Dupixent - dupilumab - EMEA/H/C/004390/II/0060 SARS-CoV-2 prefusion Spike delta TM protein, recombinant - EMEA/H/C/005754
John Joseph Borg	Member	Malta	No interests declared	
Johann Lodewijk Hillege	Member	Netherlands	No interests declared	
Paula Boudewina van Hennik	Alternate	Netherlands	No interests declared	
Ingrid Wang	Member	Norway	No interests declared	
Eva Skovlund	Alternate	Norway	No interests declared	
Ewa Balkowiec Iskra	Member	Poland	No interests declared	
Bruno Sepodes	Member (Vice-Chair)	Portugal	No interests declared	
Fatima Ventura	Alternate	Portugal	No participation in final deliberations and voting on:	COVID-19 vaccines
Simona Badoi	Member	Romania	No interests declared	
Dana Gabriela Marin	Alternate	Romania	No interests declared	
Francisek Drafi	Member	Slovakia	No interests declared	
Dorota Distlerova	Alternate	Slovakia	No interests declared	
Nevenka Trsinar Brodt	Alternate	Slovenia	No interests declared	
Maria Concepcion Prieto Yerro	Member	Spain	No interests declared	
Blanca Garcia-Ochoa	Alternate	Spain	No interests declared	
Kristina Dunder	Member	Sweden	No interests declared	
Filip Josephson	Alternate	Sweden	No interests declared	
Christian Gartner	Co-opted member	Austria	No interests declared	
Jan Mueller-Berghaus	Co-opted member	Germany	No interests declared	
Blanka Hirschlerova	Co-opted member	Czechia	No interests declared	
Sol Ruiz	Co-opted member	Spain	No interests declared	
Brigitte Mueller	Expert	Austria	No interests declared	
Ilona G. Reischl	Expert	Austria	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Harald Bernsteiner	Expert	Austria	No interests declared	
Melanie Ramberger	Expert	Austria	No interests declared	
Jakob Paur	Expert	Austria	No restrictions applicable to this meeting	
Mas Parra Paloma	Expert	Spain	No restrictions applicable to this meeting	
Angelina Doriguzzi	Expert	Austria	No restrictions applicable to this meeting	
Susanne Urach	Expert	Austria	No interests declared	
Elisabeth Fuerst	Expert	Austria	No interests declared	
Krõõt Aab	Expert	Estonia	No interests declared	
Juta Kraav	Expert	Estonia	No restrictions applicable to this meeting	
Kairi Rooma	Expert	Estonia	No interests declared	
Oyvind Holte	Expert	Norway	No interests declared	
Paolo Foggi	Expert	Italy	No interests declared	
André Elferink	Expert	Netherlands	No interests declared	
Joerg Zinserling	Expert	Germany	No interests declared	
Elina Rönnemaa	Expert	Sweden	No interests declared	
Karolina Törneke	Expert	Sweden	No interests declared	
Peter Mol	Expert	Netherlands	No interests declared	
Peter Mayer	Expert	Germany	No interests declared	
Torbjörn Callréus	Expert	Malta	No interests declared	
Vincent Gazin	Expert	France	No interests declared	
Elsa Grangier	Expert	France	No interests declared	
Anissa Benlazar	Expert	France	No interests declared	
Céline Jumeau	Expert	France	No interests declared	
Bruno Delafont	Expert	France	No participation in discussion, final deliberations and voting on:	Imfinzi - durvalumab - EMEA/H/C/004771/II/0041 Imfinzi - durvalumab - EMEA/H/C/004771/II/0046 Lynparza - olaparib - EMEA/H/C/003726/II/0053 Evusheld - tixagevimab / cilgavimab - EMEA/H/C/005788/II/0003 Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/R/0079

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				tremelimumab - EMEA/H/C/004650
Umberto CASALEGNO	Expert	France	No interests declared	
Paula Contreras Alarcón	Expert	Spain	No participation in discussion, final deliberations and voting on:	Xydalba - dalbavancin - EMEA/H/C/002840/II/0043
Maria Victoria Tudanca Pacios	Expert	Spain	No restrictions applicable to this meeting	
Lucia Lopez-Anglada Fernandez	Expert	Spain	No interests declared	
Macarena Gajardo	Expert	Spain	No interests declared	
Agustin Portela Moreira	Expert	Spain	No interests declared	
Maria Chamorro Somoza Diaz-Sarmiento	Expert	Spain	No interests declared	
Alicia Pérez González	Expert	Spain	No interests declared	
Ana Sagredo	Expert	Spain	No interests declared	
Consuelo Mejías Pavón	Expert	Spain	No interests declared	
Maria Martinez Gonzalez	Expert	Spain	No restrictions applicable to this meeting	
Irene Saugar Gomez	Expert	Spain	No interests declared	
Eva Maria Nadal Elduayen	Expert	Spain	No interests declared	
Monica Beteta Robles	Expert	Spain	No interests declared	
David Monjas Piqueras	Expert	Spain	No interests declared	
Marte Fergestad	Expert	Norway	No interests declared	
Therese Solstad Saunders	Expert	Norway	No interests declared	
Alexandru Mihail Simion	Expert	Belgium	No interests declared	
Roel Van Loock	Expert	Belgium	No interests declared	
Edwige Haelterman Brenneisen	Expert	Belgium	No interests declared	
Inne Crèvecoeur	Expert	Belgium	No interests declared	
Olga Kholmanskikh	Expert	Belgium	No interests declared	
Valerie Lescrainier	Expert	Belgium	No interests declared	
Karri Penttila	Expert	Finland	No interests declared	
Kari Punnonen	Expert	Finland	No interests declared	
Claire-Li Ding	Expert	France	No interests declared	
Sandrine Chiappini	Expert	France	No interests declared	
Martijn van Gils	Expert	Netherlands	No interests declared	
Miki Hew	Expert	Netherlands	No interests declared	
Jaap Fransen	Expert	Netherlands	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Gaja Lesnicar Pucko	Expert	Slovenia	No interests declared	
Suzana Vidic	Expert	Slovenia	No restrictions applicable to this meeting	
Janneke van Leeuwen	Expert	Netherlands	No interests declared	
Jeanette McCallion	Expert	Ireland	No interests declared	
Maura O'Donovan	Expert	Ireland	No interests declared	
Niamh Curran	Expert	Ireland	No interests declared	
Jana Schweigertova	Expert	Slovakia	No interests declared	
Eva Malikova	Expert	Slovakia	No interests declared	
Jana Klimasová	Expert	Slovakia	No restrictions applicable to this meeting	
Anna Kubandová	Expert	Slovakia	No interests declared	
Peter Sisovsky	Expert	Slovakia	No interests declared	
Poleta Luga	Expert	Germany	No interests declared	
Sarah Lang	Expert	Germany	No restrictions applicable to this meeting	
Lars Krueger	Expert	Germany	No restrictions applicable to this meeting	
Elena Grabski	Expert	Germany	No interests declared	
Linda Marchioro	Expert	Germany	No interests declared	
Hilke Zander	Expert	Germany	No interests declared	
Joerg Engelbergs	Expert	Germany	No interests declared	
Susanne Mueller-Egert	Expert	Germany	No interests declared	
Sarah Tognarelli	Expert	Germany	No restrictions applicable to this meeting	
Yasmin Molter	Expert	Germany	No interests declared	
Steffen Gross	Expert	Germany	No interests declared	
Gaby Wangorsch	Expert	Germany	No interests declared	
Maren Richter	Expert	Germany	No restrictions applicable to this meeting	
Claudia Reichmann	Expert	Germany	No interests declared	
Lukas Malte Aguirre Davila	Expert	Germany	No interests declared	
Bettina Klug	Expert	Germany	No interests declared	
Zuzana Jedlickova	Expert	Germany	No interests declared	
Verena Scheer	Expert	Germany	No interests declared	
Meera Varma	Expert	Denmark	No restrictions applicable to this meeting	
Line Praest Lauridsen	Expert	Denmark	No restrictions applicable to this meeting	
Lene Weber Vestermark	Expert	Denmark	No interests declared	
Anne-Marie Dalseg	Expert	Denmark	No interests declared	
Mette Linnert Jensen	Expert	Denmark	No interests declared	
Kristina Bech Jensen	Expert	Denmark	No interests declared	
Deirdre Mannion	Expert	Denmark	No restrictions applicable to this meeting	
Kristin Skougaard	Expert	Denmark	No interests declared	

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Thadeus Bao Quan Nguyen	Expert	Denmark	No interests declared	
Charlotte Hejl	Expert	Denmark	No restrictions applicable to this meeting	
Anne Hasle Buur	Expert	Denmark	No interests declared	
Charlotte Anderberg	Expert	Sweden	No restrictions applicable to this meeting	
Maria Winqvist	Expert	Sweden	No interests declared	
Adriana Ammassari	Expert	Italy	No interests declared	
Luca Santi	Expert	Italy	No restrictions applicable to this meeting	
Martina Perini	Expert	Italy	No restrictions applicable to this meeting	
Angela Garau	Expert	Italy	No interests declared	
Cristina Migali	Expert	Italy	No interests declared	
Antonella Isgrò	Expert	Italy	No interests declared	
Sarah Galluzzo	Expert	Italy	No interests declared	
Sabine Mayrhofer	Expert	Germany	No interests declared	
Irene Bachmann	Expert	Germany	No interests declared	
Nora Cascante Estepa	Expert	Germany	No interests declared	
Regine Magdalene Lehnert	Expert	Germany	No interests declared	
Jana Lukacisinova	Expert	Czechia	No interests declared	
Ilze Kalve	Expert	Latvia	No interests declared	
Vita Gulevska	Expert	Latvia	No interests declared	
Pia Rivetti di Val Cervo	Expert	Italy	No interests declared	
Karin Fjordén	Expert	Sweden	No part in final deliberations and voting as appropriate as regards the medicinal product:	Keytruda - pembrolizumab - EMEA/H/C/003820/II/0121 Imbruvica - ibrutinib - EMEA/H/C/003791/II/0075
Ebru Karakoc Madsen	Expert	Denmark	No restrictions applicable to this meeting	
Irene Bosselaers	Expert	Netherlands	No interests declared	
Salvatore Tranchina	Expert	Italy	No interests declared	
Sheila Killalea	Expert	Ireland	No interests declared	
Gerlienke Geurts-Voerman	Expert	Netherlands	No interests declared	
Rune Kjeken	Expert	Norway	No restrictions applicable to this meeting	
Meeting run with the help of EMA staff				

Experts were evaluated against the agenda topics or activities they participated in.

Experts from international organisations or regulatory authorities in third countries cannot participate in

the adoption of any procedural decision, scientific opinion or recommendation by the Committee at any step of the procedure.

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)*

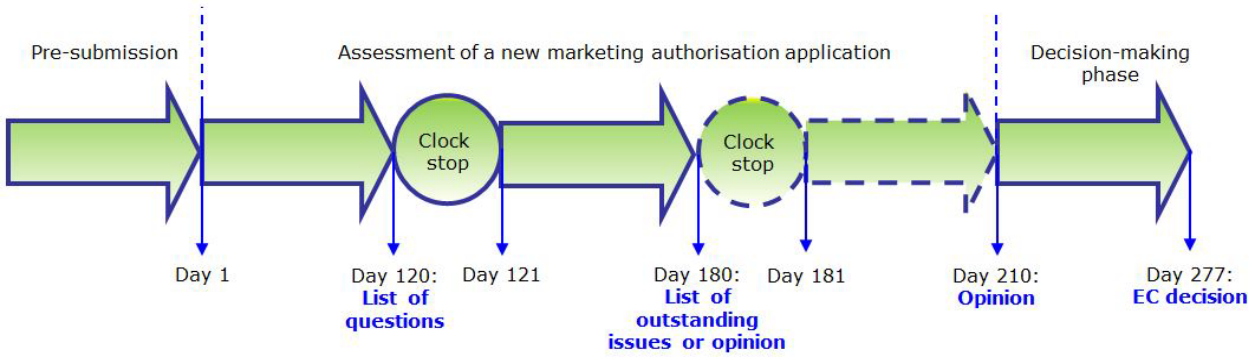
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

23 November 2022
EMA/CHMP/825886/2022

Annex to 10-13 October 2022 CHMP Minutes

Pre-submission and post-authorisations issues

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A. PRE-SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

Final Outcome of Rapporteurship allocation for October 2022: **For adoption**	Adopted

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

Bylvay - odevixibat - EMEA/H/C/004691/S/0008, Orphan Albireo, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable.
MVABEA - ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005343/S/0015 Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jean-Michel Dogné	Positive Opinion adopted by consensus together with the CHMP assessment report. The Marketing Authorisation remains under exceptional circumstances.
Qarziba - dinutuximab beta - EMEA/H/C/003918/S/0046, Orphan EUSA Pharma (Netherlands) B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. The Marketing Authorisation remains under exceptional circumstances.
ZABDENO - ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005337/S/0012 Janssen-Cilag International N.V., Rapporteur:	Positive Opinion adopted by consensus together with the CHMP assessment report. The Marketing Authorisation remains under

Johann Lodewijk Hillege, PRAC Rapporteur: Jean-Michel Dogné	exceptional circumstances.

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Lamzede - velmanase alfa - EMEA/H/C/003922/R/0029, Orphan Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Jan Neuhauser Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable.
Lokelma - sodium zirconium cyclosilicate - EMEA/H/C/004029/R/0027 AstraZeneca AB, Rapporteur: Silvijus Abramavicius, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Kirsti Villikka Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable.
Riarify - beclometasone dipropionate / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004836/R/0022 Chiesi Farmaceutici S.p.A., Informed Consent of Trimbow, Rapporteur: Janet Koenig, Co-Rapporteur: Finbarr Leacy, PRAC Rapporteur: Jan Neuhauser	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.
Semglee - insulin glargine - EMEA/H/C/004280/R/0040 Viatris Limited, Rapporteur: Martina Weise, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable.
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/R/0057 GlaxoSmithkline Biologicals SA, Rapporteur: Christophe Focke, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sonja Hrabcik	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.
Trydonis - beclometasone dipropionate / formoterol fumarate dihydrate /	Positive Opinion adopted by consensus together with the CHMP assessment report and

glycopyrronium - EMEA/H/C/004702/R/0025 Chiesi Farmaceutici S.p.A., Informed Consent of Trimbow, Rapporteur: Janet Koenig, Co-Rapporteur: Finbarr Leacy, PRAC Rapporteur: Jan Neuhauser	translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.
Zessly - infliximab - EMEA/H/C/004647/R/0025 Sandoz GmbH, Rapporteur: Eva Skovlund, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Ulla Wändel Liminga	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.

B.2.3. Renewals of Conditional Marketing Authorisations

Paxlovid - (1r,2s,5s)-n-((1s)-1-cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2s)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973/R/0023 Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Martin Huber Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable.
Retsevmo - selpercatinib - EMEA/H/C/005375/R/0018 Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst	Positive Opinion adopted by consensus together with the CHMP assessment report. The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional.
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/R/0079 AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné	Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable. Based on the review of the available information, the CHMP was of the opinion that the risk-benefit balance remains favourable and that all specific obligations have been fulfilled, therefore the CHMP recommended granting of a Marketing Authorisation not subject to specific obligations. See 9.1

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its October 2022 meeting:	
EMEA/H/C/PSUSA/00000403/202202 (bevacizumab) CAPS: **Abevmy** (EMEA/H/C/005327) (bevacizumab), Mylan IRE Healthcare Limited, Rapporteur: Jan Mueller-Berghaus **Alymsys** (EMEA/H/C/005286) (bevacizumab), Mabxience Research SL, Rapporteur: Christian Gartner **Avastin** (EMEA/H/C/000582) (bevacizumab), Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia **Aybintio** (EMEA/H/C/005106) (bevacizumab), Samsung Bioepis NL B.V., Rapporteur: Andrea Laslop **MVASI** (EMEA/H/C/004728) (bevacizumab), Amgen Technology (Ireland) Unlimited Company, Rapporteur: Eva Skovlund **Onbevzi** (EMEA/H/C/005640) (bevacizumab), Samsung Bioepis NL B.V., Rapporteur: Andrea Laslop **Oyavas** (EMEA/H/C/005556) (bevacizumab), STADA Arzneimittel AG, Rapporteur: Christian Gartner **Zirabev** (EMEA/H/C/004697) (bevacizumab), Pfizer Europe MA EEIG, Rapporteur: Eva Skovlund, PRAC Rapporteur: Anette Kirstine Stark, "25/02/2021 To: 25/02/2022"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.4 of the SmPC to amend a warning/precaution regarding anaphylactic shock. Update of section 4.8 of the SmPC to add the adverse reaction anaphylactic shock with a frequency rare, and to change the frequency of the adverse reaction hypersensitivity and infusion reactions in table 2 and 3 from not known to common. The package leaflet is updated accordingly.
EMEA/H/C/PSUSA/00010633/202203 (ribociclib) CAPS: **Kisqali** (EMEA/H/C/004213) (ribociclib), Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Marie Louise Schougaard Christiansen, "13/03/2021 To: 12/03/2022"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following changes: Update of sections 4.4 and 4.8 of the SmPC to amend a warning/precaution regarding ILD/pneumonitis and add the adverse reaction ILD/pneumonitis with a frequency common. The package leaflet is updated accordingly.
EMEA/H/C/PSUSA/00010745/202202	The CHMP, having considered in accordance with

(apalutamide) CAPS: **Erleada** (EMEA/H/C/004452) (apalutamide), Janssen-Cilag International N.V., Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Tiphaine Vaillant, "14/08/2021 To: 13/02/2022"	Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following changes: Update of sections 4.4 and 4.8 of the SmPC of apalutamide containing products to add "DRESS". The Package leaflet is updated accordingly.
EMEA/H/C/PSUSA/00010825/202203 (esketamine (for centrally authorised product only)) CAPS: **Spravato** (EMEA/H/C/004535) (esketamine), Janssen-Cilag International N.V., Rapporteur: Martina Weise, PRAC Rapporteur: Kirsti Villikka, "05/09/2021 To: 04/03/2022"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of sections 4.4 and 4.8 of the SmPC to amend a warning concerning respiratory depression and to add respiratory depression with a frequency rare. The package leaflet is updated accordingly.
EMEA/H/C/PSUSA/00010851/202203 (isatuximab) CAPS: **SARCLISA** (EMEA/H/C/004977) (isatuximab), sanofi-aventis groupe, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Maria del Pilar Rayon, "01/03/2021 To: 01/03/2022"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of section 4.4 of the SmPC to add Tumour Lysis Syndrome. The Package leaflet is updated accordingly.
EMEA/H/C/PSUSA/00010916/202202 (COVID-19 vaccine (Ad26.COV2-S [recombinant]) (COVID-19 Vaccine Janssen)) CAPS: **JCOVDEN** (EMEA/H/C/005737) (adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein), Janssen-Cilag International N.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Ulla Wändel Liminga, "24/08/2021 To: 24/02/2022"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above-mentioned medicinal product(s), concerning the following change(s): Update of section 4.8 of the SmPC to add the adverse reaction Facial Paralysis (including Bell's Palsy) with frequency 'rare'. The Package leaflet is updated accordingly.

EMEA/H/C/PSUSA/00010969/202202 (lonapegsomatropin) CAPS: **Skytrofa** (EMEA/H/C/005367) (lonapegsomatropin), Ascendis Pharma Endocrinology Division A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber, "25/08/2021 To: 25/02/2022"	The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s): Update of sections 4.4 and 4.8 of the SmPC to include a warning on anaphylactic reactions including angioedema and add anaphylactic reactions (including angioedema) as an adverse drug reaction with a frequency 'uncommon'. The Package leaflet is updated accordingly.

B.4. EPARs / WPARs

Beyfortus - nirsevimab - EMEA/H/C/005304 AstraZeneca AB, Prevention of RSV lower respiratory tract infection. Immunise infants from birth entering their first Respiratory Syncytial Virus (RSV) season for the prevention of RSV lower respiratory tract disease, 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.
Enjaymo - sutimlimab - EMEA/H/C/005776, Orphan Genzyme Europe BV, treatment of haemolysis in adult patients with cold agglutinin disease (CAD), 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.
LIVTENCITY - maribavir - EMEA/H/C/005787, Orphan Takeda Pharmaceuticals International AG Ireland Branch, treatment of cytomegalovirus (CMV) infection, 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.
Melatonin Neurim - melatonin - EMEA/H/C/005603 RAD Neurim Pharmaceuticals EEC SARL, treatment of primary insomnia, Informed Consent of Circadin, Informed consent application (Article 10c of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Mounjaro - tirzepatide -	For information only. Comments can be sent to

EMEA/H/C/005620 Eli Lilly Nederland B.V., treatment of adults with type 2 diabetes mellitus, New active substance (Article 8(3) of Directive No 2001/83/EC)	the PL in case necessary.
Mycapssa - octreotide - EMEA/H/C/005826, Orphan Amryt Pharmaceuticals DAC, treatment of acromegaly, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Pyrukynd - mitapivat - EMEA/H/C/005540, Orphan Agios Netherlands B.V., treatment of pyruvate kinase deficiency, 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.
Sorafenib Accord - sorafenib - EMEA/H/C/005921 Accord Healthcare S.L.U., treatment of hepatocellular carcinoma and renal cell carcinoma, Generic, Generic of Nexavar, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Teriflunomide Accord - teriflunomide - EMEA/H/C/005960 Accord Healthcare S.L.U., treatment of multiple sclerosis (MS), Generic, Generic of AUBAGIO, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Teriflunomide Mylan - teriflunomide - EMEA/H/C/005962 Mylan Pharmaceuticals Limited, treatment of multiple sclerosis (MS), Generic, Generic of AUBAGIO, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Teriparatide SUN - teriparatide - EMEA/H/C/005793 Sun Pharmaceutical Industries Europe B.V., treatment of osteoporosis, Hybrid application (Article 10(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Ximluci - ranibizumab - EMEA/H/C/005617 STADA Arzneimittel AG, treatment of neovascular age-related macular degeneration (AMD), Similar biological application (Article 10(4) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Zynlonta - loncastuximab tesirine - EMEA/H/C/005685, Orphan ADC Therapeutics (NL) B.V., treatment of adult	For information only. Comments can be sent to the PL in case necessary.

patients with relapsed or refractory large B-cell lymphoma, New active substance (Article 8(3) of Directive No 2001/83/EC)	
Vabysmo - faricimab - EMEA/H/C/005642 Roche Registration GmbH, treatment of neovascular (wet) age-related macular degeneration (nAMD) and visual impairment due to diabetic macular oedema (DME), 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

Alecensa - alectinib - EMEA/H/C/004164/II/0041 Roche Registration GmbH, Rapporteur: Filip Josephson Opinion adopted on 13.10.2022. Request for Supplementary Information adopted on 01.09.2022.	Positive Opinion adopted by consensus on 13.10.2022.
Ameluz - 5-aminolevulinic acid - EMEA/H/C/002204/II/0049/G Biofrontera Bioscience GmbH, Rapporteur: Janet Koenig Opinion adopted on 06.10.2022. Request for Supplementary Information adopted on 10.06.2022, 14.10.2021.	Positive Opinion adopted by consensus on 06.10.2022.
Armisarte - pemetrexed - EMEA/H/C/004109/II/0030/G Actavis Group PTC ehf, Rapporteur: Alar Irs Request for Supplementary Information adopted on 22.09.2022.	Request for supplementary information adopted with a specific timetable.
Bavencio - avelumab - EMEA/H/C/004338/II/0037/G Merck Europe B.V., Rapporteur: Filip Josephson Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable.
Benepali - etanercept - EMEA/H/C/004007/II/0065/G Samsung Bioepis NL B.V., Rapporteur: Andrea Laslop Opinion adopted on 06.10.2022. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 06.10.2022.

on 14.07.2022.	
Caelyx pegylated liposomal - doxorubicin - EMEA/H/C/000089/II/0103 Baxter Holding B.V., Rapporteur: Ondřej Slanař Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable.
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0146/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 29.09.2022.	Positive Opinion adopted by consensus on 29.09.2022.
Elaprase - idursulfase - EMEA/H/C/000700/II/0095 Takeda Pharmaceuticals International AG Ireland Branch, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 22.09.2022. Request for Supplementary Information adopted on 07.07.2022, 24.03.2022.	Positive Opinion adopted by consensus on 22.09.2022.
Entyvio - vedolizumab - EMEA/H/C/002782/II/0070/G Takeda Pharma A/S, Rapporteur: Armando Genazzani Opinion adopted on 29.09.2022. Request for Supplementary Information adopted on 21.07.2022.	Positive Opinion adopted by consensus on 29.09.2022.
Firazyr - icatibant - EMEA/H/C/000899/II/0054/G, Orphan Takeda Pharmaceuticals International AG, Rapporteur: Kristina Dunder Opinion adopted on 22.09.2022. Request for Supplementary Information adopted on 21.07.2022.	Positive Opinion adopted by consensus on 22.09.2022.
Insulin aspart Sanofi - insulin aspart - EMEA/H/C/005033/II/0010/G sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 06.10.2022.	Request for supplementary information adopted with a specific timetable.
Lyumjev - insulin lispro - EMEA/H/C/005037/II/0016 Eli Lilly Nederland B.V., Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 13.10.2022, 08.09.2022.	Request for supplementary information adopted with a specific timetable.
Nexviadyme - avalglucosidase alfa -	Positive Opinion adopted by consensus on

EMEA/H/C/005501/II/0001, Orphan Genzyme Europe BV, Rapporteur: Andrea Laslop Opinion adopted on 22.09.2022.	22.09.2022.
Nexviadyme - avalglucosidase alfa - EMEA/H/C/005501/II/0002, Orphan Genzyme Europe BV, Rapporteur: Andrea Laslop Opinion adopted on 22.09.2022.	Positive Opinion adopted by consensus on 22.09.2022.
Nexviadyme - avalglucosidase alfa - EMEA/H/C/005501/II/0003/G, Orphan Genzyme Europe BV, Rapporteur: Andrea Laslop Opinion adopted on 06.10.2022.	Positive Opinion adopted by consensus on 06.10.2022.
OPDIVO - nivolumab - EMEA/H/C/003985/II/0124/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Blanca Garcia-Ochoa Opinion adopted on 06.10.2022.	Positive Opinion adopted by consensus on 06.10.2022.
Paxlovid - (1r,2s,5s)-n-((1s)-1-cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2s)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973/II/0019/G Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable.
Pemetrexed Accord - pemetrexed - EMEA/H/C/004072/II/0020 Accord Healthcare S.L.U., Generic, Generic of Alimta, Rapporteur: John Joseph Borg Opinion adopted on 13.10.2022. Request for Supplementary Information adopted on 07.07.2022.	Positive Opinion adopted by consensus on 13.10.2022.
Phesgo - pertuzumab / trastuzumab - EMEA/H/C/005386/II/0012/G Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia Opinion adopted on 06.10.2022. Request for Supplementary Information adopted on 01.09.2022.	Positive Opinion adopted by consensus on 06.10.2022.
Qarziba - dinutuximab beta - EMEA/H/C/003918/II/0047, Orphan EUSA Pharma (Netherlands) B.V., Rapporteur: Paula Boudewina van Hennik Opinion adopted on 06.10.2022.	Positive Opinion adopted by consensus on 06.10.2022.
Remsima - infliximab -	Request for supplementary information adopted

EMEA/H/C/002576/II/0117/G Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 29.09.2022.	with a specific timetable.
SARCLISA - isatuximab - EMEA/H/C/004977/II/0017/G sanofi-aventis groupe, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable.
Spikevax - elasomeran - EMEA/H/C/005791/II/0076/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 13.10.2022.	Positive Opinion adopted by consensus on 13.10.2022.
Spikevax - elasomeran - EMEA/H/C/005791/II/0078/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 06.10.2022.	Positive Opinion adopted by consensus on 06.10.2022.
Spikevax - elasomeran - EMEA/H/C/005791/II/0079/G Moderna Biotech Spain, S.L., Co-Rapporteur: Andrea Laslop Opinion adopted on 06.10.2022.	Positive Opinion adopted by consensus on 06.10.2022.
Terrosa - teriparatide - EMEA/H/C/003916/II/0026/G Gedeon Richter Plc., Rapporteur: Daniela Philadelphy Request for Supplementary Information adopted on 29.09.2022.	Request for supplementary information adopted with a specific timetable.
Tremfya - guselkumab - EMEA/H/C/004271/II/0034/G Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable.
Ultomiris - ravulizumab - EMEA/H/C/004954/II/0030 Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa Opinion adopted on 06.10.2022.	Positive Opinion adopted by consensus on 06.10.2022.
Vaniqa - eflornithine - EMEA/H/C/000325/II/0056 Almirall S.A, Rapporteur: Jayne Crowe	Positive Opinion adopted by consensus on 22.09.2022.

Opinion adopted on 22.09.2022. Request for Supplementary Information adopted on 10.06.2022.	
Voraxaze - glucarpidase - EMEA/H/C/005467/II/0004, Orphan SERB S.A.S., Rapporteur: Ondřej Slanař Opinion adopted on 22.09.2022.	Positive Opinion adopted by consensus on 22.09.2022.
ZYNRELEF - bupivacaine / meloxicam - EMEA/H/C/005205/II/0009/G Heron Therapeutics, B.V., Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 22.09.2022.	Request for supplementary information adopted with a specific timetable.
WS2283/G **Eucreas- EMEA/H/C/000807/WS2283/0098/G** **Galvus- EMEA/H/C/000771/WS2283/0077/G** **Icandra- EMEA/H/C/001050/WS2283/0103/G** **Jalra- EMEA/H/C/001048/WS2283/0080/G** **Xiliarx- EMEA/H/C/001051/WS2283/0078/G** **Zomarist- EMEA/H/C/001049/WS2283/0100/G** Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder Opinion adopted on 06.10.2022. Request for Supplementary Information adopted on 01.09.2022.	Positive Opinion adopted by consensus on 06.10.2022.
WS2288 **Humalog- EMEA/H/C/000088/WS2288/0196** **Liprolog- EMEA/H/C/000393/WS2288/0156** Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 13.10.2022, 01.09.2022.	Request for supplementary information adopted with a specific timetable.
WS2309/G **Hexacima- EMEA/H/C/002702/WS2309/0135/G** **Hexyon- EMEA/H/C/002796/WS2309/0139/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus	Positive Opinion adopted by consensus on 22.09.2022.

Opinion adopted on 22.09.2022.	
WS2332/G **Ongentys-** **EMEA/H/C/002790/WS2332/0051/G** **Ontilyv-** **EMEA/H/C/005782/WS2332/0005/G** Bial - Portela & Cª, S.A., Lead Rapporteur: Martina Weise Opinion adopted on 22.09.2022.	Positive Opinion adopted by consensus on 22.09.2022.

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

ADCETRIS - brentuximab vedotin - EMEA/H/C/002455/II/0103, Orphan Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.8 and 5.1 of the SmPC to reflect new safety and efficacy information based on long-term data from the second interim analysis of OS (103 events) from study ECHELON-1, undertaken in previously untreated CD30+ Stage IV HL. In addition, following the completion of all specific obligations and considering the recent switch from a conditional to a full MA (variation II-99), the MAH takes the opportunity to propose the removal of the black triangle (regarding additional monitoring) from the SmPC and the Package Leaflet. Further, minor editorial changes are proposed in the SmPC and Package Leaflet and the contact details of the local representatives are being updated in the Package Leaflet." Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable.
Avonex - interferon beta-1A - EMEA/H/C/000102/II/0193 Biogen Netherlands B.V., Rapporteur: Maria Concepcion Prieto Yerro, "Update of sections 4.2 and 4.4 of the SmPC in order to update safety information for the paediatric population based on the final results of the Tecfidera Paediatric study (109MS306) (CONNECT - part 1), submitted as part of the PAM procedure P46/089, availability of data from published literature and post-marketing data form Biogen global safety database; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 13.10.2022, 16.06.2022.	Request for supplementary information adopted with a specific timetable.

Benlysta - belimumab - EMEA/H/C/002015/II/0107 GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder, "Update of section 4.4 of the SmPC based on final results from study 205646; this is an interventional Phase III Study to Evaluate the Efficacy and Safety of Belimumab Administered in Combination with Rituximab to Adult Subjects with Systemic Lupus Erythematosus (SLE). In addition, the MAH took the opportunity to implement editorial changes." Request for Supplementary Information adopted on 29.09.2022.	Request for supplementary information adopted with a specific timetable.
Betaferon - interferon beta-1b - EMEA/H/C/000081/II/0143/G Bayer AG, Rapporteur: Martina Weise, "Update of sections 4.4 and 4.8 of the SmPC based on pooled clinical trial data from six phase II-IV studies: NASPMS (Study No. 3112), Pivotal RRMS (Study No. 13103), EUSPMS (Study No.93079), BENEFIT (Study No. 304747), BEYOND (Study No. 306440) and BEYOND pilot (Study No. 307000), post-marketing experience, scientific literature and FAERS database; the Package Leaflet is updated accordingly. Update of section 4.8 of the SmPC in order to merge the existing two tables for ADRs, requested by the PRAC following the assessment of PSUSA procedure EMEA/H/C/PSUSA/00001759/202107), based on pooled data from four placebo controlled trials: NASPMS (Study No. 3112), Pivotal RRMS (Study No. 13103), EUSPMS (Study No. 93079) and BENEFIT (Study No. 304747); the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes and to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 06.10.2022.	Request for supplementary information adopted with a specific timetable.
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0139 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC of COMIRNATY 30 µg concentrate for dispersion for injection and COMIRNATY 30 µg dispersion for injection as well as section 4.8	Request for supplementary information adopted with a specific timetable. See 9.1

of the SmPC of COMIRNATY 10 µg concentrate for dispersion for injection in order to update information based on six month post (booster) dose three interim report data in patients aged 16 years of age and above from studies C4591001 and C4591031. Study C4591001 is a phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals, while study C4591031 is a phase 3 master protocol to evaluate additional dose(s) of BNT162b2 in healthy individuals previously vaccinated with BNT162b2." Request for Supplementary Information adopted on 13.10.2022.	
Esperoct - turoctocog alfa pegol - EMEA/H/C/004883/II/0013 Novo Nordisk A/S, Rapporteur: Andrea Laslop, "Update of section 4.2 of the SmPC in order to delete the statement in reference to previously untreated patients (PUPs) and section 5.1 of the SmPC in order to update information based on final results from study NN7088-3908; this is an open-label single-arm multicentre non-controlled phase 3a trial investigating safety and efficacy of turoctocog alfa pegol (N8-GP) in prophylaxis and treatment of bleeding episodes in previously untreated paediatric patients with severe haemophilia A. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted on 13.10.2022, 21.07.2022.	Request for supplementary information adopted with a specific timetable.
Extavia - interferon beta-1b - EMEA/H/C/000933/II/0116/G Novartis Europharm Limited, Informed Consent of Betaferon, Rapporteur: Martina Weise, "Update of sections 4.4 and 4.8 of the SmPC in order to expand the language regarding the risk of injection site infection; the Package Leaflet is updated accordingly. Update of section 4.8 of the SmPC to merge the existing two tables for ADRs that occurred during clinical trials and those reported post-marketing, requested by PRAC following the assessment of PSUSA procedure (PSUSA/00001759/202107); the Package Leaflet is updated accordingly. In addition, the	Request for supplementary information adopted with a specific timetable.

MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted on 13.10.2022.	
Eylea - aflibercept - EMEA/H/C/002392/II/0080 Bayer AG, Rapporteur: Alexandre Moreau, "Update of sections 4.2 and 5.1 of the SmPC in order to allow the individualisation of the treatment posology for intravitreal aflibercept in diabetic macular edema (DME) indication based on a propensity-score-matching (PSM) analyses on patient-level-data comparison of the two pivotal studies in DME (VIVID & VISTA) versus the independently conducted Protocol T study as well as supporting data from a systematic literature review and confirmatory data from the recently completed VIOLET Phase 3b study. The Package Leaflet is updated accordingly." Opinion adopted on 13.10.2022. Request for Supplementary Information adopted on 23.06.2022.	Positive Opinion adopted by consensus on 13.10.2022.
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0075 Janssen-Cilag International N.V., Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC to incorporate information specific for dose modifications for non-cardiac events and events of cardiac failure or cardiac arrhythmias events based on data pool from clinical studies which included 4 Phase II (PCYC-1102-CA, PCYC-1104-CA, PCYC-1118E, PCYC-1142-CA) and 8 Phase III studies (PCYC-1112-CA, PCYC-1115-CA, CLL3001, PCYC-1130-CA, MCL3001, PCYC-1127-CA, CLL3011, and MCL3002)." Opinion adopted on 13.10.2022. Request for Supplementary Information adopted on 21.07.2022.	Positive Opinion adopted by consensus on 13.10.2022. See 9.1
Imfinzi - durvalumab - EMEA/H/C/004771/II/0050 AstraZeneca AB, Rapporteur: Aaron Sosa Mejia, "Update of section 5.1 of the SmPC in order to include the most recent overall survival (OS) data based on final results from the CASPIAN study (D419QC00001). This is a phase III, randomized, multicenter, open-label, comparative study to determine the efficacy of durvalumab or durvalumab and tremelimumab in combination with platinum-based	Positive Opinion adopted by consensus on 29.09.2022.

chemotherapy for the first-line treatment in patients with extensive disease small-cell lung cancer (SCLC)." Opinion adopted on 29.09.2022.	
Jardiance - empagliflozin - EMEA/H/C/002677/II/0071 Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC based on a meta-analysis report for the non-interventional study EMPRISE–Europe and Asia (1245.195), undertaken to assess the effectiveness and safety of empagliflozin compared with DPP-4 inhibitors in adult patients with type 2 diabetes. The MAH took the opportunity to implement minor editorial changes in the SmPC and Package Leaflet and to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 22.09.2022.	Request for supplementary information adopted with a specific timetable.
JCOVDEN - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0047/G Janssen-Cilag International N.V., Rapporteur: Christophe Focke, "Submission of the final reports from the non-clinical studies TV-TEC-207316, TV-TEC-207437, TOX15155, TV-TEC-215524 and TOX15252, listed as category 3 in the RMP. These are non-clinical studies conducted to further characterise the potential mechanisms underlying the important identified risks of thrombosis with thrombocytopenia syndrome (TTS) and thrombocytopenia, including immune thrombocytopenia (ITP)." Opinion adopted on 13.10.2022. Request for Supplementary Information adopted on 23.06.2022.	Positive Opinion adopted by consensus on 13.10.2022.
Koselugo - selumetinib - EMEA/H/C/005244/II/0006/G, Orphan AstraZeneca AB, Rapporteur: Alexandre Moreau, "Submission of the reports for the long-term efficacy and safety updates from study D1532C00057: SPRINT Phase I and SPRINT Phase II Stratum 1 which represent the Specific Obligations SOB/003 and SOB/002, respectively, listed in the Annex II of the Product Information. SPRINT is a phase I/II study of the mitogen activated protein kinase (MEK) 1 inhibitor selumetinib (AZD6244; HYD-	Positive Opinion adopted by consensus on 13.10.2022.

Sulfate) in children with neurofibromatosis type 1 (NF1) and inoperable plexiform neurofibromas (PN)." Opinion adopted on 13.10.2022. Request for Supplementary Information adopted on 21.07.2022.	
LIBTAYO - cemiplimab - EMEA/H/C/004844/II/0031 Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Aaron Sosa Mejia, "Update of sections 4.8 and 5.1 of the SmPC in order to update the list of adverse drug reactions (ADRs) and efficacy information based on final results from study R2810-ONC-1540 in order to fulfil REC/005; this is a nonrandomized, multicenter, phase 2 study of cemiplimab in patients with advanced cutaneous squamous cell carcinoma; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Opinion adopted on 06.10.2022.	Positive Opinion adopted by consensus on 06.10.2022.
LIBTAYO - cemiplimab - EMEA/H/C/004844/II/0032 Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Aaron Sosa Mejia, "Update of sections 4.8 and 5.1 of the SmPC in order to update the list of adverse drug reactions (ADRs) and efficacy results for the BCC indication based on the primary analysis data from study R2810-ONC-1620 listed in the Annex II; this is a phase 2 study of cemiplimab in patients with advanced basal cell carcinoma who experienced progression of disease on hedgehog pathway inhibitor therapy or were intolerant of prior hedgehog pathway inhibitor therapy. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Opinion adopted on 06.10.2022.	Positive Opinion adopted by consensus on 06.10.2022.
Methylthioninium chloride Proveblue - methylthioninium chloride - EMEA/H/C/002108/II/0052/G Provepharm SAS, Rapporteur: Kristina Dunder, "Update of sections 4.2 and 5.2 of the SmPC in order to change the posology recommendations in patients with renal and hepatic impairment and update the pharmacokinetic information respectively, based on results from: an open-label, parallel group, population-matched,	Positive Opinion adopted by consensus on 13.10.2022.

single-dose study to investigate the influence of renal impairment on the pharmacokinetics of ProvayBlue (Study Report PVP-2016006). The package leaflet and labelling are updated accordingly. The MAH takes this opportunity to update the Product Information according to the QRD template v10.2. Update of sections 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information with other medicinal products and update the pharmacokinetic information respectively, based on results from: an open-label, randomized, two-period, crossover study to assess the effect of a single dose of methylene blue 5 mg/ml on the pharmacokinetics of the probe drugs midazolam, caffeine, warfarin, omeprazole and dextromethorphan in healthy subjects (Study Report PVP-2016004). The package leaflet and labelling are updated accordingly." Opinion adopted on 13.10.2022. Request for Supplementary Information adopted on 21.07.2022, 22.04.2022, 16.12.2021.	
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 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, section 4.9 of the SmPC was updated to include further guidance with regards to overdose and the MAH also took the opportunity to update section 5.1 of the SmPC to update the internet website address of the Pompe Registry." Opinion adopted on 06.10.2022. Request for Supplementary Information adopted on 10.06.2022, 07.04.2022, 20.01.2022.	Positive Opinion adopted by consensus on 06.10.2022.
NUVAXOVID - SARS-CoV-2, spike protein, recombinant, expressed in Sf9 cells derived from Spodoptera frugiperda - EMEA/H/C/005808/II/0011/G Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege, "C.I.13 (Type II): Submission of the	Positive Opinion adopted by consensus on 13.10.2022.

final clinical report from study 2019nCoV-101 (Part 1), a Phase 1/2, Randomized, Observer-Blinded Study to Evaluate the Safety and Immunogenicity of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine (SARS-CoV-2 rS) With or Without Matrix-M Adjuvant in Healthy Subjects (NCT04368988). This submission addresses the post-authorisation measures MEA 009, REC 041 and REC 042." Opinion adopted on 13.10.2022. Request for Supplementary Information adopted on 21.07.2022.	
Onpattro - patisiran - EMEA/H/C/004699/II/0025, Orphan Alnylam Netherlands B.V., Rapporteur: Kristina Dunder, "Update of sections 4.2 and 5.1 of the SmPC based on interim results from study ALN-TTR02-006 listed as a category 3 study in the RMP; this is a multicenter, open-label, extension study to evaluate the long-term safety and efficacy of patisiran in patients with familial amyloidotic polyneuropathy who have completed a prior clinical study with patisiran. In addition, the MAH took the opportunity to update section 3 of the SmPC in order to update the pH ." Request for Supplementary Information adopted on 06.10.2022, 23.06.2022.	Request for supplementary information adopted with a specific timetable.
Padcev - enfortumab vedotin - EMEA/H/C/005392/II/0002 Astellas Pharma Europe B.V., Rapporteur: Aaron Sosa Mejia, "Submission of the final report from study "An Open-label, Randomized Phase 3 Study to Evaluate Enfortumab Vedotin vs Chemotherapy in Subjects with Previously Treated Locally Advanced or Metastatic Urothelial Cancer" (EV-301) listed as a category 3 study. EV-301 is a global, open-label, randomized phase 3 study in adult subjects with locally advanced or metastatic UC who had received a platinum-containing chemotherapy and had experienced disease progression or relapse during or following treatment with PD-1 or PD-L1 inhibitors." Opinion adopted on 22.09.2022.	Positive Opinion adopted by consensus on 22.09.2022.
Paxlovid - (1r,2s,5s)-n-((1s)-1-cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2s)-	Request for supplementary information adopted with a specific timetable.

3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973/II/0010/G Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, "Update of section 4.8 of the SmPC to add hypersensitivity to the list of adverse drug reactions with frequency common, based on a cumulative search of the MAH safety database; the Package Leaflet is updated accordingly. Update of section 4.5 of the SmPC in order to add drug-drug interaction information with dabigatran (P-gp substrate) based on the clinical study results from study C4671012, a pharmacokinetic study to estimate the effect of Paxlovid on the pharmacokinetics of dabigatran; the Package Leaflet is updated accordingly. Update of section 4.5 of the SmPC in order to update the drug-drug interaction information of midazolam based on the clinical study results from study C4671013, a pharmacokinetic study to estimate the effect of Paxlovid on the pharmacokinetics of midazolam. The MAH is taking the opportunity to include editorial updates in sections 4.3 and 6.1 of the SmPC." Request for Supplementary Information adopted on 06.10.2022, 23.06.2022.	
Paxlovid - (1r,2s,5s)-n-((1s)-1-cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2s)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973/II/0016/G Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, "Update of section 4.8 of the SmPC in order to include the adverse drug reactions: nausea with frequency common, abdominal pain with frequency uncommon and malaise with frequency rare; based on the global safety database of the MAH and literature review. The Package Leaflet is updated accordingly." Opinion adopted on 13.10.2022. Request for Supplementary Information adopted on 01.09.2022.	Positive Opinion adopted by consensus on 13.10.2022.
Pegasys - peginterferon alfa-2A - EMEA/H/C/000395/II/0112 Zr Pharma& GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update	Positive Opinion adopted by consensus on 29.09.2022.

of section 4.8 of the SmPC in order to include information on post-treatment recovery in growth based on final results from study YV25718 listed as a category 3 study in the RMP; this is a Phase IIIb parallel group, open label study of pegylated interferon alfa-2a monotherapy (PEG-IFN, RO0258310) compared to untreated control in children with HBeAg-Positive Chronic Hepatitis B in the immune active phase. The RMP version 9.1 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in the Package Leaflet." Opinion adopted on 29.09.2022. Request for Supplementary Information adopted on 07.07.2022.	
Plenadren - hydrocortisone - EMEA/H/C/002185/II/0038 Takeda Pharmaceuticals International AG Ireland Branch, Rapporteur: Kristina Dunder, "Update of section 4.4 of the SmPC in order to add a warning on pheochromocytoma crisis. 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 implement other minor editorial corrections in the Annexes." Opinion adopted on 13.10.2022.	Positive Opinion adopted by consensus on 13.10.2022.
Regkirona - regdanvimab - EMEA/H/C/005854/II/0005 Celltrion Healthcare Hungary Kft., Rapporteur: Filip Josephson, "Submission of the final clinical study report for the study CT-P59 3.2 Part 2; a randomised, placebo controlled, double-blind study used to evaluate the efficacy and safety of Regkirona submitted in the initial marketing authorisation." Opinion adopted on 13.10.2022. Request for Supplementary Information adopted on 21.07.2022.	Positive Opinion adopted by consensus on 13.10.2022.
Retsevmo - selpercatinib - EMEA/H/C/005375/II/0016 Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, "Update of section 4.8 of the SmPC in order to add chylothorax and chylous ascites to the list of adverse drug reactions (ADRs) based on a review of adverse events. The Package Leaflet is updated accordingly."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 06.10.2022.	
Retsevmo - selpercatinib - EMEA/H/C/005375/II/0017 Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, "Update of section 4.5 of the SmPC in order to update drug-drug interaction information based on the final results from study J2G-MC-JZJV; this is a phase 1, single-center, open-label, drug-drug interaction (DDI) study to investigate the effect of selpercatinib on the pharmacokinetic profiles of dabigatran, a P-glycoprotein (P-gp) substrate, in healthy volunteers. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 06.10.2022.	Request for supplementary information adopted with a specific timetable.
Ronapreve - casirivimab / imdevimab - EMEA/H/C/005814/II/0007 Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2, 4.4, 5.1 and 5.2 of the SmPC in order to introduce the proposed dose for SARS-CoV-2 Omicron BA.2, BA.2.12.1, BA.4, and BA.5 subvariants along with dose preparation and infusion instructions for treatment of outpatients and post-exposure prophylaxis as well as to update efficacy and pharmacokinetic information based on pharmacokinetic (PK) modelling data from R10933-PK-21187-SR-01V2 and R10933-R10987-4800mgIV-KRM and in vitro viral neutralisation data from the updated virus neutralisation report R10933-PH-20091-SR-01V7 and its addendum; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable. See 9.1
TAGRISSO - osimertinib - EMEA/H/C/004124/II/0047 AstraZeneca AB, Rapporteur: Blanca Garcia-Ochoa, "Update of section 5.2 of the SmPC based on final results from studies ODIN-BM and ODIN-HV; these are two phase I clinical pharmacology studies conducted in EGFRm+ NSCLC patients (ODIN-BM) and healthy volunteers (ODIN-HV) to determine osimertinib	Positive Opinion adopted by consensus on 06.10.2022.

blood-brain barrier (BBB) penetration and brain distribution in patients with brain metastases and healthy volunteers with an intact BBB, respectively." Opinion adopted on 06.10.2022. Request for Supplementary Information adopted on 07.07.2022.	
Taxotere - docetaxel - EMEA/H/C/000073/II/0141 Sanofi Mature IP, Rapporteur: Alexandre Moreau, "Update of sections 4.4, 4.6 and 5.3 of the SmPC to include further information regarding genotoxicity, pregnancy/lactation exposure with associated adverse outcomes and recommendations regarding use of contraception, and update of section 5.2 of the SmPC regarding the pharmacokinetic terminal elimination half-life (t1/2). The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable.
Toviaz - fesoterodine - EMEA/H/C/000723/II/0063 Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro, "C.I.3 Update of sections 4.2, 5.1 and 5.2 of the SmPC with the results from study A0221047, to evaluate the safety and efficacy of fesoterodine in subjects aged 6 to 17 years with neurogenic detrusor overactivity as requested in the outcome of EMEA/H/C/000723/P46/030.1. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.1." Opinion adopted on 06.10.2022. Request for Supplementary Information adopted on 23.06.2022, 03.03.2022, 14.10.2021.	Positive Opinion adopted by consensus on 06.10.2022.
Translarna - ataluren - EMEA/H/C/002720/II/0068, Orphan PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC in order to update efficacy information upon the request by the CHMP following the outcome of P46/026 based on final results from study PTC124-GD-045-DMD (Study 045); this is an open-label, single-arm, phase 2 study designed to evaluate the	Request for supplementary information adopted with a specific timetable.

ability of ataluren treatment to increase dystrophin protein levels in muscle cells of subjects with nonsense mutation duchenne muscular dystrophy (nmDMD).” Request for Supplementary Information adopted on 06.10.2022.	
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. In addition, the MAH is taking this opportunity to introduce editorial changes in the SmPC and to update the list of local representatives in the Package Leaflet.” Opinion adopted on 22.09.2022. Request for Supplementary Information adopted on 16.06.2022, 17.02.2022.	Positive Opinion adopted by consensus on 22.09.2022.
Veklury - remdesivir - EMEA/H/C/005622/II/0037/G Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, “Grouped variations to update sections 4.5 and 5.2 of the SmPC to update prescribing information related to interactions with other medicinal products, effect of intrinsic factors and COVID-19 disease on the pharmacokinetics (PK) of Veklury and its metabolites in the adult population. This variation covers the Recommendations 9, 11, 12 and 13 listed at the time of the conditional marketing authorisation (EMEA/H/C/005622/0000) for Veklury. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some linguistic amendments.” Opinion adopted on 13.10.2022. Request for Supplementary Information adopted on 23.06.2022.	Positive Opinion adopted by consensus on 13.10.2022.

Veltassa - patiromer - EMEA/H/C/004180/II/0029 Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Jayne Crowe, "Update of sections 4.2 and 4.5 of the SmPC in order to introduce new drug-drug interaction information based on results from four in vitro studies: RLY-TR-0174, titled "In Vitro Evaluation of Potential RLY5016S and Immunosuppressant Drug-Drug Interactions"; RLY-TR-018, titled "In Vitro Evaluation of Potential Drug-Drug Interactions Between Patiromer and Sevelamer Hydrochloride"; "In Vitro Evaluation of Drug-Drug Interactions of commonly prescribed renal and cardiovascular Drugs with Patiromer DS" and "Drug-drug interactions of commonly prescribed renal and cardiovascular Drugs with Patiromer DS in a simulated GI tract passage study". The Package Leaflet is updated accordingly." Opinion adopted on 06.10.2022. Request for Supplementary Information adopted on 01.09.2022, 19.05.2022.	Positive Opinion adopted by consensus on 06.10.2022.
Xarelto - rivaroxaban - EMEA/H/C/000944/II/0096 Bayer AG, Rapporteur: Kristina Dunder, "Submission of the final report from study 15786 (COMPASS LTOLE). This is a phase 3, multicenter, randomized, double-blind, double-dummy, active comparator, event-driven study, in which subjects were randomized 1:1:1 to rivaroxaban 2.5 mg bid/ASA 100 mg od, or rivaroxaban 5 mg bid, or ASA 100 mg od." Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable.
WS2241/G **Advagraf- EMEA/H/C/000712/WS2241/0065/G** **Modigraf- EMEA/H/C/000954/WS2241/0039/G** Astellas Pharma Europe B.V., Lead Rapporteur: Jayne Crowe, "Update of sections 4.4, 4.5 and 4.8 of the SmPC in order to add a warning on the adverse reaction Thrombotic microangiopathy (TMA) based on a cumulative review of fatal cases of TMA during treatment with tacrolimus, requested by the PRAC following the assessment of the PSUR (EMEA/H/C/00002839/202103).	Positive Opinion adopted by consensus on 06.10.2022.

Update of section 4.5 of the SmPC in order to add the drug-drug interaction between tacrolimus and caspofungin based on post-marketing safety report and literature. Update of section 5.2 of the SmPC in order to add that tacrolimus is metabolised by the cytochrome P450-3A5 (CYP3A5) based on post-marketing safety report and literature. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement some editorial changes. ” Opinion adopted on 06.10.2022. Request for Supplementary Information adopted on 10.06.2022.	
WS2244 **Nuwiq-EMEA/H/C/002813/WS2244/0048** **Vihuma-EMEA/H/C/004459/WS2244/0030** Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus, “Update of sections 4.8 and 5.1 of the SmPC in order to add safety and efficacy data based on the final CSR from the category 3 study GENA-21b; a prospective, open-label, multicentre phase 3b study to assess the efficacy and safety of personalized prophylaxis with Human-cl rhFVIII in previously treated adult patients with severe haemophilia A. Further, upon request by the CHMP following the assessment of study GENA-05 (P46 013 and P46 014), the MAH is updating the numbers of evaluated subjects in SmPC section 4.8 and is removing of the sentence “A prospective open-label clinical study in PUPs with severe haemophilia A (<1% FVIII:C) is ongoing” in section 5.1 of the SmPC. The Package Leaflet is updated accordingly.” Opinion adopted on 13.10.2022. Request for Supplementary Information adopted on 01.09.2022, 16.06.2022, 05.05.2022.	Positive Opinion adopted by consensus on 13.10.2022. See 9.1
WS2321 **CONTROLOC Control-EMEA/H/C/001097/WS2321/0040** **PANTOZOL Control-EMEA/H/C/001013/WS2321/0042** **SOMAC Control-EMEA/H/C/001098/WS2321/0041** Takeda GmbH, Lead Rapporteur: Silvijus Abramavicius, “Update of sections 4.4 and 4.8 of the SmPC in order to add “Severe Cutaneous	Request for supplementary information adopted with a specific timetable.

Adverse Reactions (SCARs)" information and to add "Acute Generalised Exanthematous Pustulosis (AGEP)" to the list of adverse drug reactions (ADRs) with frequency "not know" based on post-marketing experience, adverse reaction databases and literature; the Package Leaflet is updated accordingly. In addition, the MAH proposes to update section 4.5 of the SmPC to introduce information regarding Drug-Laboratory Interactions. Furthermore, the MAH took the opportunity to implement editorial changes and to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 06.10.2022.	
WS2334 **Dovato-EMEA/H/C/004909/WS2334/0034** **Juluca-EMEA/H/C/004427/WS2334/0046** **Tivicay-EMEA/H/C/002753/WS2334/0082** **Triumeq-EMEA/H/C/002754/WS2334/0108** ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC in order to update information on pregnancy and breast-feeding based on supporting published medical literature data on DolPHIN-1 (Dolutegravir in pregnant HIV mothers and their neonates, NCT02245022). In addition, administrative changes were included in section 5.3 of the SmPC of Tivicay and Juluca." Opinion adopted on 22.09.2022.	Positive Opinion adopted by consensus on 22.09.2022.
WS2336 **Gardasil-EMEA/H/C/000703/WS2336/0100** **Gardasil 9-EMEA/H/C/003852/WS2336/0058** Merck Sharp & Dohme B.V., Lead Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC to add the effect of vaccination campaigns on the reduction in the incidence of Juvenile-onset Recurrent Respiratory Papillomatosis (JoRRP) based upon published observational studies. In addition, the MAH took the opportunity to introduce minor editorial changes to the SmPC." Opinion adopted on 13.10.2022.	Positive Opinion adopted by consensus on 13.10.2022.
WS2342/G **Prezista-**	Request for supplementary information adopted with a specific timetable.

EMEA/H/C/000707/WS2342/0119/G Rezolsta- EMEA/H/C/002819/WS2342/0049/G Symtuza- EMEA/H/C/004391/WS2342/0046/G Janssen-Cilag International N.V., Lead Rapporteur: Johann Lodewijk Hillege, "Update of section 4.8 of the SmPC in order to add 'crystal nephropathy' to the list of adverse drug reactions (ADRs) with frequency rare based on recent post-marketing data; the Package Leaflets are updated accordingly. In addition, the MAH proposes to update sections 4.4 and 4.6 of the SmPC in order to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding; the Package Leaflets are updated accordingly." Request for Supplementary Information adopted on 29.09.2022.	

B.5.3. CHMP-PRAC assessed procedures

Apexxnar - pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - EMEA/H/C/005451/II/0002 Pfizer Europe MA EEIG, Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Jean-Michel Dogné, "Update of sections 4.5, 4.8 and 5.1 of the SmPC to add information regarding the co-administration of Apexxnar with seasonal quadrivalent influenza vaccine (QIV) based on final study results from study B7471004, "A Phase 3, Randomized, Double-Blind Trial to Evaluate the Safety and Immunogenicity of a 20 valent Pneumococcal Conjugate Vaccine (20vPnC) When Coadministered with Seasonal Inactivated Influenza Vaccine (SIIV) in Adults ≥65 Years of Age." listed as a category 3 study in the RMP. The Package Leaflet is updated accordingly. The updated RMP version 1.1 has also been submitted." Opinion adopted on 13.10.2022. Request for Supplementary Information adopted on 21.07.2022, 19.05.2022.	Positive Opinion adopted by consensus on 13.10.2022.
EVUSHELD - tixagevimab / cilgavimab - EMEA/H/C/005788/II/0003 AstraZeneca AB, Rapporteur: Jan Mueller-	Request for supplementary information adopted with a specific timetable.

Berghaus, PRAC Rapporteur: Kimmo Jaakkola, "Update of sections 4.2, 4.8, 4.9, 5.1 and 5.2 of the SmPC in order to change the posology recommendations in the pre-exposure prophylaxis indication based on study TACKLE (D8851C00001). The Package Leaflet is updated accordingly. The RMP version 2 has also been submitted." Request for Supplementary Information adopted on 13.10.2022.	See 9.1
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." Request for Supplementary Information adopted on 29.09.2022, 07.07.2022, 10.03.2022.	Request for supplementary information adopted with a specific timetable.
Fintepla - fenfluramine - EMEA/H/C/003933/II/0015, Orphan Zogenix ROI Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, "To update sections 4.2 and 5.2 of the SmPC to update the safety information based on final results from study ZX008-1903 listed as a category 3 study in the RMP; this is a Phase 1, Open-Label, Single-Dose Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of ZX008 (Fenfluramine Hydrochloride) in Subjects with Varying Degrees of Hepatic Impairment. The primary objective of this study was to compare the PK of a single dose of ZX008 (fenfluramine HCl) in subjects with varying degrees of hepatic impairment with that of healthy matched control subjects.	Request for supplementary information adopted with a specific timetable.

The updated RMP version 2.7 has also been submitted." Request for Supplementary Information adopted on 29.09.2022.	
GIVLAARI - givosiran - EMEA/H/C/004775/II/0011/G, Orphan Alnylam Netherlands B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Martin Huber, "Update of section 5.3 of the SmPC based on final results from study AS1-GLP18-007 listed as a category 3 study in the RMP; This is a 104-week Subcutaneous Injection Carcinogenicity Study in Sprague Dawley Rats. Update of section 5.3 of the SmPC based on final results from study AS1-GLP18-004; This is a 26-week Subcutaneous Injection Carcinogenicity Study in TgRasH2 Mice. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 29.09.2022.	Request for supplementary information adopted with a specific timetable.
GIVLAARI - givosiran - EMEA/H/C/004775/II/0013/G, Orphan Alnylam Netherlands B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Martin Huber, "Submission of the final reports from studies ALN-AS1-003 (Study 003) and ALN-AS1-002 (Study 002) listed as a category 3 studies in the RMP. Study 003 is a phase 3 randomized, double-blind, placebo-controlled multicenter study with an open-label extension to evaluate the efficacy and safety of givosiran in patients with acute hepatic porphyrias, while study 002 is a multicenter, open-label extension study to evaluate the long-term safety and clinical activity of subcutaneously administered ALN AS1 in patients with acute intermittent porphyria who have completed a previous clinical study with ALN-AS1. The RMP version 2.2 has also been submitted." Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable.
Invokana - canagliflozin - EMEA/H/C/002649/II/0060 Janssen-Cilag International N.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber,	Positive Opinion adopted by consensus on 29.09.2022.

"Submission of the final report from non-clinical studies 1 and 2, listed as category 3 studies in the RMP, in order to fulfil MEA/007.2. Nonclinical study 1 was designed to evaluate the effects of canagliflozin on ketone clearance and production; nonclinical study 2 objective is to evaluate the effects of canagliflozin on ketone clearance and production during prolonged fast. The RMP version 9.1 has also been submitted." Opinion adopted on 29.09.2022.	
Jyseleca - filgotinib - EMEA/H/C/005113/II/0018 Galapagos N.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of sections 4.4, 4.6 and 5.1 of the SmPC in order to update information on fertility based on interim results from studies GLPG0634-CL-227 (MANTA Ray) and GS-US-418-4279 (MANTA) listed as a category 3 study in the RMP. The Package Leaflet and Annex II are updated accordingly. The RMP version 4.1 has also been submitted." Opinion adopted on 29.09.2022. Request for Supplementary Information adopted on 01.09.2022.	Positive Opinion adopted by consensus on 29.09.2022.
Kaftrio - ivacaftor / tezacaftor / elexacaftor - EMEA/H/C/005269/II/0017/G, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber, "C.I.4 Update of section 5.3 of the SmPC in order to update the non-clinical information based on final results from a 2-year oral carcinogenicity study in rats (VX-445-TX-015) evaluating the carcinogenic potential of up to 10 mg/kg/day of elexacaftor. An updated RMP (version 6.0) has also been submitted to include the completion of the 2-year carcinogenicity study in rats as well as to update the post-market pregnancy safety information collection form following EMEA/H/C/WS2048. C.I.13 To submit the final report of Tezacaftor Juvenile Toxicity study (VX-661-TX-038)." Opinion adopted on 29.09.2022. Request for Supplementary Information adopted on 07.07.2022, 05.05.2022, 10.02.2022.	Positive Opinion adopted by consensus on 29.09.2022.

Kisplyx - lenvatinib - EMEA/H/C/004224/II/0052 Eisai GmbH, Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: David Olsen, "Update of section 4.8 of the SmPC based on pooled safety data including results of study 307, an ongoing, multicenter, randomised, open-label study that is being conducted to compare the efficacy and safety of lenvatinib in combination with everolimus or pembrolizumab versus sunitinib as first-line (1L) treatment in adults with advanced renal cell carcinoma (RCC). The provision of the CSR addresses the post-authorisation measure MEA/FSR 009.3. The Package Leaflet is updated accordingly. An updated RMP version 15.0 has been submitted." Request for Supplementary Information adopted on 29.09.2022.	Request for supplementary information adopted with a specific timetable.
NINLARO - ixazomib - EMEA/H/C/003844/II/0041, Orphan Takeda Pharma A/S, Rapporteur: Armando Genazzani, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from study NSMM-5001 (INSIGHT) listed as a Specific Obligation in the Annex II of the Product Information. This is a global, prospective, non-interventional, observational study of presentation, treatment patterns, and outcomes in multiple myeloma patients. The Annex II and the RMP (submitted version 9.0) are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted on 29.09.2022.	Request for supplementary information adopted with a specific timetable.
Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0033 AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "Update of section 5.1 of the SmPC based on interim results from the PK/PD study listed as a specific obligation in the Annex II in order to fulfil SOB 1 and SOB 3; this is a PK and PK/PD Analysis of Intravenously Administered Andexanet after dosing to steady state with a factor Xa inhibitor, rivaroxaban or Apixaban, in healthy subjects and patients who have acute major bleeding. In addition, the MAH took the opportunity to implement editorial changes in	Request for supplementary information adopted with a specific timetable.

Annex II of the SmPC. The RMP version 3.0 has also been submitted." Request for Supplementary Information adopted on 13.10.2022.	
Paxlovid - (1r,2s,5s)-n-((1s)-1-cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2s)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973/II/0007 Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Martin Huber, "Submission of the final report from study C4671010 listed as a category 3 study in the RMP. This is a phase I, non-randomized, open label study to assess the pharmacokinetics, safety and tolerability of PF-07321332 boosted with ritonavir in adults with moderate hepatic impairment and individuals with normal hepatic function. The RMP version 2.2 has been approved." Opinion adopted on 29.09.2022. Request for Supplementary Information adopted on 01.09.2022, 10.06.2022.	Positive Opinion adopted by consensus on 29.09.2022.
Polivy - polatuzumab vedotin - EMEA/H/C/004870/II/0018, Orphan Roche Registration GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from study GO29365 listed as a category 3 study in the RMP in order to address MEA/002. This is a phase Ib/II, multicenter, open-label study evaluating the safety, tolerability, and anti-tumour activity of polatuzumab vedotin in combination with rituximab or obinutuzumab plus bendamustine in patients with R/R follicular lymphoma or R/R diffuse large B-cell lymphoma. The RMP version 3.0 has also been submitted." Request for Supplementary Information adopted on 29.09.2022.	Request for supplementary information adopted with a specific timetable.
Scintimun - besilesomab - EMEA/H/C/001045/II/0015 CIS BIO International, PRAC Rapporteur: Maria del Pilar Rayon, "Submission of the final report from the clinical study AG-2012 - Non interventional controlled survey on the impact of Scintimun administered for scintigraphic imaging on diagnostic thinking and management of patient with suspicion of	Positive Opinion adopted by consensus on 29.09.2022.

peripheral osteomyelitis, listed as a category 3 study in the RMP - MEA 08.4. An updated RMP version 15 was submitted." Opinion adopted on 29.09.2022. Request for Supplementary Information adopted on 10.06.2022.	
Trecondi - treosulfan - EMEA/H/C/004751/II/0013, Orphan medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Fátima Ventura, PRAC Rapporteur: Julia Pallos, "Update of section 5.3 of the SmPC in order to update the description of non-clinical information regarding musculoskeletal and connective tissue disorders in form of lympho-histiocytic infiltration in the skeletal muscles and renal and urinary disorders which show up as haematuria. These new determinations are based on results from study LPT 37259. A revised RMP version 1.2 was submitted." Opinion adopted on 29.09.2022. Request for Supplementary Information adopted on 07.07.2022.	Positive Opinion adopted by consensus on 29.09.2022.
Vokanamet - canagliflozin / metformin - EMEA/H/C/002656/II/0064 Janssen-Cilag International N.V., Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, "Submission of the final report from non-clinical studies 1 and 2, listed as category 3 studies in the RMP in order to fulfil MEA/006.2. Nonclinical study 1 was designed to evaluate the effects of canagliflozin on ketone clearance and production; nonclinical study 2 objective is to evaluate the effects of canagliflozin on ketone clearance and production during prolonged fast. The RMP version 9.1 has also been submitted." Opinion adopted on 29.09.2022.	Positive Opinion adopted by consensus on 29.09.2022.
WS2318/G **Ebymect-** **EMEA/H/C/004162/WS2318/0058/G** **Edistride-** **EMEA/H/C/004161/WS2318/0056/G** **Forxiga-** **EMEA/H/C/002322/WS2318/0077/G** **Qtern-** **EMEA/H/C/004057/WS2318/0036/G** **Xigduo-** **EMEA/H/C/002672/WS2318/0068/G** AstraZeneca AB, Lead Rapporteur: Kristina	Request for supplementary information adopted with a specific timetable.

Dunder, Lead PRAC Rapporteur: Mari Thorn, "C.I.4 Update of section 4.4 of the SmPC in order to remove the potential risk of Lower Limb Amputation (LLA) based on studies D1690C00018, D1690C00019, DECLARE, DAPA-HF, DAPA-CKD, and DELIVER. The Package Leaflet are 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. In addition, the MAH took the opportunity to update the list of local representatives in the Qtern Package Leaflet. C.I.11.z Submission of an updated RMP in order to align the EU RMPs for the FDCs Xigduo, Ebymect and Qtern, to recently approved updates to the Forxiga EU RMP. C.I.z Update of section 4.5 of the SmPC to include a further PI harmonisation to address the consideration raised by PRAC and CHMP during the ongoing dapagliflozin procedure PSUSA/00010029/202110. The Forxiga RMP and Edistride RMP version 28 have been submitted. The Qtern RMP version 7 has been submitted. The Xigduo RMP and Ebymect RMP version 13 have been submitted." Request for Supplementary Information adopted on 29.09.2022.	

B.5.4. PRAC assessed procedures

PRAC Led **Cancidas - caspofungin - EMEA/H/C/000379/II/0078** Merck Sharp & Dohme B.V., PRAC Rapporteur: Jo Robays, PRAC-CHMP liaison: Karin Janssen van Doorn, "Submission of an updated RMP version 4.2 in order to remove safety concerns and align it with the EU GVP Module V (Revision 2)." Opinion adopted on 29.09.2022. Request for Supplementary Information adopted on 01.09.2022.	Positive Opinion adopted by consensus on 29.09.2022.
PRAC Led **Entyvio - vedolizumab - EMEA/H/C/002782/II/0073**	Request for supplementary information adopted with a specific timetable.

Takeda Pharma A/S, PRAC Rapporteur: Adam Przybylkowski, PRAC-CHMP liaison: Ewa Balkowiec Iskra, "Submission of the final report from study MLN0002_401 listed as a category 3 study in the RMP in order to fulfil MEA/001.2; this is an international observational prospective cohort study comparing vedolizumab to other biologic agents in patients with ulcerative colitis or Crohn's disease. The RMP version 8.0 has also been submitted." Request for Supplementary Information adopted on 29.09.2022.	
PRAC Led **HEPLISAV B - hepatitis B surface antigen - EMEA/H/C/005063/II/0015** Dynavax GmbH, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from the study HBV-26: Post-Marketing Observational Surveillance Study to Evaluate the Incidence of New-Onset Immune-mediated Diseases, Herpes Zoster, and Anaphylaxis, listed as a category 3 post-authorisation safety study (PASS) in the RMP. This is a post-marketing observational surveillance study comparing the incidence of new-onset immune-mediated diseases, herpes zoster, and anaphylaxis in recipients of HEPLISAV B with recipients of another hepatitis B vaccine. The RMP version 1.3 has also been submitted. The requested variation proposed amendments to the Risk Management Plan (RMP)." Opinion adopted on 29.09.2022. Request for Supplementary Information adopted on 10.06.2022.	Positive Opinion adopted by consensus on 29.09.2022.
PRAC Led **Idacio - adalimumab - EMEA/H/C/004475/II/0017** Fresenius Kabi Deutschland GmbH, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 6 in order to propose a continuation of the observational registry (RABBIT) study #1 (Study Identifier: FKS0-000-RAB) and the cancelation of the observational registry (IBD UK) (Study Identifier: FKS0-000-IBD). In addition, the MAH took the opportunity to align the RMP with the current approved RMP	Positive Opinion adopted by consensus on 29.09.2022.

of the reference product." Opinion adopted on 29.09.2022.	
PRAC Led **Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0090** Genzyme Europe BV, PRAC Rapporteur: Nathalie Gault, PRAC-CHMP liaison: Alexandre Moreau, "Update of SmPC section 4.8 to include the new ADRs "somnolence", "throat irritation" and "infusion site pruritus" with the frequency 'not known', and SmPC section 4.7 to include "somnolence", and "tremor" and "hypotension" for consistency, based on the final report from non-interventional PASS Pompe Safety Sub-Registry - AGLU06909/LTS13930. This final study report is submitted to address the assessment report conclusion of the Pompe registry report 2020 (MEA024.15 and MEA025.15 Annual Pompe Registry Report 2020). The Package Leaflet is updated accordingly." Opinion adopted on 29.09.2022. Request for Supplementary Information adopted on 05.05.2022.	Positive Opinion adopted by consensus on 29.09.2022.
PRAC Led **Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0054** Orexigen Therapeutics Ireland Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of the final report from study NB-542 listed as a category 3 PASS in the RMP. This is a cross-sectional survey aimed to evaluate the effectiveness of the Mysimba Physician Prescribing Checklist (PPC) among physicians in the EU. The RMP version 12.6 has also been submitted." Request for Supplementary Information adopted on 29.09.2022, 10.06.2022, 10.02.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **NUVAXOVID - SARS-CoV-2, spike protein, recombinant, expressed in Sf9 cells derived from Spodoptera frugiperda - EMEA/H/C/005808/II/0022** Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of sections 4.4 and 4.8 of	Positive Opinion adopted by consensus on 29.09.2022.

the SmPC in order to add a new warning on pericarditis and myocarditis and to add pericarditis and myocarditis to the list of adverse drug reactions (ADRs) with frequency not known following the outcome of MEA/014.4 based on PRAC assessment on pericarditis and myocarditis. The Package Leaflet is updated accordingly." Opinion adopted on 29.09.2022.	
PRAC Led **Obizur - susoctocog alfa - EMEA/H/C/002792/II/0049** Baxalta Innovations GmbH, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report for study 241501 listed as a category 2 study in the RMP in order to fulfil SOB/001.4. This is a prospective and retrospective, non-interventional post-authorisation safety study (PASS) to evaluate the safety and effectiveness of Obizur in real-life practice. The RMP version 6.0 has also been submitted." Request for Supplementary Information adopted on 29.09.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **PecFent - fentanyl - EMEA/H/C/001164/II/0054** Kyowa Kirin Holdings B.V., Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of an updated RMP (version 7.1) in line with the outcome of the last PSUR single assessment (PSUSA) procedure (PSUSA 00001369/202004) finalised in January 2021 in order to update the key messages of the educational materials in line with Instanyl (fentanyl). As a result, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated accordingly. Finally, the MAH took the opportunity to bring the RMP in line with revision 2 of GVP module V on 'Risk management systems' and the product information in line with the latest quality review of documents (QRD) template (version 10.2). The requested variation proposed amendments to the Annex II and to the Risk Management Plan (RMP)." Opinion adopted on 29.09.2022. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 29.09.2022.

on 07.07.2022, 10.03.2022, 28.10.2021.	
PRAC Led **Praluent - alirocumab - EMEA/H/C/003882/II/0072** sanofi-aventis groupe, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from study ALIROC07997 listed as a category 3 study in the RMP. This is a post-authorisation safety study (PASS) using healthcare databases to monitor the safety of alirocumab in HIV patients. The RMP version 7.0 has also been submitted." Opinion adopted on 29.09.2022.	Positive Opinion adopted by consensus on 29.09.2022.
PRAC Led **Spikevax - elasomeran - EMEA/H/C/005791/II/0077** Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marie Louise Schougaard Christiansen, PRAC-CHMP liaison: Thalia Marie Estrup Blicher, "Update of section 4.8 of the SmPC to include 'Acute and Delayed urticaria' as an adverse reaction, with the frequency 'Rare', as requested by the PRAC in the 13th Safety Summary Report (EMEA/H/C/005791/MEA/011.12). The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 29.09.2022.	Request for supplementary information adopted with a specific timetable.
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	Positive Opinion adopted by consensus on 29.09.2022.

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." Opinion adopted on 29.09.2022. Request for Supplementary Information adopted on 07.07.2022, 10.03.2022.	
PRAC Led **WS2306** **Aripiprazole Mylan Pharma-EMEA/H/C/003803/WS2306/0020** Mylan Pharmaceuticals Limited, Generic, Generic of Abilify, Lead Rapporteur: Eva Skovlund, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "To align the safety concerns in the RMP with the reference product. In addition, nationally authorised product has been included in the RMP for the company." Request for Supplementary Information adopted on 29.09.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **WS2320** **Stribild-EMEA/H/C/002574/WS2320/0120** **Truvada-EMEA/H/C/000594/WS2320/0177** Gilead Sciences Ireland UC, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "To update Annex II and the RMP for Truvada and Stribild to version 18.1 and 14.1 to remove of the paediatric additional Risk Minimisation Measures (aRMMs) for HIV indication. In addition, the MAH took the opportunity to introduce changes to the PI." Request for Supplementary Information adopted on 29.09.2022.	Request for supplementary information adopted with a specific timetable.

B.5.5. CHMP-CAT assessed procedures

Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0003, ATMP Bristol-Myers Squibb Pharma EEIG, Rapporteur:	Request for supplementary information adopted with a specific timetable.

Concetta Quintarelli, CHMP Coordinator: Armando Genazzani Request for Supplementary Information adopted on 07.10.2022, 15.07.2022.	
Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0057, ATMP Amgen Europe B.V., Rapporteur: Maija Tarkkanen, CHMP Coordinator: Johanna Lähteenvuo, "Update to sections 4.4 and 4.8 of the SmPC to revise the safety instructions regarding the risk of disseminated herpetic infection adverse drug reactions following an MAH review of aggregate safety data of herpetic and disseminated herpetic infections that were reported in patients who were not immunocompromised and those who were immunocompromised. The Package Leaflet is updated accordingly." Opinion adopted on 13.10.2022, 07.10.2022.	Positive Opinion adopted by consensus on 13.10.2022.
Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0053, Orphan, ATMP Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang, "Submission of the results from study CCTL019H2301 (BELINDA) listed as an obligation in the Annex II of the Product Information. This is a randomised open-label parallel-group multicenter Phase III trial to evaluate the efficacy and safety of tisagenlecleucel in adult patients with relapsed or refractory B-cell aggressive NHL after failure of rituximab and anthracycline containing first-line immune-chemotherapy. The Annex II is updated accordingly." Opinion adopted on 13.10.2022, 07.10.2022. Request for Supplementary Information adopted on 13.05.2022.	Positive Opinion adopted by consensus on 13.10.2022. See 9.1
Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0059, Orphan, ATMP Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang, "Update of section 5.1 of the SmPC based on a subgroup analysis from CCTL019B2401 (B2401) disease registry listed as a PAES (ANX006) in the Annex II; this is a non-interventional study to evaluate the efficacy and safety of Kymriah in ALL patients below the age of 3 years.	Positive Opinion adopted by consensus on 13.10.2022. See 9.1

In addition, the MAH took the opportunity to update Annex II.D of the SmPC to reflect the fulfilment of the PAES." Opinion adopted on 13.10.2022, 07.10.2022. Request for Supplementary Information adopted on 15.07.2022.	

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

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

WS2311/G **Advagraf-** **EMEA/H/C/000712/WS2311/0068/G** **Modigraf-** **EMEA/H/C/000954/WS2311/0043/G** Astellas Pharma Europe B.V., Lead Rapporteur: Jayne Crowe Opinion adopted on 06.10.2022.	Positive Opinion adopted by consensus on 06.10.2022.
WS2314 **Aerius-EMEA/H/C/000313/WS2314/0103** **Azomyr-** **EMEA/H/C/000310/WS2314/0107** **Neoclarityn-** **EMEA/H/C/000314/WS2314/0101** Organon N.V., Duplicate, Duplicate of Allex (SRD), Azomyr, Opulis (SRD), Lead Rapporteur: Christophe Focke Opinion adopted on 22.09.2022.	Positive Opinion adopted by consensus on 22.09.2022.
WS2315/G **Biktarvy-** **EMEA/H/C/004449/WS2315/0051/G** **Descovy-** **EMEA/H/C/004094/WS2315/0058/G** **Genvoya-** **EMEA/H/C/004042/WS2315/0084/G** **Odefsey-** **EMEA/H/C/004156/WS2315/0055/G** **Vemlidy-** **EMEA/H/C/004169/WS2315/0041/G** Gilead Sciences Ireland UC, Lead Rapporteur: Bruno Sepodes, Request for Supplementary Information adopted on 06.10.2022.	Request for supplementary information adopted with a specific timetable.
WS2328 **HyQvia-EMEA/H/C/002491/WS2328/0082**	Request for supplementary information adopted with a specific timetable.

Kiovig-EMEA/H/C/000628/WS2328/0119 Takeda Manufacturing Austria AG, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 13.10.2022.	
WS2341 **Aflunov-EMEA/H/C/002094/WS2341/0081** **Foclivia-EMEA/H/C/001208/WS2341/0078** Seqirus S.r.l, Lead Rapporteur: Armando Genazzani Opinion adopted on 29.09.2022.	Positive Opinion adopted by consensus on 29.09.2022.
WS2350/G **Neupro-EMEA/H/C/000626/WS2350/0094/G** UCB Pharma S.A., Lead Rapporteur: Bruno Sepodes Opinion adopted on 13.10.2022.	Positive Opinion adopted by consensus on 13.10.2022.
WS2352 **Mirapexin-EMEA/H/C/000134/WS2352/0103** **Sifrol-EMEA/H/C/000133/WS2352/0094** Boehringer Ingelheim International GmbH, Lead Rapporteur: Thalia Marie Estrup Blicher Request for Supplementary Information adopted on 13.10.2022.	Request for supplementary information adopted with a specific timetable.
WS2354/G **Abseamed-EMEA/H/C/000727/WS2354/0100/G** **Binocrit-EMEA/H/C/000725/WS2354/0099/G** **Epoetin alfa Hexal-EMEA/H/C/000726/WS2354/0099/G** Sandoz GmbH, Lead Rapporteur: Alexandre Moreau Opinion adopted on 13.10.2022.	Positive Opinion adopted by consensus on 13.10.2022.

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

Norvir - ritonavir - EMEA/H/C/000127/II/0163 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.2 of the SmPC in order to modify administration based on final results from three bioavailability and bioequivalence studies: M11-472, M12-279, and M11-475; the Package	The MAH withdrew the procedure on 12.10.2022.

Leaflet and Labelling are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.” Withdrawal request submitted on 12.10.2022.	
GONAL-f - follitropin alfa - EMEA/H/C/000071/II/0154/G Merck Europe B.V., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 21.07.2022, 22.04.2022. Withdrawal request submitted on 30.09.2022.	The MAH withdrew the procedure on 30.09.2022.

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

latanoprost - EMEA/H/C/005933 Reduction of elevated intraocular pressure (IOP)
dabrafenib - EMEA/H/C/005885, Orphan Novartis Europharm Limited, Treatment of glioma
trametinib - EMEA/H/C/005886, Orphan Novartis Europharm Limited, Treatment of paediatric patients aged 1 year and older with glioma
tocilizumab - EMEA/H/C/005984 treatment of rheumatoid arthritis, active systemic juvenile idiopathic arthritis (sJIA), juvenile idiopathic polyarthritis (pJIA), chimeric antigen receptor (CAR) T cell-induced cytokine release syndrome (CRS) and COVID-19
fezolinetant - EMEA/H/C/005851 treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause
zilucoplan - EMEA/H/C/005450, Orphan UCB Pharma S.A., treatment of generalised myasthenia gravis in adults

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

Esperoct - turoctocog alfa pegol - EMEA/H/C/004883/X/0016 Novo Nordisk A/S, Rapporteur: Andrea Laslop,

"Extension application to add two new strengths of 4000 IU and 5000 IU powder and solvent for solution for injection."

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

Boehringer Ingelheim International GmbH, Rapporteur: Finbarr Leacy, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica Mirošević Skvrce, "Extension application to add a new strength of 25 mg soft capsule grouped with a type II variation C.I.6.a to add a new indication of treatment of fibrosing Interstitial Lung Diseases (ILDs) in children and adolescents from 6 to 17 years of age, based on results from study 1199 0337 (InPedILD); a randomised, placebo-controlled, double-blind, multicentre, multinational, phase III clinical trial undertaken to evaluate dose-exposure and safety of nintedanib on top of standard of care in children and adolescents (6 to 17 years old) with clinically significant fibrosing ILD. 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. In addition, the MAH took the opportunity to implement minor editorial changes to the list of local representatives in the Package Leaflet. The updated RMP version 12.0 is also submitted."

Olumiant - baricitinib - EMEA/H/C/004085/X/0035/G

Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski, "Extension application to introduce a new strength (1 mg film-coated tablet), grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment, as monotherapy or in combination with conventional synthetic disease modifying antirheumatic drugs (DMARDs), of active juvenile idiopathic arthritis (JIA) in patients 2 years of age and older who have had an inadequate response or intolerance to one or more prior conventional synthetic or biologic DMARDs, based on final results from the pivotal study JAHV (I4V-MC-JAHV); this is a multicentre, double-blind, randomised, placebo-controlled, medication-withdrawal Phase 3 study in children from 2 years to less than 18 years of age with JIA who have had an inadequate

response or intolerance to treatment with at least 1 cDMARD or bDMARD. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance.
Version 15.1 of the RMP has also been submitted. ”

Viagra - sildenafil -
EMEA/H/C/000202/X/0115
Upjohn EESV, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Maria Concepcion Prieto Yerro, “Extension application to introduce a new pharmaceutical form (orodispersible film).”

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

lenadogene nolparvovec -
EMEA/H/C/005047, Orphan, ATMP
GenSight Biologics S.A., treatment of vision loss due to Leber Hereditary Optic Neuropathy (LHON)
List of Questions adopted on 19.02.2021.

in vitro diagnostic medical device -
EMEA/H/D/006107
In-vitro qualitative immunohistochemical detection of programmed death-ligand 1 (PD-L1)
Request for Supplementary Information adopted on 15.09.2022.

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

Brineura - cerliponase alfa -
EMEA/H/C/004065/S/0038, Orphan
BioMarin International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Mari Thorn

Increlex - mecasermin -
EMEA/H/C/000704/S/0078
Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Kirsti Villikka

Strensiq - asfotase alfa -
EMEA/H/C/003794/S/0059, Orphan
Alexion Europe SAS, Rapporteur: Armando Genazzani, PRAC Rapporteur: Rhea Fitzgerald

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

Aimovig - erenumab -
EMEA/H/C/004447/R/0024
Novartis Europharm Limited, Rapporteur: Kristina Dunder, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Kirsti Villikka

Carmustine Obvius - carmustine -
EMEA/H/C/004326/R/0009
Obvius Investment B.V, Generic, Rapporteur: Elita Poplavska, PRAC Rapporteur: Jan Neuhauser

Hefiya - adalimumab -
EMEA/H/C/004865/R/0038
Sandoz GmbH, Duplicate, Duplicate of Hyrimoz, Rapporteur: Daniela Philadelphy, Co-Rapporteur: Finbarr Leacy, PRAC Rapporteur: Ulla Wändel Liminga

Hyrimoz - adalimumab -
EMEA/H/C/004320/R/0037
Sandoz GmbH, Rapporteur: Daniela Philadelphy, Co-Rapporteur: Finbarr Leacy, PRAC Rapporteur: Ulla Wändel Liminga

Pemetrexed Krka - pemetrexed -
EMEA/H/C/003958/R/0009
KRKA, d.d., Novo mesto, Generic, Generic of Alimta, Rapporteur: Hrefna Gudmundsdottir, PRAC Rapporteur: Tiphaine Vaillant

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

Adempas - riociguat -
EMEA/H/C/002737/II/0037
Bayer AG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola, "Extension of indication to include treatment of pulmonary arterial hypertension (PAH) in paediatric patients aged 6 to less than 18 years of age with WHO Functional Class (FC) I to III in combination with endothelin receptor antagonists with or without prostanoids for ADEMPAS, based on results from pivotal study PATENT-CHILD (Study 15681); this is a Phase III, Open-label, individual dose titration study to

evaluate safety, tolerability and pharmacokinetics of riociguat in children from 6 to less than 18 years of age with PAH; As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 8.1 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."

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

UCB Pharma S.A., Rapporteur: Finbarr Leacy, Co-Rapporteur: Christophe Focke, PRAC Rapporteur: Liana Gross-Martirosyan,

"Extension of indication to include treatment of adults with active axial spondyloarthritis (axSpA), including non-radiographic axial spondyloarthritis (nr-axSpA) and ankylosing spondylitis (AS, radiographic axial spondyloarthritis), based on interim results from two interventional and controlled phase III clinical studies: AS0010 (BE MOBILE 1) and AS0011 (BE MOBILE 2), which provide evidence of the efficacy and safety of bimekizumab in axSpA (nr-axSpA and AS), both compared to placebo treatment. Further supportive data is provided by the results of a phase 2a exploratory study (AS0013), a phase 2b, dose-ranging study (AS0008) and its ongoing follow-on phase 2b open-label extension (OLE) study (AS0009). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.2 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.2 rev.1."

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

UCB Pharma S.A., Rapporteur: Finbarr Leacy, Co-Rapporteur: Christophe Focke, PRAC Rapporteur: Liana Gross-Martirosyan,

"Extension of indication to include treatment of active psoriatic arthritis in adult patients who have had an inadequate response or who have been intolerant to one or more DMARDs for BIMZELX, based on interim results of a Phase III study in biological DMARD naïve study

participants (PA0010; BE OPTIMAL) and the final results of the Phase III study in study participants who are inadequate responders (inadequate response or intolerant) to ≤2 prior TNF inhibitors (PA0011; BE COMPLETE). Both Phase III studies are interventional studies aimed to evaluate the efficacy and safety of bimekizumab. For PA0010, the Initial Treatment Period was placebo- and no inferential active reference (adalimumab)-controlled, while PA0011 was placebo-controlled. Further supportive data comprise the results of a Phase 1 study (PA0007), a Phase 2b dose-finding study (PA0008) and a Phase 2 open label extension study (PA0009). A Phase 3 open-label extension study is currently ongoing (PA0012). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC have been updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.2 rev.1. As part of the application the MAH is requesting a 1-year extension of the market protection." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)	
NexoBrid - concentrate of proteolytic enzymes enriched in bromelain - EMEA/H/C/002246/II/0058, Orphan MediWound Germany GmbH, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, "Extension of current indication for removal of eschar in adults with deep partial- and full-thickness thermal burns to the paediatric population for NexoBrid based on interim results from study MW2012-01-01 (CIDS study), listed as study MW2012-01-01 is a 3-stage, multi-centre, multi-national, randomised, controlled, open label, 2 arm study aiming to demonstrate the superiority of NexoBrid treatment over SOC treatment in paediatric patients (aged 0 to 18 years) with deep partial thickness (DPT) and full thickness (FT) thermal burns of 1% to 30% of total body surface area (TBSA). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated accordingly. Version 9 of the RMP has also been submitted."	

OPDIVO - nivolumab - EMEA/H/C/003985/II/0125/G

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

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

Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension of indication to include treatment of new indication for slowing the rate of decline in pulmonary function in adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) for RoActemra, based on final results from the pivotal Phase III study WA29767 (focuSSced) entitled, "A Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Assess the Efficacy and Safety of Tocilizumab Versus Placebo in Patients With Systemic Sclerosis" and the supportive Phase II/III study WA27788 (faSScinate) entitled, "A Phase II/III, Multicenter, Randomized, Double-blind, Placebo-controlled Study To Assess The Efficacy And Safety Of Tocilizumab Versus Placebo In Patients With Systemic Sclerosis".
As a consequence, sections 4.1, 4.2, 4.4, 4.8,

5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 28 of the RMP has also been submitted.”	
Rubraca - rucaparib - EMEA/H/C/004272/II/0036 Clovis Oncology Ireland Limited, Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Ulla Wändel Liminga, “Extension of indication to include maintenance treatment of adult patients with advanced (FIGO Stages III and IV) epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to first-line platinum-based chemotherapy for RUBRACA, based on interim results from study CO-338-087 (ATHENA); this is a Phase III, randomized, double-blind, dual placebo controlled study of rucaparib as monotherapy and in combination with nivolumab in patients with newly diagnosed EOC, FTC, or PPC who have responded to their first-line treatment (surgery and platinum-based chemotherapy). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 6.3 of the RMP has also been submitted. As part of the application, the MAH is requesting a 1-year extension of the market protection.” Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)	
Spikevax - elasomeran - EMEA/H/C/005791/II/0083/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marie Louise Schougaard Christiansen, “Extension of indication to include a 50-µg booster dose of Spikevax bivalent Original/Omicron BA.1 in children (6 to < 12 years), based on interim results from study P204; this is a Phase 2/3, Three-Part, Open-Label, Dose-Escalation, Age De-escalation and Randomized, Observer-Blind, Placebo-Controlled Expansion Study to Evaluate the Safety, Tolerability, Reactogenicity, and Effectiveness of mRNA-1273 SARS-CoV-2 Vaccine in Healthy Children 6 Months to Less Than 12 Years of Age; As a consequence, sections 2, 4.1, 4.2, 4.4, 4.8, 5.1 and 6.6 of the	

SmPC are updated. The Package Leaflet is updated in accordance. Version 4.5 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement editorial changes. To update sections 4.8, 5.1 and 6.6 of the SmPC to include additional immunogenicity data for the paediatric population (6 to < 18 years) based on Real-World Safety studies."	
Tenkasi - oritavancin - EMEA/H/C/003785/II/0037 Menarini International Operations Luxembourg S.A., Rapporteur: Janet Koenig, PRAC Rapporteur: Adam Przybylkowski, "Extension of indication to include treatment of paediatric population, aged between 3 months and less than 18 years for Tenkasi (oritavancin) 400 mg based on interim results from study TMC-ORI-11-01; this is a multicenter, open-label, dose-finding study of oritavancin single dose infusion in paediatric subjects less than 18 years of age with suspected or confirmed bacterial infections. The purpose of this Phase 1 study is to evaluate the safety, tolerability and PK of oritavancin in paediatric subjects and determine the optimal dose for a Phase 2 trial in paediatric subjects with ABSSSI. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 5.0 of the RMP has also been submitted. In addition, the MAH is also taking this opportunity to update the contact details of the local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.2 rev 1."	
Ultomiris - ravulizumab - EMEA/H/C/004954/II/0032 Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Kimmo Jaakkola, "Extension of indication to include the treatment of adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin 4 (AQP4) antibody-positive, based on interim results from study ALXN1210-NMO-307; this is a phase 3, external placebo-controlled, open-label, multicenter study to evaluate the efficacy and safety of ravulizumab in adult patients with	

NMOSD. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 6.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

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

Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Mari Thorn,
"Extension of indication to include treatment of adolescents for weight management for Wegovy based on final results from study NN9536-4451; this trial was conducted to assess the effect and safety of semaglutide in the paediatric population in order to address the unmet need for treatment of adolescents ages 12 to <18 years with obesity.
As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 8.0 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.2."

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

Bristol-Myers Squibb Pharma EEIG, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst,
"Extension of indication to include in combination with nivolumab the treatment of adolescents (12 years of age and older) for advanced (unresectable or metastatic) melanoma, based on the pivotal study CA209070; this is a multicentre, open-label, single arm, phase 1/2 trial of nivolumab +/- ipilimumab in children, adolescents and young adults with recurrent or refractory solid tumours or lymphomas. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 38.0 of the RMP has also been submitted."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Besremi - ropeginterferon alfa-2b -

EMEA/H/C/004128/II/0026 AOP Orphan Pharmaceuticals GmbH, Rapporteur: Janet Koenig	
CEVENFACTA - eptacog beta (activated) - EMEA/H/C/005655/II/0001 Laboratoire Francais du Fractionnement et des Biotechnologies, Rapporteur: Andrea Laslop	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0146/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	See B.5.1
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0148/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0149/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
Defitelio - defibrotide - EMEA/H/C/002393/II/0059, Orphan Gentium S.r.l., Rapporteur: Kristina Dunder	
Fasturtec - rasburicase - EMEA/H/C/000331/II/0064/G sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege	
Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0029 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz	
Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0060/G Merck Sharp & Dohme B.V., Rapporteur: Kristina Dunder	
Ivabradine Accord - ivabradine - EMEA/H/C/004241/II/0016/G Accord Healthcare S.L.U., Generic, Generic of Procoralan, Rapporteur: Anastasia Mountaki	
JCOVDEN - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0064 Janssen-Cilag International N.V., Rapporteur: Christophe Focke	

Jivi - damoctocog alfa pegol - EMEA/H/C/004054/II/0025/G Bayer AG, Rapporteur: Thalia Marie Estrup Blicher	
NUVAXOVID - SARS-CoV-2, spike protein, recombinant, expressed in Sf9 cells derived from Spodoptera frugiperda - EMEA/H/C/005808/II/0025/G Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege	
NUVAXOVID - SARS-CoV-2, spike protein, recombinant, expressed in Sf9 cells derived from Spodoptera frugiperda - EMEA/H/C/005808/II/0027 Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege	
Ozurdex - dexamethasone - EMEA/H/C/001140/II/0043/G AbbVie Deutschland GmbH & Co. KG, Rapporteur: Maria Concepcion Prieto Yerro	
Paxlovid - (1r,2s,5s)-n-((1s)-1-cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2s)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973/II/0028/G Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race	
ReFacto AF - moroctocog alfa - EMEA/H/C/000232/II/0165/G Pfizer Europe MA EEIG, Rapporteur: Thalia Marie Estrup Blicher	
Spikevax - elasomeran - EMEA/H/C/005791/II/0084/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus"B.I.a.6.a (Type II): Addition of a new strain (Omicron BA.4-5) resulting in a new Spikevax bivalent Original/Omicron BA.4-5 (50 µg elasomeran/50 µg davesomeran)/mL 0.1 mg/mL dispersion for injection presentation. The Annex A, the SmPC, the Annex II, the labelling and the Package Leaflet are updated accordingly.	See 9.1
Strensiq - asfotase alfa - EMEA/H/C/003794/II/0060/G, Orphan Alexion Europe SAS, Rapporteur: Armando	

Genazzani

TEZSPIRE - tezepelumab - EMEA/H/C/005588/II/0001
AstraZeneca AB, Rapporteur: Finbarr Leacy, PRAC Rapporteur: Eva Jirsová

TRODELVY - sacituzumab govitecan - EMEA/H/C/005182/II/0017
Gilead Sciences Ireland UC, Rapporteur: Jan Mueller-Berghaus

Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0042
Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege

Ultomiris - ravulizumab - EMEA/H/C/004954/II/0033/G
Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa

Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0107
MCM Vaccine B.V., Rapporteur: Christophe Focke

Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0109
MCM Vaccine B.V., Rapporteur: Christophe Focke

Zercepac - trastuzumab - EMEA/H/C/005209/II/0021
Accord Healthcare S.L.U., Rapporteur: Sol Ruiz

WS2298/G
Actraphane- EMEA/H/C/000427/WS2298/0092/G
Actrapid- EMEA/H/C/000424/WS2298/0085/G
Actrapid- EMEA/H/W/005779/WS2298/0001/G
Insulatard- EMEA/H/C/000441/WS2298/0090/G
Insulatard- EMEA/H/W/005780/WS2298/0001/G

Levemir-
EMEA/H/C/000528/WS2298/0105/G
Mixtard-
EMEA/H/C/000428/WS2298/0093/G
Protaphane-
EMEA/H/C/000442/WS2298/0089/G
Ryzodeg-
EMEA/H/C/002499/WS2298/0050/G
Tresiba-
EMEA/H/C/002498/WS2298/0057/G
Xultophy-
EMEA/H/C/002647/WS2298/0046/G
Novo Nordisk A/S, Lead Rapporteur: Thalia Marie Estrup Blicher

WS2303/G
Saxenda-
EMEA/H/C/003780/WS2303/0033/G
Victoza-
EMEA/H/C/001026/WS2303/0064/G
Xultophy-
EMEA/H/C/002647/WS2303/0045/G
Novo Nordisk A/S, Lead Rapporteur: Johann Lodewijk Hillege

WS2326/G
Hexacima-
EMEA/H/C/002702/WS2326/0138/G
Hexyon-
EMEA/H/C/002796/WS2326/0142/G
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

WS2359
HyQvia-EMEA/H/C/002491/WS2359/0085
Kiovig-EMEA/H/C/000628/WS2359/0120
Takeda Manufacturing Austria AG, Lead Rapporteur: Jan Mueller-Berghaus

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

COMIRNATY - tozinameran -
EMEA/H/C/005735/II/0145
BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "To update sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to add recommendations and data for subsequent and booster doses based on real world evidence (RWE) data as well as interim study results from both sub-study E (SSE) and sub-study D (SSD) C4591031 following procedure II/0140 assessment.

The Package Leaflet is updated accordingly.”
Cotellic - cobimetinib - EMEA/H/C/003960/II/0028 Roche Registration GmbH, Rapporteur: Filip Josephson, “Update of section 4.8 of the SmPC in order to add “Pruritus”, “Dry skin” and “Oedema peripheral” to the list of adverse drug reactions (ADRs) with frequency “Very common” based on post-marketing experience and the final results from study ML29733; this is an Open-label, single-center, Phase II study evaluating the efficacy and safety of single-agent cobimetinib in patients with histiocytic disorders whose tumours were 1) BRAF V600 wildtype or 2) BRAF V600E mutant and were intolerant to, or unable to access, BRAF inhibitors. The Package Leaflet is updated accordingly.”
Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0030 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz, “Update of section 4.8 of the SmPC in order to add Guillain Barré syndrome (GBS), syncope and pre-syncope to the list of adverse drug reactions (ADRs) based on the assessment of the global safety database; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the Package Leaflet in order to align it with the information in the SmPC.”
LUTATHERA - lutetium (177Lu) oxodotreotide - EMEA/H/C/004123/II/0038, Orphan Advanced Accelerator Applications, Rapporteur: Janet Koenig, “Update of sections 2, 4.2, 4.4, 4.5, 4.6, 4.8, 4.9, 5.1, 5.2, 5.3, 6.2, 6.4, 6.5, 6.6, 11 and 12 of the SmPC to align the Lutathera product information to that of the latest Core Data Sheet (CDS) version 2.0. In addition, the MAH is also taking the opportunity to propose additional corrections and changes to align with the QRD template. This application is also used as an opportunity to propose editorial updates to the product information (PI) to improve the language throughout the SmPC and patient leaflet.”
Opsumit - macitentan -

EMEA/H/C/002697/II/0047, Orphan
Janssen-Cilag International N.V., Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 4.8 of the SmPC in order to add 'flushing' to the list of adverse drug reactions (ADRs) with frequency 'common' based on a cumulative review of cases (post-marketing, clinical studies, registry) and literature; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the SmPC."

Revolade - eltrombopag - EMEA/H/C/001110/II/0070
Novartis Europharm Limited, Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 5.1 of the SmPC based on primary analysis results from study TAPER (CETB115J2411). This is a Phase II, open-label, prospective, single-arm, study to assess ability of eltrombopag to induce sustained remission in subjects with immune thrombocytopenia (ITP) who are refractory or relapsed after first-line steroids. In addition, the MAH took the opportunity to implement editorial changes in the SmPC."

Skyrizi - risankizumab - EMEA/H/C/004759/II/0028
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Finbarr Leacy, "Update of section 4.8 of the SmPC in order to add eczema, rash and urticaria to the list of adverse drug reactions (ADRs) based on a thorough evaluation of all events of rash, eczema and urticaria, including clinical trial and post-marketing data from the global safety database; the Package Leaflet is updated accordingly."

Tabrecta - capmatinib - EMEA/H/C/004845/II/0002
Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa, "Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on hypersensitivity reactions and add hypersensitivity to the list of adverse drug reactions (ADRs) with frequency uncommon, based on cumulative assessment of hypersensitivity cases in studies CINC280A2201, CINC280X1101, CINC280X2102, CINC280A2108, CINC280A2103 (post-DDI phase only), and CINC280A2105 (post-DDI phase only) and MAH global safety

database.
The Package Leaflet is updated accordingly."

Tegsedi - inotersen -
EMEA/H/C/004782/II/0034, Orphan
Akcea Therapeutics Ireland Limited, Rapporteur: Martina Weise, "Submission of the final report from study ISIS 420915-CS3, listed as a category 3 in the RMP. This is an Open-Label Extension Study to Assess the Long-Term Safety and Efficacy of ISIS 420915 in Patients with Familial Amyloid Polyneuropathy (FAP)."

TRODELVY - sacituzumab govitecan -
EMEA/H/C/005182/II/0018/G
Gilead Sciences Ireland UC, Rapporteur: Jan Mueller-Berghaus, "Grouped application comprising two type II variations as follows:
- To update sections 4.8 and 5.2 to address the commitment on providing bioanalytical study reports for antidrug-antibody (ADA) and neutralising antibody (NAb) determination for both studies IMMU- 132-01 and IMMU-132-05, the NAb assay method validation report as well as an integrated summary of immunogenicity.
- To update sections 4.8 and 5.2 to address the commitment to provide data on the impact of concomitant medications including UGT1A1 inhibitors/inducers on SN-38 PK based on the future PopPK model refinement."

Xevudy - sotrovimab -
EMEA/H/C/005676/II/0010/G
Glaxosmithkline Trading Services Limited, Rapporteur: Thalia Marie Estrup Blicher, "C.I.4: Update of sections 4.4 and 5.1 of the SmPC based on results from study reports PC-22-0108 on the in vitro activity of sotrovimab against Omicron spike variants encoding epitope substitutions in a pseudotyped virus assay, PC-22-0116 on the in vitro activity of sotrovimab against the SARS-CoV-2 XD variant in a live virus assay, PC-22-0117 on the in vitro activity of sotrovimab against the SARS-CoV-2 Omicron BA.2.12.1, BA.4 and BA.5 variants in a live virus assay, and PC-22-0124 on the in vitro activity of sotrovimab against the Omicron BA.2.75 spike variant in a pseudotyped virus assay. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI.
C.I.13: Submission of the final study report PC-22-0101 on the in vivo activity of S309

encoding the hamster Fc region in a Syrian golden hamster model of SARS-CoV-2 Omicron BA.2 infection.
C.I.13: Submission of the final study report PC-22-0126 on the in vivo activity of VIR-7831-WT in a Syrian golden hamster model of SARS-CoV-2 Omicron BA.5. infection."

WS2368
Invokana-
EMEA/H/C/002649/WS2368/0061
Vokanamet-
EMEA/H/C/002656/WS2368/0066
Janssen-Cilag International N.V., Lead Rapporteur: Martina Weise, "To update section 4.4 of the SmPC in order amend an existing warning on the diabetic ketoacidosis, to indicate that glucosuria may persist longer than expected and that DKA may be prolonged after discontinuation of canagliflozin in some patients based on a cumulative review of literature, MAH global safety database, preclinical and clinical pharmacology data, and clinical study data including cases reports."

B.6.10. CHMP-PRAC assessed procedures

Cablivi - caplacizumab -
EMEA/H/C/004426/II/0040, Orphan
Ablynx NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Jan Neuhauser, "Update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC in order to update information on long-term efficacy and safety based on final results from study ALX0681-C302/LTS16371 - Prospective Follow-up Study for Patients who Completed Study ALX0681-C301 (HERCULES) to Evaluate Long-term Safety and Efficacy of Caplacizumab (Post-HERCULES), listed as a category 3 study in the RMP. The Post-HERCULES study was a Phase III, 36-month follow-up study from HERCULES (parent study) to evaluate the long-term outcomes as well as the safety and efficacy of repeat use of caplacizumab in patients who experienced a recurrence of aTTP.
The RMP version 3.0 has also been submitted."

Ocrevus - ocrelizumab -
EMEA/H/C/004043/II/0034/G
Roche Registration GmbH, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Brigitte

Keller-Stanislawski, "Submission of the final report from study BN29739 (VELOCE) listed as a category 3 study in the RMP. This is a phase 3b, multicentre, randomized, parallel-group, open-label study to evaluate the effectiveness of vaccinations in patients with relapsing forms of multiple sclerosis (RMS) undergoing treatment with ocrelizumab. Submission of the final report from studies MA30005 (CASTING) and MN30035 (CHORDS). These are prospective, multicenter, international, interventional, open-label phase 3b studies to assess the efficacy and safety of ocrelizumab in patients with relapsing multiple sclerosis who have a suboptimal response to an adequate course of disease-modifying treatment. The RMP version 8.0 has also been submitted."	
Omnitrope - somatropin - EMEA/H/C/000607/II/0073 Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, "Update of section 4.4 of the SmPC in order to add a new warning on scoliosis following PRAC recommendation from procedure EMEA/H/C/PSUSA/00002772/202003 based on final results from study EP00-401 listed as a category 3 study in the RMP; this is a prospective, open-label, non-comparative, multicenter, Phase IV study to monitor the long-term safety and efficacy of Omnitrope in short children born small for gestational age (SGA), in particular the diabetogenic potential and immunogenicity of rhGH therapy. The Package Leaflet is updated accordingly. The RMP version 12.0 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the SmPC."	
Repatha - evolocumab - EMEA/H/C/003766/II/0061 Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola, "Update of sections 4.8 and 5.1 of the SmPC in order to update safety information and include long-term safety and efficacy data based on final results from study 20130295 and study 20160250 listed as category 3 studies in the RMP; these are phase 3b, multicenter, open-label extension (OLE) studies designed to assess	

the long-term safety of evolocumab in subjects who completed the FOURIER study (study 20110118). The RMP version 8.0 has also been submitted."	
Sancuso - granisetron - EMEA/H/C/002296/II/0061 Kyowa Kirin Holdings B.V., Rapporteur: Silvijus Abramavicius, PRAC Rapporteur: Rugile Pilviniene, "Update of sections 4.4, 4.6, 4.7, 4.8, 4.10 and 5.3 of the SmPC in order to add 'Serotonin syndrome' and 'Application site Reactions' to the list of adverse drug reactions (ADRs) with frequency unknow; as well as 'Application site Irritation' with frequency 'Uncommon' based on post-marketing data and literature. The MAH also proposes to update sections 4.4 and 4.5 of the SmPC to add drug-drug interaction information with buprenorphine/Opioids and serotonergic medicinal products based on post-marketing data and literature. The Package Leaflet has been updated accordingly. The RMP version 5 has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes in the SmPC."	
Xenpozyme - olipudase alfa - EMEA/H/C/004850/II/0001/G, Orphan Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber, "Grouped application comprising two type II variations as follows: - To update section 4.6 of the SmPC in order to include a recommendation to conduct a pregnancy test for women of childbearing potential (WOCP) prior to treatment initiation based on embryo-foetal study in mice (study TER0694). In addition, the MAH proposes an update of section 5.3 of the SmPC based on a re-calculation of exposure margins for the embryo-foetal study. The MAH also proposes to align the SmPC with the updated CCDS. - To update sections 4.6 and 5.3 of the SmPC in order to include data in lactating mice based on final results from study MSSM-1120 - Evaluation of Olipudase alfa Transfer Into Milk of Lactating Mice. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted."	

B.6.11. PRAC assessed procedures

PRAC Led

Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0117

GlaxoSmithkline Biologicals SA, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Karin Janssen van Doorn, "Submission of the interim report from study EPI-HPV-099 (217743). This is an observational, retrospective database post-authorisation safety study (PASS) assessing trends and changes over time in incidence of anal cancer and feasibility for a case-control study in European countries that introduced Cervarix in their National Immunisation Programme.
The study was set up to address the missing information on the impact and effectiveness of Cervarix against anal lesions and cancer in the Cervarix RMP. The RMP version 26 has also been submitted."

PRAC Led

Darzalex - daratumumab - EMEA/H/C/004077/II/0063, Orphan

Janssen-Cilag International N.V., Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, PRAC-CHMP liaison: Bruno Sepodes, "Update of section 4.4 of the SmPC in order to update the warnings and precautions for myocardial infarction and ocular events following PSUSA/00010498/202111, based on the cumulative review of the relevant cases retrieved from the MAH's global safety database, clinical database, epidemiological evaluation and literature review.
The Package Leaflet is updated accordingly."

PRAC Led

Deltyba - delamanid - EMEA/H/C/002552/II/0061, Orphan

Otsuka Novel Products GmbH, PRAC Rapporteur: Jo Robays, PRAC-CHMP liaison: Christophe Focke, "Update of sections 4.2 and 4.4 of the SmPC in order to update treatment duration based on final results from EU PASS (protocol no. 242-12-402), listed as a category 3 study in the RMP. This is a "A Multicentre, EU-wide, Non-Interventional Post-Authorisation Study to Assess the Safety and Usage of

Delamanid in Routine Medical Practice in Multidrug-Resistant Tuberculosis (MDR-TB) Patients". This treatment registry was for monitoring and documenting Deltyba use in routine medical practice and aimed to assess compliance with the recommendations in the authorised product information when prescribed as part of an appropriate combination regimen (ACR) for the treatment of MDR-TB.
The Package Leaflet is updated accordingly. The RMP version 4.2 has also been submitted. In addition, the MAH took the opportunity to update Annex II section D of the SmPC."

PRAC Led

JCOVDEN - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0065

Janssen-Cilag International N.V., PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 5.1 in order to update the clinical exposure and risk sections."

PRAC Led

Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0092

Genzyme Europe BV, RAC Rapporteur: Nathalie Gault, PRAC-CHMP liaison: Alexandre Moreau, "Update of sections 4.6 and 5.3 of the SmPC in order to update information on pregnancy, lactation and fertility following the request by PRAC in the AR for MEA/024.17 and MEA/025.17 and in PSUSA/00000086/202109; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

PRAC Led

Neulasta - pegfilgrastim - EMEA/H/C/000420/II/0121

Amgen Europe B.V., PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report from PASS study 20170701 listed as a category 3 study in the RMP. This is a cross-sectional survey study to Assess the Effectiveness of the Neulasta Patient Alert Card and to Measure Medication Errors Related to the Use of the Neulasta On-Body Injector. The RMP version 9.0 has also been submitted."

PRAC Led

NUVAXOVID - SARS-CoV-2, spike protein, recombinant, expressed in Sf9 cells derived from Spodoptera frugiperda - EMEA/H/C/005808/II/0028

Novavax CZ, a.s., PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 2.1 due to reclassification of myocarditis and/or pericarditis from important potential risk to important identified."

PRAC Led

Saxenda - liraglutide - EMEA/H/C/003780/II/0034

Novo Nordisk A/S, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report from study NN8022-4246 listed as a category 3 study in the RMP. This is an in-market utilisation non-interventional PASS of liraglutide used for weight management in the UK using the CPRD Primary Care Database. The RMP version 33.0 has also been submitted."

PRAC Led

Synagis - palivizumab - EMEA/H/C/000257/II/0131

AstraZeneca AB, PRAC Rapporteur: Marie Louise Schougaard Christiansen, PRAC-CHMP liaison: Thalia Marie Estrup Blicher, "Submission of an updated RMP version 2.0 in order to remove from the list of safety concerns "Anaphylaxis, Anaphylactic shock, and Hypersensitivity" and "Medication error of mixing lyophilised and liquid palivizumab before injection". In addition, the MAH took the opportunity to apply the revised template."

PRAC Led

TOBI Podhaler - tobramycin - EMEA/H/C/002155/II/0053, Orphan

Mylan IRE Healthcare Limited, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 8.0 following the request by PRAC in the AR for PSUSA/00009315/202106 in order to update it based on the guidance provided in the GVP and to remove the safety concerns as well as to reflect the finalisation of study CTBM100C2407

and the transfer of ownership."

PRAC Led
Zydelig - idelalisib -
EMEA/H/C/003843/II/0056
Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the final report from study GS-EU-313-4172 listed as a category 3 study in the RMP. This is a non-interventional study to assess the safety profile of idelalisib in patients with refractory follicular lymphoma (FL) with primary objective to assess the overall safety profile of idelalisib monotherapy in patients with refractory FL."

PRAC Led
WS2369
Filgrastim Hexal-
EMEA/H/C/000918/WS2369/0066
Zarzio-EMEA/H/C/000917/WS2369/0067
Sandoz GmbH, Lead PRAC Rapporteur: Menno van der Elst, "C.I.11.z - To amend the RMP to reduce the list of safety concerns and remove risks which are well characterised and already included in the product information, following PRAC Assessment Report of PSUR P14 (EMEA/H/C/PSUSA/00001391/202109) dated 05-May-2022. Additionally, the due date of the final study report EP06-501 (MEA007) has been updated .
Furthermore, the MAH took the opportunity to introduce the following editorial changes:
- Removal of pharmaceutical forms and strengths no longer registered in Japan;
- Editorial changes in Part V "Risk minimisation measures"."

B.6.12. CHMP-CAT assessed procedures

Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel -
EMEA/H/C/004731/II/0007/G, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Concetta Quintarelli, CHMP Coordinator: Armando Genazzani

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

WS2263
Blitzima-
EMEA/H/C/004723/WS2263/0060
Truxima-
EMEA/H/C/004112/WS2263/0063
Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz

WS2325
Adjupanrix-
EMEA/H/C/001206/WS2325/0080
Ambirix-
EMEA/H/C/000426/WS2325/0123
Bexsero-
EMEA/H/C/002333/WS2325/0116
Cervarix-
EMEA/H/C/000721/WS2325/0116
Fendrix-
EMEA/H/C/000550/WS2325/0080
Infanrix hexa-
EMEA/H/C/000296/WS2325/0319
Menveo-
EMEA/H/C/001095/WS2325/0114
Mosquirix-
EMEA/H/W/002300/WS2325/0063
Rotarix-EMEA/H/C/000639/WS2325/0126
Shingrix-
EMEA/H/C/004336/WS2325/0060
Synflorix-
EMEA/H/C/000973/WS2325/0173
Twinrix Adult-
EMEA/H/C/000112/WS2325/0158
Twinrix Paediatric-
EMEA/H/C/000129/WS2325/0159
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke

WS2331
Descovy-
EMEA/H/C/004094/WS2331/0059
Emtriva-
EMEA/H/C/000533/WS2331/0140
Odefsey-
EMEA/H/C/004156/WS2331/0056
Gilead Sciences Ireland UC, Lead Rapporteur:

Bruno Sepodes, "To update sections 4.4 and 4.6 of the SmPC to implement modifications of the HIV SmPC/PL to update wording related to the risk of HIV transmission in accordance with the January 2022 CHMP adoption of an update to the Product Information for all approved HIV products, recommending the removal of the disease information relating to sexual transmission of HIV and amendment of the sections relating to breast-feeding. The MAH has taken the opportunity to update the contact details of the local representative listed in the Package Leaflet for Estonia, Latvia, Lithuania and Romania. An editorial change has also been made to the SmPC and Patient Information Leaflet for Emtriva 10 mg/ml oral solution to correct an error in the sodium content."	
WS2333 **Ambirix-** **EMEA/H/C/000426/WS2333/0124** **Twinrix Adult-** **EMEA/H/C/000112/WS2333/0159** **Twinrix Paediatric-** **EMEA/H/C/000129/WS2333/0160** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke	
WS2345 **Hexacima-** **EMEA/H/C/002702/WS2345/0137** **Hexyon-** **EMEA/H/C/002796/WS2345/0141** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus	
WS2360 **HBVAXPRO-** **EMEA/H/C/000373/WS2360/0079** **Vaxelis-EMEA/H/C/003982/WS2360/0108** Merck Sharp & Dohme B.V., Lead Rapporteur: Jan Mueller-Berghaus	
WS2363/G **Copalia-** **EMEA/H/C/000774/WS2363/0127/G** **Dafiro-** **EMEA/H/C/000776/WS2363/0131/G** **Exforge-** **EMEA/H/C/000716/WS2363/0126/G** Novartis Europharm Limited, Lead Rapporteur:	

Thalia Marie Estrup Blicher

WS2370
Nuwiq-EMEA/H/C/002813/WS2370/0051
Vihuma-
EMEA/H/C/004459/WS2370/0033
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus

WS2379/G
Lixiana-
EMEA/H/C/002629/WS2379/0039/G
Roteas-
EMEA/H/C/004339/WS2379/0026/G
Daiichi Sankyo Europe GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro

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

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

B.7.2. Monthly Line listing for Type I variations

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

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

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

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

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

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

E. Annex E - EMA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

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

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

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

G. ANNEX G

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

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

G.2. PRIME

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

G.2.1. List of procedures concluding at 10-13 October 2022 CHMP plenary:

Neurology		
Nicardipine (SME)	Treatment of non-traumatic subarachnoid haemorrhage in patients undergoing surgery	The CHMP granted eligibility to PRIME and adopted the critical summary report.

G.2.2. List of procedures starting in October 2022 for November 2022 CHMP adoption of outcomes

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