21 February 2022
EMA/CHMP/60787/2022
Human Medicines Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 21-24 February 2022

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

21 February 2022, 09:00 – 19:30, virtual meeting/room 1C

22 February 2022, 08:30 – 19:30, virtual meeting/room 1C

23 February 2022, 08:30 – 19:30, virtual meeting/room 1C

24 February 2022, 08:30 – 15:00, virtual meeting/room 1C

Disclaimers

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

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

Note on access to documents

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

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 21-24 February 2022. See February 2022 CHMP minutes (to be published post March 2022 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 21-24 February 2022.

1.3. Adoption of the minutes

CHMP minutes for 24-27 January 2022.

Minutes from PReparatory and Organisational Matters (PROM) meeting held on 14 February 2022.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

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

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

Scope: Oral explanation

Action: Oral explanation to be held on 23 February 2022 at 16:00

Participation of patient representatives.

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

2.2. Re-examination procedure oral explanations

2.2.1. Ipique - bevacizumab - EMEA/H/C/005433

Rotterdam Biologics B.V.; indicated in adults for the treatment of neovascular macular degeneration associated with aging and diabetes.

Scope: Oral explanation

Action: Oral explanation to be held on 22 February 2022 at 09:00

Opinion adopted on 11.11.2021. List of Outstanding Issues adopted on 20.05.2021. List of Questions adopted on 17.09.2020.

2.3. Post-authorisation procedure oral explanations

No items

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

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

treatment of homocystinuria

Scope: Opinion

Action: For adoption

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

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

treatment of multiple sclerosis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 27.01.2022.

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

treatment of multiple sclerosis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 27.01.2022. List of Questions adopted on 14.10.2021.

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

treatment of multiple sclerosis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 27.01.2022. List of Questions adopted on 14.10.2021.

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

treatment of multiple sclerosis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 27.01.2022.

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

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

Scope: Opinion

Action: For adoption

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

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

treatment of patients with diabetes mellitus who require intravenous insulin

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 25.03.2021. List of Questions adopted on 23.07.2020.

3.1.8. difelikefalin - EMEA/H/C/005612

treatment of pruritus

Scope: Opinion

Action: For adoption

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

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

Accelerated assessment

Immunocore Ireland Limited; treatment of uveal melanoma

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 25.01.2022. List of Questions adopted on 09.11.2021.

3.1.10. relugolix - EMEA/H/C/005353

treatment of adult patients with advanced prostate cancer.

Scope: Opinion

Action: For adoption

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

3.1.11. daridorexant - EMEA/H/C/005634

treatment of insomnia

Scope: Opinion

Action: For adoption

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

3.1.12. sitagliptin - EMEA/H/C/005598

treatment of type 2 diabetes mellitus

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 16.12.2021, 16.09.2021, 20.05.2021. List of Questions adopted on 17.09.2020.

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

treatment of diabetes mellitus

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 27.01.2022. List of Questions adopted on 16.09.2021.

3.1.14. rimegepant - EMEA/H/C/005725

management of migraine

Scope: Opinion

Action: For adoption

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

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

3.2.1. insulin human - Article 58 - EMEA/H/W/005779

treatment of diabetes mellitus

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 11.11.2021.

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

prevention of venous thromboembolic events

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 12.11.2020.

3.2.3. insulin human - Article 58 - EMEA/H/W/005780

treatment of diabetes mellitus

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 11.11.2021.

3.2.4. molnupiravir - EMEA/H/C/005789

Treatment of coronavirus disease 2019 (COVID-19)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 16.12.2021.

3.2.5. pirfenidone - EMEA/H/C/005873

indicated in adults for the treatment of mild to moderate idiopathic pulmonary fibrosis (IPF).

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 16.09.2021.

3.2.6. bevacizumab - EMEA/H/C/005574

Treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer.
First-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer.
First-line treatment of patients with advanced and/or metastatic renal cell cancer.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.04.2021.

3.2.7. ranibizumab - EMEA/H/C/005610

treatment of neovascular age-related macular degeneration in adults

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 16.09.2021.

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

3.3.1. sutimlimab - Orphan - EMEA/H/C/005776

Genzyme Europe BV; treatment of haemolysis in adult patients with cold agglutinin disease (CAD)

Scope: List of questions

Action: For adoption

3.3.2. gozetotide - EMEA/H/C/005488

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

Scope: List of questions

Action: For adoption

3.3.3. bardoxolone methyl - Orphan - EMEA/H/C/005869

Reata Ireland Limited; treatment of chronic kidney disease

Scope: List of questions

Action: For adoption

3.3.4. lutetium (177lu) vipivotide tetraxetan - EMEA/H/C/005483

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

Scope: List of questions

Action: For adoption

3.3.5. pegfilgrastim - EMEA/H/C/005587

treatment of neutropenia

Scope: List of questions

Action: For adoption

3.3.6. tirzepatide - EMEA/H/C/005620

treatment of adults with type 2 diabetes mellitus

Scope: List of questions

Action: For adoption

3.3.7. fosdenopterin - Orphan - EMEA/H/C/005378

Accelerated assessment

Comharsa Life Sciences Ltd; treatment of molybdenum cofactor deficiency type A

Scope: List of questions

Action: For adoption

3.3.8. plerixafor - EMEA/H/C/005943

treatment of lymphoma and multiple myeloma

Scope: List of questions

Action: For adoption

3.3.9. ruxolitinib - EMEA/H/C/005843

treatment of non-segmental vitiligo

Scope: List of questions

Action: For adoption

3.3.10. spesolimab - EMEA/H/C/005874

treatment of flares in adult patients with generalised pustular psoriasis

Scope: List of questions

Action: For adoption

3.3.11. teriflunomide - EMEA/H/C/005960

treatment of multiple sclerosis (MS)

Scope: List of questions

Action: For adoption

3.3.12. deucravacitinib - EMEA/H/C/005755

treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy

Scope: List of questions

Action: For adoption

3.3.13. bevacizumab - EMEA/H/C/005534

Treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer.
First-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer.
First-line treatment of patients with advanced and/or metastatic renal cell cancer.

Scope: List of questions

Action: For adoption

3.3.14. olipudase alfa - PRIME - Orphan - EMEA/H/C/004850

Accelerated assessment

Genzyme Europe BV; Treatment of non-Central Nervous System (CNS) manifestations of Acid Sphingomyelinase Deficiency (ASMD) in paediatric and adult patients.

Scope: List of questions

Action: For adoption

3.3.15. loncastuximab tesirine - Orphan - EMEA/H/C/005685

FGK Representative Service GmbH; treatment of adult patients with relapsed or refractory large B-cell lymphoma

Scope: List of questions

Action: For adoption

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

3.4.1. teriparatide - EMEA/H/C/005793

treatment of osteoporosis

Scope: Letter by the applicant dated 3 February 2022, requesting an extension to the clock stop to respond to the list of questions adopted in May 2021.

Action: For adoption

List of Questions adopted on 20.05.2021.

3.4.2. mobocertinib - EMEA/H/C/005621

Treatment of adult patients with epidermal growth factor receptor (EGFR) exon 20 insertion mutation-positive locally advanced or metastatic non-small cell lung cancer (NSCLC).

Scope: Letter by the applicant dated 01 February 2022, requesting an extension to the clock stop to respond to the list of questions adopted in November 2021.

Action: For adoption

List of Questions adopted on 11.11.2021.

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

Y-Mabs Therapeutics A/S; treatment of neuroblastoma

Scope: Request by the applicant dated 03 February 2022 for an extension to the clock stop to respond to the list of questions adopted in September 2021.

Action: For adoption

List of Questions adopted on 16.09.2021.

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

indicated for in vitro labelling of kits for radiopharmaceutical preparation

Scope: Request by the applicant dated 18 February 2022 for an extension to the clock stop to respond to the list of questions adopted in December 2021.

Action: For adoption

List of Questions adopted on 16.12.2021.

3.4.5. trastuzumab - EMEA/H/C/005880

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

Scope: Request by the applicant dated 17 February 2022 for an extension to the clock stop to respond to the list of outstanding issues adopted in January 2022.

Action: For adoption

List of Outstanding Issues adopted on 27.01.2022

3.4.6. trastuzumab - EMEA/H/C/005066

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

Scope: Request by the applicant dated 17 February 2022 for an extension to the clock stop to respond to the list of outstanding issues adopted in January 2022.

Action: For adoption

List of Outstanding Issues adopted on 27.01.2022, 25.03.2021, 10.12.2020. List of Questions adopted on 19.09.2019.

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

3.5.1. Aduhelm - aducanumab - EMEA/H/C/005558

Biogen Netherlands B.V.; Alzheimer's disease

Scope: Appointment of rapporteurs, re-examination timetable

Action: For adoption

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

Opinion adopted on 16.12.2021. List of Outstanding Issues adopted on 22.07.2021. List of Questions adopted on 25.02.2021.

3.6. Initial applications in the decision-making phase

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

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

Scope: Update on the status of this application.

Action: For adoption

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

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

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

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

Scope: List of Questions

Action: For adoption

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

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

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

4.1.1. Ilumetri - tildrakizumab - EMEA/H/C/004514/X/0023

Almirall S.A

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension application to introduce a new strength (200 mg solution for injection)."

Action: For adoption

List of Questions adopted on 11.11.2021.

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

Eli Lilly Nederland B.V.

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

Scope: "Extension application. The RMP is updated (version 11.1) accordingly."

Action: For adoption

List of Questions adopted on 14.10.2021.

4.1.3. Nucala - mepolizumab - EMEA/H/C/003860/X/0042

GlaxoSmithKline Trading Services Limited

Rapporteur: Peter Kiely, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension application to introduce a new strength of 40 mg for Nucala solution for injection in a pre-filled syringe for subcutaneous use to be used in children aged 6 to 11 years."

Action: For adoption

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

16.09.2021.

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

Novo Nordisk A/S

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber

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

Action: For adoption

List of Outstanding Issues adopted on 27.01.2022. List of Questions adopted on 14.10.2021.

4.1.5. Xofluza - baloxavir marboxil - EMEA/H/C/004974/X/0003/G

Roche Registration GmbH

Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Sonja Hrabcik

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

Action: For adoption

List of Questions adopted on 16.09.2021.

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

No items

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

4.3.1. Calquence - acalabrutinib - EMEA/H/C/005299/X/0009/G

AstraZeneca AB

Rapporteur: Filip Josephson, PRAC Rapporteur: Željana Margan Koletić

Scope: "Extension application to introduce a new pharmaceutical form, film-coated tablet. A.6 - To change the ATC Code of acalabrutinib from L01XE51 to L01EL02."

Action: For adoption

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

No items

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

No items

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

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

5.1.1. Beovu - brolucizumab - EMEA/H/C/004913/II/0010

Novartis Europharm Limited

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include treatment of visual impairment due to DME for Beovu; as a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 11.11.2021.

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

Camurus AB

Rapporteur: Peter Kiely, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Tiphaine Vaillant

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

Action: For adoption

5.1.3. Cabometyx - cabozantinib - EMEA/H/C/004163/II/0023

Ipsen Pharma

Rapporteur: Ingrid Wang, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include monotherapy treatment of adults and adolescent patients aged 12 years and older, with locally advanced or metastatic differentiated thyroid carcinoma (DTC), refractory or not eligible to radioactive iodine (RAI) who have progressed during or after prior systemic therapy for CABOMETYX; 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 6.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 11.11.2021.

5.1.4. 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

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

Merck Sharp & Dohme B.V.

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

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

Action: For adoption

Request for Supplementary Information adopted on 14.10.2021.

5.1.6. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0110

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication for Keytruda in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery of adults with locally advanced, inflammatory, or early-stage triple-negative breast

cancer at high-risk of recurrence; as a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 37.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 11.11.2021.

5.1.7. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0111

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication to include the adjuvant treatment of adults and adolescents aged 12 years and older with stage IIB, stage IIC or stage III melanoma and to include the treatment of adolescents aged 12 years and older with advanced melanoma for Keytruda; as a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 36.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 11.11.2021.

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

Regeneron Ireland Designated Activity Company (DAC)

Rapporteur: Sinan B. Sarac, 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

5.1.9. Opdivo - nivolumab - EMEA/H/C/003985/II/0100

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication for Opdivo to include adjuvant treatment of adults with muscle invasive urothelial carcinoma (MIUC) who are at high risk of recurrence after undergoing radical resection of MIUC; 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 23.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 11.11.2021, 24.06.2021.

5.1.10. Opdivo - nivolumab - EMEA/H/C/003985/II/0107

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of indication to include in combination with fluoropyrimidine- and platinum-based combination chemotherapy the first-line treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC) for OPDIVO based on study CA209648; as a consequence, sections 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 25.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 11.11.2021.

5.1.11. Polivy - polatuzumab vedotin - Orphan - EMEA/H/C/004870/II/0012

Roche Registration GmbH

Rapporteur: Alexandre Moreau, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Annika Folin

Scope: "Extension of the indication to include: Polivy in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone, is indicated for the treatment of adult patients with previously untreated diffuse large B-cell lymphoma (DLBCL) based on the efficacy and safety data from the Pivotal Phase III study GO39942 (POLARIX). This submission fulfills SOB003 thus supporting the switch from CMA to full MA. Annexes I, II, IIIB are revised. The RMP is also updated."

Action: For adoption

5.1.12. Retsevmo - selpercatinib - EMEA/H/C/005375/II/0011

Eli Lilly Nederland B.V.

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

Scope: "Extension of indication to include the first-line treatment of RET fusion-positive NSCLC for Retsevmo based on results from study LIBRETTO-001, an open-label, multicentre, global Phase 1/2 study of selpercatinib in patients with RET-altered advanced solid tumours; as a consequence, sections 4.1, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

5.1.13. Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0041

Moderna Biotech Spain, S.L.

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop

Scope: "Extension of indication to include use in children 6-11 years of age for Spikevax, based on data from study mRNA-1273-P204, an ongoing Phase 2/3, 2-part, open-label, dose-escalation, age de-escalation and subsequent randomized, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of mRNA-1273 in healthy children; 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."

Action: For adoption

Request for Supplementary Information adopted on 16.12.2021.

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

Eli Lilly Nederland B.V.

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

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

Action: For adoption

Request for Supplementary Information adopted on 27.01.2022, 14.10.2021, 24.06.2021, 25.02.2021.

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

Pfizer Europe MA EEIG

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant

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

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021.

5.1.16. Yescarta - axicabtagene ciloleucel - Orphan - ATMP - EMEA/H/C/004480/II/0042

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Claire Beuneu, CHMP Coordinators: Jan Mueller-Berghaus and Karin Janssen van Doorn, PRAC Rapporteur: Anette Kirstine Stark

Scope: "Extension of indication to include the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after three or more lines of systemic therapy. Consequently, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC, Annex II (Section D) and Package Leaflet are proposed to be updated. As a consequence, the RMP (version 5.1) has been updated to align with the indication extension.
In addition, the applicant has taken the opportunity to make minor editorial corrections throughout the SmPC and package leaflet to align with the current Quality Review of Documents (QRD) template." 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 05.11.2021.

5.1.17. Yescarta - axicabtagene ciloleucel - Orphan - ATMP - EMEA/H/C/004480/II/0046

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Claire Beuneu, CHMP Coordinators: Jan Mueller-Berghaus and Karin Janssen van Doorn, PRAC Rapporteur: Anette Kirstine Stark

Scope: "Extension of indication to include treatment of adult patients with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) for Yescarta; 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 5.3 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the product information with minor editorial changes." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

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

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication to include treatment of paediatric patients aged birth to less than 18 years for Zerbaxa, based on final results from studies MK-7625A-034 (A Phase 2, Randomized, Active Comparator-Controlled, Double-Blind Clinical Trial to Study the Safety and Efficacy of Ceftolozane/Tazobactam Versus Meropenem in Pediatric Subjects with Complicated Urinary Tract Infection, Including Pyelonephritis) and MK-7625A-035 (A Phase 2, Randomized, Active Comparator-Controlled, Double-Blind Clinical Trial to Study the Safety and Efficacy of Ceftolozane/Tazobactam Plus Metronidazole Versus Meropenem in Pediatric Subjects with Complicated Intra-Abdominal Infection).
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 14.10.2021.

5.1.19. WS2065
Delstrigo - doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746/WS2065/0026
Pifeltro - doravirine - EMEA/H/C/004747/WS2065/0019

Merck Sharp & Dohme B.V.

Lead Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "Extension of indication to include the new indication to the paediatric population weighing at least 35 kgs for PIFELTRO and DELSTRIGO. Sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.1 of the RMP for each product have also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial corrections and to update the list of local representatives in the Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 11.11.2021.

5.1.20. WS2113
Opdivo - nivolumab - EMEA/H/C/003985/WS2113/0108
Yervoy - ipilimumab - EMEA/H/C/002213/WS2113/0090

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of indication to include first-line treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC) for Opdivo in combination with Yervoy; 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 24.0 of the Opdivo RMP and version 33.0 of the Yervoy RMP have also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 11.11.2021.

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

No items

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

No items

6. Medical devices

6.1. Ancillary medicinal substances - initial consultation

No items

6.2. Ancillary medicinal substances – post-consultation update

No items

6.3. Companion diagnostics – initial consultation

No items

6.4. Companion diagnostics – follow-up consultation

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. niraparib tosylate monohydrate, abiraterone acetate - H0005932

is indicated with prednisone or prednisolone for the treatment of adult patients with prostate cancer who have progressed to metastatic castration resistant prostate cancer (mCRPC) and are positive for HRR gene alteration (germline and/or somatic).

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

Action: For adoption

8.1.2. polihexanide - H0005858

Treatment of Acanthamoeba keratitis

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

Action: For adoption

8.1.3. Request for combination pack – H0005999

Treatment of advanced breast cancer

Scope: Request for combination pack

Action: For adoption

8.2. Priority Medicines (PRIME)

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

8.2.1. List of applications received

Action: For information

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

9. Post-authorisation issues

9.1. Post-authorisation issues

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

BioNTech Manufacturing GmbH

Rapporteur: Filip Josephson

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

Action: For adoption

Request for Supplementary Information adopted on 27.01.2022.

9.1.2. Comirnaty - tozinameran - EMEA/H/C/005735/II/0104

BioNTech Manufacturing GmbH

Rapporteur: Filip Josephson

Scope: "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update immunogenicity, safety and efficacy information regarding heterologous vaccination (both in the primary series and for booster vaccinations) based on published literature data; the Package Leaflet is updated accordingly.
In addition, the MAH took the opportunity to make minor editorial changes throughout the product information."

Action: For adoption

9.1.3. Comirnaty - tozinameran - EMEA/H/C/005735/II/0111

BioNTech Manufacturing GmbH

Rapporteur: Filip Josephson

Scope: "Update of section 4.2 of the SmPC of Comirnaty 30 microgram/dose to lower the age of the booster dose from adults 18 years of age and older to adults and adolescents 12 years of age and older, based on real world evidence collected by the Ministry of Health of Israel. The Package Leaflet is updated accordingly.
In addition, the MAH took the opportunity to make minor editorial changes throughout the product information (SmPC and package leaflet)."

Action: For adoption

9.1.4. Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0042

Moderna Biotech Spain, S.L.

Rapporteur: Jan Mueller-Berghaus

Scope: "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include information on heterologous boosting using a 50 ug dose of Spikevax to boost subjects that have previously completed a primary vaccination series with any authorised COVID-19 vaccine, based on data from the DMID study 21-0012, a Phase 1/2 heterologous SARS-CoV-2 vaccine dosing (mRNA-1273 booster) study of the various vaccines authorised in the US under Emergency Use Authorisation in participants $\geqslant$ 18 years old (NCT04889209). In addition, the MAH took the opportunity to make minor editorial changes/corrections throughout the product information."

Action: For adoption

Request for Supplementary Information adopted on 27.01.2022, 16.12.2021.

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

Moderna Biotech Spain, S.L.

Rapporteur: Jan Mueller-Berghaus

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

Action: For adoption

9.1.6. Defitelio - defibrotide - EMEA/H/C/002393/S/0057

Gentium S.r.l.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: annual re-assessment

Action: For adoption

9.1.7. Vivanza – vardenafil – EMEA/H/C/000488

Bayer AG; treatment of erectile dysfunction

Rapporteur: Maria Concepcion Prieto Yerro, Co-rapporteur: Johann Lodewijk Hillege

Scope: Withdrawal of marketing authorisation

Action: For information

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

9.1.8. Remicade EMEA/H/C/000240, Flixabi EMEA/H/C/004020, Inflectra EMEA/H/C/002778, Remsima EMEA/H/C/002576, Zessly EMEA/H/C/004647 - Infliximab

MAHs: various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Use of live vaccines in infants exposed in utero or during breastfeeding. The DHPC, communication plan and PRAC advice have been adopted via written procedure on 14.02.2022

Action: For information

9.1.9. Skysona – elivaldogene autotemcel – EMEA/C/H/003690

bluebird bio (Netherlands) B.V.; treatment of early cerebral adrenoleukodystrophy

Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder

Scope: Withdrawal of marketing authorisation

Action: For information

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

10. Referral procedures

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

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

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

No items

13.2. Innovation Task Force briefing meetings

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

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

Action: For adoption

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

14.3.1. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP February 2022 meeting to CHMP for adoption:

- 20 reports on products in scientific advice and protocol assistance
- 16 reports on products in pre-authorisation procedures
- 2 reports on products in post-authorisation procedures
- 6 reports on products in plasma master file

Action: For adoption

14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 15-16 February 2022.

Action: For adoption

14.3.3. Scientific Advice Working Party (SAWP)

Chair: Anja Schiel

Report from the SAWP meeting held on 07-10 February 2022. Table of conclusions

Action: For information

Scientific advice letters:

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

14.3.4. Oncology Working Party (ONCWP)

Chairs: Sinan B. Sarac/Paolo Foggi

Proposal for the list of new members for the Oncology Working Party under the new Working Parties Operational Model (WOM).

Action: For adoption

14.3.5. SWP Response to CMDh regarding medicinal products with genotoxic potential

SWP answered questions from CMDh in 2020 on how to deal with the duration of contraception after completion of a therapy using potentially genotoxic medicines. Member states are now receiving variations with regards to these recommendations. CMDh proposed an amendment to the published Q&A.

Action: For adoption

14.3.6. Re-evaluation of Bisphenol A (BPA) - SWP comment to EFSA public consultation

Summary: EFSA launched an open consultation on the draft scientific opinion on the re-evaluation of the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs with a proposed new TDI value. SWP will provide comments on the draft opinion to share with EFSA some of the concerns related to the methodology and safety assessment that led to the establishment of this new TDI value.

Action: For discussion

14.3.7. SAG Infectious Diseases Group

Appointment of SAG Infectious Diseases Group based on outcome of the election organised by the SAG, in accordance to the SAG-ID rules of procedure

Action: For endorsement

14.4. Cooperation within the EU regulatory network

14.4.1. Revision of pharmaceutical legislation

Follow-up on new Pharmaceutical Strategy

Action: For discussion

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Update on COVID-19

Action: For information

15.1.2. COVID-19 vaccine (inactivated, adjuvanted, adsorbed) - EMEA/H/C/006019

prevention of coronavirus disease-2019 (COVID-19)

Scope: Rolling review 1st interim opinion

Action: For adoption

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)*

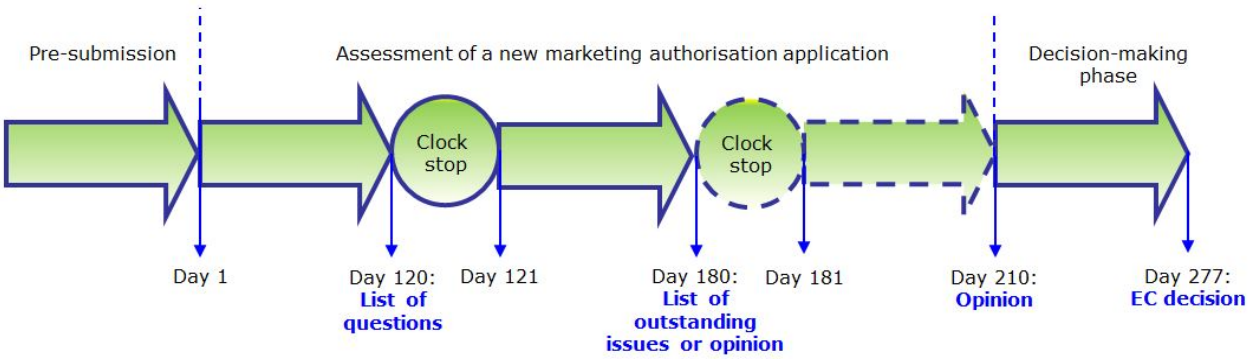
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

21 February 2022
EMA/CHMP/60811/2022

Annex to 21-24 February 2022 CHMP Agenda

Pre-submission and post-authorisations issues

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A. PRE-SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

Final Outcome of Rapporteurship allocation for February 2022: **For adoption**

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

Information related to pre-submission of initial applications cannot be released at the present time as these contain commercially confidential information.

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

B.1.1. Annual reassessment for products authorised under exceptional circumstances

Defitelio - defibrotide - EMEA/H/C/002393/S/0057, Orphan Gentium S.r.l., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga	See 9.1
Lojuxta - lomitapide - EMEA/H/C/002578/S/0048 Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 16.12.2021.	
Obiltoxaximab SFL - obiltoxaximab - EMEA/H/C/005169/S/0004, Orphan SFL Pharmaceuticals Deutschland GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Liana Gross-Martirosyan	
Obizur - susoctocog alfa - EMEA/H/C/002792/S/0044 Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski	
Vedrop - tocofersolan - EMEA/H/C/000920/S/0041 Recordati Rare Diseases, Rapporteur: Agnes	

Gyurasics, PRAC Rapporteur: Melinda Palfi

Vyndaqel - tafamidis -
EMEA/H/C/002294/S/0076, Orphan
Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Tiphaine Vaillant

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Mavenclad - cladribine -
EMEA/H/C/004230/R/0022
Merck Europe B.V., Rapporteur: Thalia Marie Estrup Blicher, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Blitzima - rituximab -
EMEA/H/C/004723/R/0049
Celltrion Healthcare Hungary Kft., Duplicate, Duplicate of Truxima, Rapporteur: Sol Ruiz, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Anette Kirstine Stark

Fampyra - fampridine -
EMEA/H/C/002097/R/0050
Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Liana Gross-Martirosyan

Imraldi - adalimumab -
EMEA/H/C/004279/R/0050
Samsung Bioepis NL B.V., Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Ulla Wändel Liminga

Kalydeco - ivacaftor -
EMEA/H/C/002494/R/0106, Orphan
Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Maria del Pilar Rayon
Request for Supplementary Information adopted on 16.12.2021.

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

PRAC Rapporteur: Eva A. Segovia
Request for Supplementary Information adopted on 16.12.2021.

Kyntheum - brodalumab - EMEA/H/C/003959/R/0019
LEO Pharma A/S, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Eva A. Segovia
Request for Supplementary Information adopted on 27.01.2022.

Rydapt - midostaurin - EMEA/H/C/004095/R/0023, Orphan
Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Ingrid Wang, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/R/0024, ATMP
CO.DON AG, Rapporteur: Lisbeth Barkholt, Co-Rapporteur: Heli Suila, CHMP Coordinators: Kristina Dunder and Outi Mäki-Ikola, PRAC Rapporteur: Brigitte Keller-Stanislawski
Request for Supplementary Information adopted on 10.12.2021.

Tecentriq - atezolizumab - EMEA/H/C/004143/R/0069
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

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

Vosevi - sofosbuvir / velpatasvir / voxilaprevir - EMEA/H/C/004350/R/0053
Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ana Sofia Diniz Martins

Xermelo - telotristat ethyl - EMEA/H/C/003937/R/0032, Orphan
Ipsen Pharma, Rapporteur: Martina Weise, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur:

Adam Przybylkowski

B.2.3. Renewals of Conditional Marketing Authorisations

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

Zolgensma - onasemnogene abeparvovec -
EMEA/H/C/004750/R/0021, Orphan,
ATMP
Novartis Gene Therapies EU Limited,
Rapporteur: Carla Herberts, Co-Rapporteur:
Egbert Flory, CHMP Coordinators: Johann
Lodewijk Hillege and Jan-Mueller-Berghaus,
PRAC Rapporteur: Ulla Wändel Liminga

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at
the PRAC meeting held on 07-10 February 2022
PRAC:

Signal of erythema multiforme

Xtandi **–** Enzalutamide

Rapporteur: Maria Concepcion Prieto Yerro,
Co-Rapporteur: Filip Josephson, PRAC
Rapporteur: Eva A. Segovia
PRAC recommendation on a variation
Action: For adoption

Signal of non-overt disseminated
intravascular coagulation (DIC)

Gazyvaro – Obinutuzumab

Rapporteur: Sinan B. Sarac, Co-Rapporteur:
Alexandre Moreau, PRAC Rapporteur: Annika
Folin
PRAC recommendation on a variation
Action: For adoption

Signal of tumour lysis syndrome

Nexavar – Sorafenib

Rapporteur: Filip Josephson, Co-Rapporteur:
Fatima Ventura, PRAC Rapporteur: Annika
Folin
PRAC recommendation on a variation
Action: For adoption

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its February 2022 meeting:

EMEA/H/C/PSUSA/00000476/202106
(cabazitaxel)
CAPS:
Cabazitaxel Accord (EMEA/H/C/005178) (cabazitaxel), Accord Healthcare S.L.U., Rapporteur: Hrefna Gudmundsdottir
Jevtana (EMEA/H/C/002018) (cabazitaxel), sanofi-aventis groupe, Rapporteur: Alexandre Moreau
NAPS:
NAPs - EU
PRAC Rapporteur: Tiphaine Vaillant, "17/12/2019 To: 17/06/2021"

EMEA/H/C/PSUSA/00001702/202106
(ibandronic acid, sodium ibandronate)
CAPS:
Bondronat (EMEA/H/C/000101) (ibandronic acid), Atnahs Pharma Netherlands B.V., Rapporteur: Thalia Marie Estrup Blicher
Bonviva (EMEA/H/C/000501) (ibandronic acid), Atnahs Pharma Netherlands B.V., Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Anette Kirstine Stark, "25/06/2018 To: 24/06/2021"

EMEA/H/C/PSUSA/00009255/202107
(perampanel)
CAPS:
Fycompa (EMEA/H/C/002434) (perampanel), Eisai GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, "22/07/2020 To: 22/07/2021"

EMEA/H/C/PSUSA/00010379/202107
(nivolumab)
CAPS:
OPDIVO (EMEA/H/C/003985) (nivolumab), Bristol-Myers Squibb Pharma EEIG, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Brigitte Keller-Stanislawski, "03/07/2020 To: 03/07/2021"

EMEA/H/C/PSUSA/00010712/202107
(neratinib)
CAPS:
Nerlynx (EMEA/H/C/004030) (neratinib), Pierre Fabre Medicament, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Menno van der Elst,

"16/07/2020 To: 16/07/2021"	
EMEA/H/C/PSUSA/00010922/202107 (icosapent ethyl) CAPS: **Vazkepa** (EMEA/H/C/005398) (icosapent ethyl), Amarin Pharmaceuticals Ireland Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, "26/07/2020 To: 25/07/2021"	
EMEA/H/C/PSUSA/00010924/202107 (remimazolam) CAPS: **Byfavo** (EMEA/H/C/005246) (remimazolam), PAION Netherlands B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Rhea Fitzgerald, "22/01/2021 To: 22/07/2021"	

B.4. EPARs / WPARs

Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731, Orphan, ATMP Bristol-Myers Squibb Pharma EEIG, treatment of large B-cell lymphoma, diffuse large B-cell lymphoma (DLBCL), primary mediastinal large B-cell lymphoma (PMBCL) and follicular lymphoma grade 3B (FL3B), 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.
Dasatinib Accord - dasatinib - EMEA/H/C/005446 Accord Healthcare S.L.U., treatment of leukaemia, Generic, Duplicate, Generic of Sprycel, Duplicate of Dasatinib Accordpharma, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Dasatinib Accordpharma - dasatinib - EMEA/H/C/005317 Accord Healthcare S.L.U., treatment of leukaemia, Generic, Generic of Sprycel, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Paxlovid - (1r,2s,5s)-n-{(1s)-1-cyano-2-[(3s)-2-oxopyrrolidin-3-yl]ethyl}-6,6-dimethyl-3- [3-methyl-n-(trifluoroacetyl)-l-valyl]-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973	For information only. Comments can be sent to the PL in case necessary.

Pfizer Europe MA EEIG, treatment of COVID-19, New active substance (Article 8(3) of Directive No 2001/83/EC)	
Sondelbay - teriparatide - EMEA/H/C/005827 Accord Healthcare S.L.U., treatment of osteoporosis, 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.
Stimufend - pegfilgrastim - EMEA/H/C/004780 Fresenius Kabi Deutschland GmbH, treatment of neutropenia, 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.
Vildagliptin/Metformin hydrochloride Accord Healthcare - vildagliptin / metformin hydrochloride - EMEA/H/C/005738 Accord Healthcare S.L.U., treatment of type 2 diabetes mellitus, Generic, Generic of Eucreas, Generic application (Article 10(1) 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

Alymsys - bevacizumab - EMEA/H/C/005286/II/0007/G Mabxience Research SL, Rapporteur: Christian Gartner	
Apidra - insulin glulisine - EMEA/H/C/000557/II/0088/G Sanofi-Aventis Deutschland GmbH, Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 03.02.2022.	Request for supplementary information adopted with a specific timetable.
Azacitidine Accord - azacitidine - EMEA/H/C/005147/II/0009 Accord Healthcare S.L.U., Generic, Generic of Vidaza, Rapporteur: Hrefna Gudmundsdottir Opinion adopted on 17.02.2022.	Positive Opinion adopted by consensus on 17.02.2022.
Bexsero - meningococcal group B vaccine (recombinant, component, adsorbed) - EMEA/H/C/002333/II/0106	Positive Opinion adopted by consensus on 10.02.2022.

GSK Vaccines S.r.l, Rapporteur: Kristina Dunder Opinion adopted on 10.02.2022.	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0056/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, " C.I.11.b, (Type II)- To submit additional data to complete characterisation of the active substance and finished product, which are a condition to the Marketing Authorisation (Special Obligation SO1) C.I.11.b, (Type II)- To submit additional data to enhance the control strategy, including the active substance and finished product specifications, which are a condition to the Marketing Authorisation (Special Obligation SO2) Request for Supplementary Information adopted on 16.12.2021, 14.10.2021.	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0092/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 03.02.2022.	Positive Opinion adopted by consensus on 03.02.2022.
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0108/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 10.02.2022.	Positive Opinion adopted by consensus on 10.02.2022.
COVID-19 Vaccine Janssen - adenovirus type 26 encoding the sars-cov-2 spike glycoprotein - EMEA/H/C/005737/II/0037 Janssen-Cilag International N.V., Rapporteur: Christophe Focke Opinion adopted on 10.02.2022.	Positive Opinion adopted by consensus on 10.02.2022.
Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0062 Organon N.V., Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 16.12.2021.	
Enbrel - etanercept - EMEA/H/C/000262/II/0243/G Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro Request for Supplementary Information adopted on 03.02.2022, 02.09.2021.	Request for supplementary information adopted with a specific timetable.

Fluad Tetra - influenza vaccine (surface antigen, inactivated, adjuvanted) - EMEA/H/C/004993/II/0021 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz Request for Supplementary Information adopted on 13.01.2022.	
Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0024 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz Opinion adopted on 17.02.2022.	Positive Opinion adopted by consensus on 17.02.2022.
Herzuma - trastuzumab - EMEA/H/C/002575/II/0038 Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 03.02.2022. Request for Supplementary Information adopted on 20.05.2021.	Positive Opinion adopted by consensus on 03.02.2022.
Imfinzi - durvalumab - EMEA/H/C/004771/II/0036 AstraZeneca AB, Rapporteur: Sinan B. Sarac Opinion adopted on 17.02.2022. Request for Supplementary Information adopted on 09.12.2021.	Positive Opinion adopted by consensus on 17.02.2022.
Invokana - canagliflozin - EMEA/H/C/002649/II/0058 Janssen-Cilag International N.V., Rapporteur: Martina Weise Opinion adopted on 03.02.2022.	Positive Opinion adopted by consensus on 03.02.2022.
Jivi - damoctocog alfa pegol - EMEA/H/C/004054/II/0019/G Bayer AG, Rapporteur: Thalia Marie Estrup Blicher Request for Supplementary Information adopted on 10.02.2022, 07.10.2021.	Request for supplementary information adopted with a specific timetable.
Lamzede - velmanase alfa - EMEA/H/C/003922/II/0023/G, Orphan Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 03.02.2022.	Request for supplementary information adopted with a specific timetable.
Lysodren - mitotane - EMEA/H/C/000521/II/0024 HRA Pharma Rare Diseases, Rapporteur: Blanca Garcia-Ochoa Request for Supplementary Information adopted	

on 13.01.2022, 02.09.2021.	
Ogivri - trastuzumab - EMEA/H/C/004916/II/0040 Viatris Limited, Rapporteur: Karin Janssen van Doorn Request for Supplementary Information adopted on 17.02.2022.	Request for supplementary information adopted with a specific timetable.
Olanzapine Apotex - olanzapine - EMEA/H/C/001178/II/0045 Apotex Europe BV, Generic, Generic of Zyprexa, Rapporteur: John Joseph Borg Opinion adopted on 17.02.2022. Request for Supplementary Information adopted on 13.01.2022, 02.09.2021.	Positive Opinion adopted by consensus on 17.02.2022.
Perjeta - pertuzumab - EMEA/H/C/002547/II/0063 Roche Registration GmbH, Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 17.02.2022.	Request for supplementary information adopted with a specific timetable.
Polivy - polatuzumab vedotin - EMEA/H/C/004870/II/0014/G, Orphan Roche Registration GmbH, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 03.02.2022.	Request for supplementary information adopted with a specific timetable.
POTELIGEO - mogamulizumab - EMEA/H/C/004232/II/0013/G, Orphan Kyowa Kirin Holdings B.V., Rapporteur: Paula Boudewina van Hennik Opinion adopted on 17.02.2022. Request for Supplementary Information adopted on 13.01.2022.	Positive Opinion adopted by consensus on 17.02.2022.
Rekovelle - follitropin delta - EMEA/H/C/003994/II/0030 Ferring Pharmaceuticals A/S, Rapporteur: Jean-Michel Race Opinion adopted on 17.02.2022. Request for Supplementary Information adopted on 13.01.2022.	Positive Opinion adopted by consensus on 17.02.2022.
Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0055/G CSL Behring GmbH, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 17.02.2022.	Request for supplementary information adopted with a specific timetable.

Revestive - teduglutide - EMEA/H/C/002345/II/0055, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Thalia Marie Estrup Blicher Request for Supplementary Information adopted on 17.02.2022, 16.12.2021.	Request for supplementary information adopted with a specific timetable.
Senshio - ospemifene - EMEA/H/C/002780/II/0042/G Shionogi B.V., Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 10.02.2022.	Request for supplementary information adopted with a specific timetable.
SIBNAYAL - potassium citrate / potassium hydrogen carbonate - EMEA/H/C/005407/II/0002/G Advicenne, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 10.02.2022.	Positive Opinion adopted by consensus on 10.02.2022.
Skyrizi - risankizumab - EMEA/H/C/004759/II/0019/G AbbVie Deutschland GmbH & Co. KG, Rapporteur: Peter Kiely Opinion adopted on 03.02.2022.	Positive Opinion adopted by consensus on 03.02.2022.
Soliris - eculizumab - EMEA/H/C/000791/II/0118/G, Orphan Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa Opinion adopted on 03.02.2022.	Positive Opinion adopted by consensus on 03.02.2022.
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0038/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 17.02.2022.	Request for supplementary information adopted with a specific timetable.
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0046 Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 10.02.2022.	Positive Opinion adopted by consensus on 10.02.2022.
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0051/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus	
Spikevax - COVID-19 mRNA vaccine	

(nucleoside-modified) - EMEA/H/C/005791/II/0052/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus	
Supemtek - quadrivalent influenza vaccine (recombinant, prepared in cell culture) - EMEA/H/C/005159/II/0005/G Sanofi Pasteur, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 10.02.2022. Request for Supplementary Information adopted on 16.12.2021.	Positive Opinion adopted by consensus on 10.02.2022.
Thyrogen - thyrotropin alfa - EMEA/H/C/000220/II/0109/G Genzyme Europe BV, Rapporteur: Peter Kiely Opinion adopted on 10.02.2022. Request for Supplementary Information adopted on 16.12.2021.	Positive Opinion adopted by consensus on 10.02.2022.
Trogarzo - ibalizumab - EMEA/H/C/004961/II/0016/G Theratechnologies Europe Limited, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 17.02.2022, 25.11.2021.	Request for supplementary information adopted with a specific timetable.
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0093/G MCM Vaccine B.V., Rapporteur: Christophe Focke Opinion adopted on 10.02.2022.	Positive Opinion adopted by consensus on 10.02.2022.
VEYVONDI - vonicog alfa - EMEA/H/C/004454/II/0020 Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 16.12.2021.	
Votrient - pazopanib - EMEA/H/C/001141/II/0071/G Novartis Europharm Limited, Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 17.02.2022.	Request for supplementary information adopted with a specific timetable.
Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/II/0027/G Pfizer Ireland Pharmaceuticals, Rapporteur:	

Ingrid Wang Request for Supplementary Information adopted on 13.01.2022, 02.12.2021, 28.10.2021, 09.09.2021.	
Zutectra - human hepatitis B immunoglobulin - EMEA/H/C/001089/II/0050 Biotest Pharma GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 10.02.2022. Request for Supplementary Information adopted on 02.12.2021.	Positive Opinion adopted by consensus on 10.02.2022.
WS2189 **Advate-EMEA/H/C/000520/WS2189/0113** **ADYNOVI-EMEA/H/C/004195/WS2189/0026** Takeda Manufacturing Austria AG, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 13.01.2022.	
WS2190 **Lixiana-EMEA/H/C/002629/WS2190/0036** **Roteas-EMEA/H/C/004339/WS2190/0023** Daiichi Sankyo Europe GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro Request for Supplementary Information adopted on 17.02.2022.	Request for supplementary information adopted with a specific timetable.
WS2199 **Infanrix hexa-EMEA/H/C/000296/WS2199/0311** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke	

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

AYVAKYT - avapritinib - EMEA/H/C/005208/II/0014, Orphan Blueprint Medicines (Netherlands) B.V., Rapporteur: Blanca Garcia-Ochoa, "Submission of the final report from study BLU-285-1101 listed as a Specific Obligation in the Annex II of the Product Information. This is an interventional Phase 1 study, designed to evaluate the safety, tolerability, PK, pharmacodynamics, and preliminary antineoplastic activity of avapritinib administered orally in patients with unresectable GIST or other relapsed or refractory solid	Request for supplementary information adopted with a specific timetable.

tumours. The Annex II is updated accordingly." Request for Supplementary Information adopted on 10.02.2022.	
Caprelsa - vandetanib - EMEA/H/C/002315/II/0052 Genzyme Europe BV, Rapporteur: Alexandre Moreau, "Update of section 4.4 of the SmPC in order to amend an existing warning on renal failure based on the safety signal evaluation report. In addition, the MAH took the opportunity to update the contact details for local representative in DE in the Package Leaflet."	
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0101 UCB Pharma S.A., Rapporteur: Kristina Dunder, "C.I.4: Update of section 4.6 of the SmPC in order to update information on pregnancy based on non-interventional data from the UCB Global Safety Database on prospective Cimzia-exposed pregnancies with known outcomes; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 17.02.2022, 11.11.2021.	Request for supplementary information adopted with a specific timetable.
Cometriq - cabozantinib - EMEA/H/C/002640/II/0049, Orphan Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning on hypertension and add hypertensive crisis to the list of adverse drug reactions (ADRs) with frequency not known based on literature review and post-marketing and clinical data. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 03.02.2022.	Request for supplementary information adopted with a specific timetable.
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0093 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information after booster dose, based on interim results from study C4591031, this is a randomized, placebo-controlled, phase 3 booster efficacy study involving participants ≥ 16 years of age who completed the primary series of BNT162b2 30 µg in study C4591001. The Package Leaflet and	See 9.1

Labelling are updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes throughout the product information." Request for Supplementary Information adopted on 27.01.2022.	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0104 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update immunogenicity, safety and efficacy information regarding heterologous vaccination (both in the primary series and for booster vaccinations) based on published literature data; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes throughout the product information."	See 9.1
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0111 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC of Comirnaty 30 microgram/dose to lower the age of the booster dose from adults 18 years of age and older to adults and adolescents 12 years of age and older, based on real world evidence collected by the Ministry of Health of Israel. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes throughout the product information (SmPC and package leaflet)."	See 9.1
Darzalex - daratumumab - EMEA/H/C/004077/II/0053, Orphan Janssen-Cilag International N.V., Rapporteur: Sinan B. Sarac, "C.I.4 Update of section 5.1 of the SmPC in order to update PFS and OS (CCO 19/2/2021) data based on interim results from study MMY3008; This is a Phase 3, randomized, open-label, active controlled, parallel-group, multicentre study in adults with newly diagnosed MM not eligible for ASCT comparing DRd vs Rd. The Marketing authorisation holder (MAH) took the opportunity to make minor formatting and linguistic changes in the PI." Request for Supplementary Information adopted	

on 07.10.2021, 02.09.2021.	
Edarbi - azilsartan medoxomil - EMEA/H/C/002293/II/0030/G Takeda Pharma A/S, Rapporteur: Johann Lodewijk Hillege, "Group of variations: · Type II C.I.4. - Update of SmPC sections 4.2, 4.8 and 5.1 with paediatric clinical data from study AR14.001 (PIP study 8) following the outcome of procedure EMEA/H/C/002293/P46/012. · Type II C.I.4. - Update of SmPC section 5.2 with paediatric clinical data from study TAK-491_109 (PIP study 7) following the outcome of procedure EMEA/H/C/002293/P46/011. · Type II C.I.4. - Update of SmPC section 5.3 with data from juvenile animal toxicity studies. · Type II C.I.4. - Update of SmPC section 4.5 with drug-drug interaction information from clinical pharmacology studies TAK-491-013 and TAK-563-004. Furthermore, the MAH is taking the opportunity to update the PI in line with the latest QRD template version 10.2, update the local representatives for Ireland, Slovenia and United Kingdom in the Package Leaflet (PL) and update minor editorial/typographical to Product information." Request for Supplementary Information adopted on 09.12.2021.	
Eylea - aflibercept - EMEA/H/C/002392/II/0073 Bayer AG, Rapporteur: Alexandre Moreau, "C.I.13 Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority. PFS design change." Request for Supplementary Information adopted on 16.12.2021, 16.09.2021.	
Eylea - aflibercept - EMEA/H/C/002392/II/0076 Bayer AG, Rapporteur: Alexandre Moreau, "Submission of the final report from study AZURE, a randomised PAES in patients with neovascular (wet) AMD with the primary objective of comparing the standard regime of injections every 8 weeks with a reactive regimen based on visual and anatomic outcomes, based on a CHMP approved	Positive Opinion adopted by consensus on 17.02.2022.

protocol." Opinion adopted on 17.02.2022. Request for Supplementary Information adopted on 13.01.2022.	
Eylea - aflibercept - EMEA/H/C/002392/II/0078 Bayer AG, Rapporteur: Alexandre Moreau, "Update of the PI in line with the latest QRD template version 10.2, text reduction, and correction of a typo." Opinion adopted on 10.02.2022.	Positive Opinion adopted by consensus on 10.02.2022.
Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0123 Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 6.6 of the SmPC in order to modify administration instructions based on pre-existing data from the clinical trials AGAL-01-002-98, AGAL-005-99, AGAL-008-00, AGAL-02503 and AGAL-016-01 that already serve as the basis for the currently approved SmPC. In addition, section 5.1 of the SmPC is updated in order to add further information on Fabry patients included in the clinical trials. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 10.02.2022.	Request for supplementary information adopted with a specific timetable.
Feraccru - ferric maltol - EMEA/H/C/002733/II/0033 Norgine B.V., Rapporteur: Maria Concepcion Prieto Yerro, "to remove haemoglobin threshold from section 4.4 'Special warnings and precautions for use' of summary of product characteristics for Feraccru Capsules 30 mg, deleting the reference made that states "Feraccru is not recommended for use in patients with haemoglobin (Hb) <9.5 g/dl.""" Request for Supplementary Information adopted on 03.02.2022, 21.10.2021, 22.07.2021.	Request for supplementary information adopted with a specific timetable.
Fetcroja - cefiderocol - EMEA/H/C/004829/II/0006/G Shionogi B.V., Rapporteur: Filip Josephson, "Submission of the final report from the in vitro RIS correlation study S-649266-PF-415-N (REC 003), to address CYP3A4 induction by cefiderocol. In addition, the MAH submitted the final report of in vitro study S-649266-CPK-008-C to	

investigate the DDI between cefiderocol as a CYP3A4 inducer and Midazolam using physiologically-based pharmacokinetic model." Request for Supplementary Information adopted on 13.01.2022, 11.11.2021.	
Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0053 MSD Vaccins, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to update long-term effectiveness and immunogenicity data following the final results of the Gardasil 9 long-term follow-up (LTFU) study V503-002-20 listed as a category 3 study in the RMP. In addition, the applicant took the opportunity to make some minor editorial changes (spacings) and included the updated long-term follow-up data received for the qHPV vaccine following V501-167 extension study. The Package Leaflet is updated accordingly."	
Glivec - imatinib - EMEA/H/C/000406/II/0129 Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa, "C.I.4, Update of section 4.8 of the SmPC in order to add pemphigus with frequency rare and osteonecrosis with frequency uncommon to the list of adverse drug reactions based on an analysis of pre-clinical data, scientific literature, clinical trial datasets, Novartis pharmacovigilance database, EVDAS and other safety databases. The Package Leaflet is updated accordingly. The MAH is also taking the opportunity to align section 4 of the PL with the already approved ADR section of the SmPC as a number of ADRs is not reflected accurately." Opinion adopted on 17.02.2022.	Positive Opinion adopted by consensus on 17.02.2022.
Imfinzi - durvalumab - EMEA/H/C/004771/II/0039/G AstraZeneca AB, Rapporteur: Sinan B. Sarac, "Update of section 4.2 of the SmPC in order to update the recommendation for dose modification for the adverse reaction myocarditis based on NCCN guideline recommendations (2021) and findings in a Global Patient Safety Database, and update of section 4.8 of the SmPC to further clarify the medical concept of the adverse reaction	

encephalitis, by revising the footnote of the ADR table for encephalitis”	
Imfinzi - durvalumab - EMEA/H/C/004771/II/0040 AstraZeneca AB, Rapporteur: Sinan B. Sarac, “Update of section 5.1 of the SmPC in order to update efficacy data based on the results of the 5-year follow-up analysis of the PACIFIC study (a randomised, double blind, placebo controlled, multicentre study in patients with locally advanced, unresectable NSCLC). In addition, the MAH took the opportunity to include analyses of the exploratory endpoints to meet the commitment (recommendation) to submit exploratory analyses from the PACIFIC study.” Opinion adopted on 17.02.2022.	Positive Opinion adopted by consensus on 17.02.2022.
Jardiance - empagliflozin - EMEA/H/C/002677/II/0062/G Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, “Update of section 5.1 of the SmPC with the results of clinical study EMPULSE (1245-0204), a multicentre, randomised, double-blind, 90-day superiority trial to evaluate the effect on clinical benefit, safety and tolerability of once daily oral EMPagliflozin 10 mg compared to placebo, initiated in patients hospitalised for acUte heart faiLure (de novo or decompensatied chronic HF) who have been StabilisEd (EMPULSE). In addition, the MAH took the opportunity to implement editorial changes in the SmPC.” Request for Supplementary Information adopted on 10.02.2022.	Request for supplementary information adopted with a specific timetable.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0114 Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, “Update of sections 5.1 of the SmPC in order to update efficacy information based on final results from study KEYNOTE-087 listed as an imposed PAES in the Annex II; this is a multicentre, single-arm, multi-cohort, non-randomized Phase 2 study of IV pembrolizumab in participants with relapsed or refractory classical Hodgkin lymphoma (cHL).” Opinion adopted on 17.02.2022. Request for Supplementary Information adopted on 18.11.2021.	Positive Opinion adopted by consensus on 17.02.2022.

Kovaltry - octocog alfa - EMEA/H/C/003825/II/0038 Bayer AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of the SmPC sections 4.8 and 5.1 to include data from the LEOPOLD Kids Part B (previously submitted as Art 46; an addendum on biomarker data is included in this submission) and Extension study results included as part of this submission. In addition, an editorial revision in section 4.2 and a clarification in section 6.5 of the SmPC are proposed. Section 4 of the Package is updated accordingly. A correction of a typo in the Greek product information is also included. The Risk Management Plan for Kovaltry is updated using Revision 2.0.1 of the template format." Request for Supplementary Information adopted on 02.12.2021.	
Kyprolis - carfilzomib - EMEA/H/C/003790/II/0051/G, Orphan Amgen Europe B.V., Rapporteur: Blanca Garcia-Ochoa, "A.6 The ATC code of the product is updated C.I.4, Update of section 4.2 of the SmPC in order to modify administration instructions of daratumumab when Kyprolis is dosed in combination with daratumumab and dexamethasone, based on results from efficacy and safety studies MMY2040 (ongoing phase 2), MMY1001 (completed phase 1b) and CANDOR (ongoing phase 3)." Request for Supplementary Information adopted on 11.11.2021, 22.07.2021.	
MenQuadfi - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/005084/II/0013 Sanofi Pasteur, Rapporteur: Andrea Laslop, "Update of section 5.1 of the SmPC in order to add data on the immunogenicity of serogroup C based on the final results from study MEQ00065; this is a study to compare the immunogenicity and safety of serogroup C of a single dose of Menquadfi to Nimenrix or NeisVac in meningococcal naïve toddlers 12-23 months of age." Opinion adopted on 17.02.2022.	Positive Opinion adopted by consensus on 17.02.2022.
Obizur - susoctocog alfa - EMEA/H/C/002792/II/0042	

Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, "Submission of the final report from OBIZUR study 241502. This is a Phase 3, multicentre, single-arm, open-label study of the efficacy and safety of B-Domain deleted recombinant porcine factor VIII (BAX 802) in subjects with congenital haemophilia A with factor VIII inhibitors undergoing surgical or other invasive procedures. No changes to the PI are proposed."
Request for Supplementary Information adopted on 16.12.2021.

Ocaliva - obeticholic acid - EMEA/H/C/004093/II/0030, Orphan
Intercept Pharma International Limited, Rapporteur: Blanca Garcia-Ochoa, "Update of section 4.3 of the SmPC in order to include contraindication in patients with decompensated cirrhosis (e.g., Child-Pugh Class B or C) or a prior decompensation event based on the MAH's conclusion that it will not be feasible to establish the safety and efficacy of Ocaliva in these patients from either of the ongoing studies 747-302 and 747-401 listed as Specific Obligations in Annex II. Consequently, dosing instructions for patients with CP-B and CP-C cirrhosis are no longer applicable and section 4.2 has been updated accordingly.
In addition, section 4.4 of the SmPC to include a new warning on monitoring and management of patients for possible progression of PBC and other hepatic adverse reactions.
The MAH also took the opportunity to remove the outdated term "primary biliary cirrhosis" from section 4.1 and to make editorial changes to sections 4.8, 4.9, 5.1 and Annex IIE to improve clarity and correct typographical errors. The Package Leaflet is updated accordingly.
Furthermore, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2"
Request for Supplementary Information adopted on 16.12.2021, 16.09.2021.

Plenadren - hydrocortisone - EMEA/H/C/002185/II/0034
Takeda Pharmaceuticals International AG, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC to add bradycardias a new ADR with frequency unknown."

Request for Supplementary Information adopted on 28.10.2021.	
Repatha - evolocumab - EMEA/H/C/003766/II/0057 Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC based on the final study report from study 20120124 (HAUSER-OLE); an open-label, single-arm, multicentre study to evaluate the safety, tolerability and efficacy of evolocumab for low-density lipoprotein (LDL-C) Reduction, as add-on to diet and lipid-lowering therapy, in paediatric subjects from 10 to 17 years of age with heterozygous familial hypercholesterolemia (heFH) or homozygous familial hypercholesterolemia (HoFH) HAUSER-OLE (final analysis). The provision of the final study report addresses the requirements of Article 46 of the Paediatric Regulation." Opinion adopted on 10.02.2022.	Positive Opinion adopted by consensus on 10.02.2022.
Repatha - evolocumab - EMEA/H/C/003766/II/0058 Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, "C.I.4 Update to section 5.1 of the SmPC following the results of interventional study 20160184. It was a double-blind, placebo-controlled, randomized study evaluating the effect of evolocumab on coronary atherosclerotic plaques as assessed by optical coherence tomography (OCT) following 50 weeks of treatment in subjects with non-ST-elevation acute coronary syndrome (NSTE-ACS) who take maximally tolerated statin therapy." Request for Supplementary Information adopted on 17.02.2022.	Request for supplementary information adopted with a specific timetable.
Roclanda - latanoprost / netarsudil - EMEA/H/C/005107/II/0002 Santen Oy, Rapporteur: Jayne Crowe, "C.I.4, Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study PG324-CS303; this is a prospective, double-masked, randomized, multicentre, active-controlled, parallel-group, 6-month study assessing the safety and ocular hypotensive efficacy of Roclanda compared to bimatoprost + timolol in subjects with elevated intraocular pressure that was insufficiently controlled and/or deemed to	

be in need of combination IOP-lowering therapy. The Package Leaflet is updated accordingly."	
Ronapreve - casirivimab / imdevimab - EMEA/H/C/005814/II/0001 Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.1 and 5.1 of the SmPC in order to update information on the in vitro neutralization activity of casirivimab/imdevimab against the SARS-CoV-2 B.1.1.529 (Omicron) variant." Request for Supplementary Information adopted on 10.02.2022.	Request for supplementary information adopted with a specific timetable.
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0042 Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include information on heterologous boosting using a 50 ug dose of Spikevax to boost subjects that have previously completed a primary vaccination series with any authorised COVID-19 vaccine, based on data from the DMID Study 21-0012, a Phase 1/2 heterologous SARS-CoV-2 vaccine dosing (mRNA-1273 booster) study of the various vaccines authorized in the US under Emergency Use Authorisation in participants ≥ 18 years old (NCT04889209). In addition, the MAH took the opportunity to make minor editorial changes/corrections throughout the product information." Request for Supplementary Information adopted on 27.01.2022, 16.12.2021.	See 9.1
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0047 Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, "Update of section 5.1 of the SmPC in order to introduce data on the immunogenicity of Spikevax against the B.1.617.2 (Delta) variant in adults and children, based on cross-neutralisation data from studies mRNA-1273-P301 (an ongoing Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older - NCT04470427), mRNA-1273-P201B (Part B of an ongoing Phase 2a,	See 9.1

Randomized, Observer-Blind, Placebo-Controlled, Dose-Confirmation Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older - NCT04405076), and mRNA-1273-P204 (an ongoing Phase 2/3, 2-part, open-label, dose-escalation, age de-escalation and subsequent randomized, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of mRNA-1273 in healthy children - NCT04796896)."	
Spravato - esketamine - EMEA/H/C/004535/II/0012 Janssen-Cilag International N.V., Rapporteur: Martina Weise, "Update to the SmPC section 4.2 and section 5.1, based on the findings in Chinese subjects from a recently completed efficacy Phase 3 study in adults with treatment-resistant depression." Request for Supplementary Information adopted on 10.02.2022.	Request for supplementary information adopted with a specific timetable.
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 inmunopersistence and booster data based on final results from study B1971035 listed as 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." Request for Supplementary Information adopted on 17.02.2022.	Request for supplementary information adopted with a specific timetable.
Tysabri - natalizumab - EMEA/H/C/000603/II/0131 Biogen Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, "C.I.4 Type II Update of sections 5.1 and 5.2 of the SmPC in order to update efficacy and pharmacokinetic information based on final results from study 101MS329 (NOVA) part 1. This is a randomized, controlled phase 3b study of efficacy, safety and	Positive Opinion adopted by consensus on 10.02.2022.

tolerability of 6-Week Extended Interval Dosing (EID) of Natalizumab in subjects with Relapsing-Remitting Multiple Sclerosis Switching From Treatment With 4-Week Natalizumab Standard Interval Dosing (SID) in Relation to Continued SID Treatment." Opinion adopted on 10.02.2022.	
Vaborem - meropenem / vaborbactam - EMEA/H/C/004669/II/0010/G Menarini International Operations Luxembourg S.A., Rapporteur: Filip Josephson, "A grouped application including 8 type II variations (C.I.4) and 1 type II variation (C.I.13): Update of section 4.5 of the SmPC based on the results of a series of non-clinical drug-drug interaction studies undertaken with vaborbactam or meropenem. The Package Leaflet has been updated accordingly. In addition, the MAH has submitted non-clinical data on the phototoxicity potential of meropenem from a 3T3 neutral red uptake phototoxicity test." Request for Supplementary Information adopted on 17.02.2022, 25.11.2021, 11.03.2021.	Request for supplementary information adopted with a specific timetable.
Veklury - remdesivir - EMEA/H/C/005622/II/0026/G Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, "Grouped variation updating sections 4.6, 5.2 and 5.3 of the SmPC in order to update information in these sections considering new nonclinical data requested at the time of the initial conditional marketing application (EMEA/H/C/005622)." Opinion adopted on 03.02.2022. Request for Supplementary Information adopted on 02.12.2021.	Positive Opinion adopted by consensus on 03.02.2022.
Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0204 Gilead Sciences Ireland UC, Rapporteur: Jean-Michel Race, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Nathalie Gault, "Submission of final study report for study GS-US-174-0144, listed as category 3 study in the RMP for Viread. This is a randomized, double-blind evaluation of the antiviral efficacy, safety and tolerability of Tenofovir disporoxil fumarate. This application fulfils the Article 46 commitment to provide the final week 192 study results for clinical measure 'Study 5'	

(Study GS_US_174-0144) listed in the PIP. Section 5.1 of the SmPC is being amended accordingly. Additionally, the risk minimisation measures for paediatrics are being removed from the RMP and Annex II of the PI. The Package Leaflet has been updated accordingly. The MAH took the opportunity to implement minor linguistic amendments throughout the PI. In addition, the expression of lactose content in Annex I for the tablets was changed, to refer to lactose base (not as monohydrate), in line with current practice. The RMP version 25.1 has been submitted." Request for Supplementary Information adopted on 11.11.2021, 08.07.2021.	
WS2154 **CONTROLOC Control-** **EMEA/H/C/001097/WS2154/0038** **PANTOLOC Control (SRD)-** **EMEA/H/C/001100/WS2154/0043** **PANTOZOL Control-** **EMEA/H/C/001013/WS2154/0040** **SOMAC Control-** **EMEA/H/C/001098/WS2154/0039** Takeda GmbH, Lead Rapporteur: Romaldas Mačiulaitis, "C.1.4 - Update of section 4.8 of the SmPC to update the existing term "Interstitial nephritis" to "Tubulointerstitial nephritis (TIN)" in line with the updated Company Core Data Sheet. In addition, section 4.4 of the SmPC for centralised authorised products is updated with the Excipient warning for Sodium as per EMA guideline EMA/CHMP/302620/2017/EN Rev. 1. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the PL and to bring the PI in line with the last QRD template (version 10.1). This procedure also includes NAPs as listed in Annex B." Request for Supplementary Information adopted on 09.12.2021.	
WS2183 **Infanrix hexa-** **EMEA/H/C/000296/WS2183/0310** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke, "Update of sections 2 and 4.3 of the SmPC for Infanrix	Request for supplementary information adopted with a specific timetable.

Hexa in order to remove the residue formaldehyde. The PL is updated accordingly. Moreover, these sections are also been updated for the removal of some residues currently mentioned in the Product Information (PI) of some of GSK's DTPa/dTpa combined vaccines (NAPs). In addition, the MAH took the opportunity to align the PI to the Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal product for human use" (sections 2, 4.4 and 6.1 of the SmPC). The MAH also took the opportunity to introduce some additional minor changes to the PI and to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 03.02.2022.	

B.5.3. CHMP-PRAC assessed procedures

Alunbrig - brigatinib / brigatinib - EMEA/H/C/004248/II/0037 Takeda Pharma A/S, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of section 5.1 of the SmPC in order to update efficacy information based on final results from study AP26113-13-301 listed as a PAES in the Annex II; this is a randomised, open-label, multicentre phase III study comparing brigatinib versus crizotinib in patients with advanced ALK-positive NSCLC who have not previously received ALK-directed therapy; The RMP version 6.0 has also been submitted." Opinion adopted on 17.02.2022. Request for Supplementary Information adopted on 13.01.2022, 30.09.2021.	Positive Opinion adopted by consensus on 17.02.2022.
Erleada - apalutamide - EMEA/H/C/004452/II/0017 Janssen-Cilag International N.V., Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Tiphaine Vaillant, "Update of section 5.3 of the SmPC in order to update non-clinical information based on final results from study TOX11338 listed as PAM (EMEA/H/C/004452/MEA/006); this is a 2-year carcinogenicity study of JNJ-56021927-AAA by oral gavage in rats; The RMP version 4.1 has also been submitted. In addition, the MAH has taken this opportunity to include general	Positive Opinion adopted by consensus on 10.02.2022.

information in the RMP regarding study TITAN (PCR3002)." Opinion adopted on 10.02.2022. Request for Supplementary Information adopted on 02.12.2021.	
Halaven - eribulin - EMEA/H/C/002084/II/0060 Eisai GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update efficacy and pharmacokinetic information based on results from clinical studies E7389-A001-113, E7389-G000-223 and E7389-G000-213 in the paediatric population (6 months to <18 years); the Package Leaflet is updated accordingly. The RMP version 6.0 has also been submitted." Opinion adopted on 10.02.2022.	Positive Opinion adopted by consensus on 10.02.2022.
IBRANCE - palbociclib - EMEA/H/C/003853/II/0037 Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark, "Submission of an updated RMP version 1.8 in order to remove the Important Potential Risk Hyperglycaemia based on the study results from A5481027, a PAM adopted at the initial MA; this is a multicentre, randomized, double-blind, phase 3 study of palbociclib plus letrozole versus placebo plus letrozole for the treatment of previously untreated Asian postmenopausal women with ER-positive, HER2-negative advanced breast cancer to evaluate the effect of palbociclib on hyperglycaemia - category 3 study." Request for Supplementary Information adopted on 10.02.2022.	Request for supplementary information adopted with a specific timetable.
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	Request for supplementary information adopted with a specific timetable.

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)."
Request for Supplementary Information adopted on 10.02.2022.

Lojuxta - lomitapide - EMEA/H/C/002578/II/0046
Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "To propose an alternative study (LILITH) to the currently agreed protocol for the CAPTURE study. The new study proposes an evaluation of the effect of lomitapide treatment on major adverse cardiovascular events (MACE) in patients with homozygous familial hypercholesterolemia. Consequential submission of an updated RMP (version 6.4) and Annex IID of the Product Information. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2"
Request for Supplementary Information adopted on 16.12.2021, 22.07.2021, 09.04.2021.

Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0024, Orphan
Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of sections 4.8, 5.1 and 5.2 of the SmPC based on the final results from study B176103; this is a single-arm, open-label, phase 4 study evaluating the QT interval, pharmacokinetics, and safety of gemtuzumab ozogamicin as a single-agent regimen in patients with relapsed or refractory CD33-positive Acute Myeloid Leukemia. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to introduce some editorial changes in the product information."

Natpar - parathyroid hormone - EMEA/H/C/003861/II/0029, Orphan
Takeda Pharmaceuticals International AG, Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Rhea Fitzgerald, "Submission of the final results of study SHP634-101: An Open-

Label, Randomized, Crossover Study to Assess the Pharmacokinetic and Pharmacodynamic Profiles of Once-Daily and Twice-Daily Dose Regimens of recombinant human Parathyroid Hormone (rhPTH[1-84]) Administered Subcutaneously to Subjects with Hypoparathyroidism. Further clinical evaluation of an alternative dosing regimen is no longer warranted, as outlined in the current specific obligation (study SHP634-403). The conditional marketing authorisation can therefore be converted into a standard marketing authorisation (no longer subject to a specific obligation) valid for 5 years." Request for Supplementary Information adopted on 11.11.2021, 24.06.2021.	
Nerlynx - neratinib - EMEA/H/C/004030/II/0027 Pierre Fabre Medicament, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Menno van der Elst, "Update of section 5.1 of the SmPC in order to update the pharmacokinetic information with descriptive diarrhoea characteristics based on final results from study PUMA-NER-6201 (CONTROL), listed as a category 3 study in the RMP; this is an Open-Label Study to Characterize the Incidence and Severity of Diarrhea in Patients with Early Stage HER2+ Breast Cancer Treated with Neratinib and Loperamide. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to introduce editorial updates in section 4.2 of the SmPC." Request for Supplementary Information adopted on 10.02.2022.	Request for supplementary information adopted with a specific timetable.
Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0022/G Alexion Europe SAS, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4, 4.8 and 5.1 of the SmPC based the final study report from study 14-505 (ANNEXA-4). This is a Prospective, open-label study of andexanet alfa in patients receiving a factor Xa inhibitor who have acute major bleeding to confirm safety and efficacy in patients with acute major bleeds. The provision of this study report fulfils Specific Obligation 001, and as a consequence it has been deleted in the Annex II. The package leaflet was	

updated accordingly and the applicant took the opportunity to implement editorial changes in the Annexes. The revised RMP version 2.4 has also been submitted.
Change to the summary of pharmacovigilance system due to change in QPPV."
Request for Supplementary Information adopted on 16.12.2021, 16.09.2021.

Oxlumo - lumasiran - EMEA/H/C/005040/II/0008, Orphan
Alnylam Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to clarify administration instructions, remove an existing warning on metabolic acidosis in patients with severe or end stage renal impairment, update the description of adverse reactions injection site reactions, abdominal pain and immunogenicity, update efficacy, pharmacokinetic information based on interim results from a category 3 study in the RMP ILLUMINATE-C (ALN-GO1-005): A single arm study to evaluate efficacy, safety, pharmacokinetics, and pharmacodynamics of lumasiran in patients with advanced primary hyperoxaluria type 1 (PH1) and, in addition, based on available long-term efficacy and safety data from ongoing phase 3 studies ALN-GO1-003 in PH1 patients >6 years old and ALN-GO1-004 in PH1 patients <6 years old, and open-label extension study ALN-GO1-002. The Package Leaflet is updated accordingly. The RMP version 1.1 has also been submitted."

Prolia - denosumab - EMEA/H/C/001120/II/0093
Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.2 and 4.4 of the SmPC in order to change the posology recommendation for paediatric population and add a new warning on hypercalcaemia in paediatric patients with osteogenesis imperfecta following an urgent safety measure regarding the risk of hypercalcaemia reported very commonly in ongoing clinical trials in paediatric patients with osteogenesis imperfecta (OI) treated with denosumab; the Package Leaflet is updated accordingly. The RMP version 29.0 has also been submitted. In addition, the MAH took the

opportunity to update the list of local representatives in the Package Leaflet and to implement minor editorial changes in the Labelling.”	
Reagila - cariprazine - EMEA/H/C/002770/II/0023 Gedeon Richter Plc., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ana Sofia Diniz Martins, “Update of sections 4.4, 4.5, 4.6 and 5.2 of the SmPC in order to update pharmacokinetic information based on final results from RGH-188-302 (CAROLA) study listed as a category 3 study in the RMP; this is an open-label, single-arm, fixed-sequence, phase 1 trial in female schizophrenia patients to investigate the effect of multiple-dose administration of cariprazine on the pharmacokinetics of a combined oral contraceptive containing ethinylestradiol and levonorgestrel; the Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to implement minor editorial changes in sections 4.8 and 5.3 of the SmPC and in the PL. The requested variation proposed amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP).” Opinion adopted on 10.02.2022. Request for Supplementary Information adopted on 28.10.2021.	Positive Opinion adopted by consensus on 10.02.2022.
TOOKAD - padeliporfin - EMEA/H/C/004182/II/0015 STEBA Biotech S.A, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maia Uusküla, “Submission of the Clinical Study Report for category 1 study: Post-authorisation efficacy study (PAES) CLIN1001 PCM301FU5, A European Randomised Phase 3 Study to Assess the Efficacy and Safety of TOOKAD Soluble for Localised Prostate Cancer compared to Active Surveillance. The Annex II has been updated to remove reference to this study. The RMP version 8.0 is approved.” Opinion adopted on 10.02.2022. Request for Supplementary Information adopted on 30.09.2021.	Positive Opinion adopted by consensus on 10.02.2022.
XOSPATA - gilteritinib - EMEA/H/C/004752/II/0007, Orphan	Request for supplementary information adopted with a specific timetable.

Astellas Pharma Europe B.V., Rapporteur: Ingrid Wang, PRAC Rapporteur: Martin Huber, "Submission of the report of an integrated analysis to demonstrate the safety of long-term treatment with gilteritinib when all patients enrolled in studies 2215-CL-0101, 2215-CL-0102 and 2215-CL-0301 have completed at least 3 years of treatment with gilteritinib or have withdrawn prior to completing at least 3 years of treatment. The studies refer to: 1) study 2215-CL-0101: a phase 1/2 open-label, dose escalation study investigating the safety, tolerability, pharmacokinetics, and pharmacodynamics of ASP2215 (gilteritinib) in patients with relapsed or refractory acute myeloid leukaemia (AML); 2) study 2215-CL-0102: a phase 1 open-label, dose escalation study investigating the safety, tolerability, pharmacokinetics, and pharmacodynamics of ASP2215 in Japanese patients with relapsed or refractory AML; 3) study 2215-CL-0301: a phase 3 open-label, multicentre, randomized study of ASP2215 versus salvage chemotherapy in patients with relapsed or refractory AML with FMS-like tyrosine kinase 3 (FLT3) mutation. The RMP (version 2.0) is updated in order to address the missing information regarding the safety of Xospata (gilteritinib)." Request for Supplementary Information adopted on 10.02.2022.	
Zejula - niraparib - EMEA/H/C/004249/II/0033, Orphan GlaxoSmithKline (Ireland) Limited, Rapporteur: Ingrid Wang, PRAC Rapporteur: Jan Neuhauser, "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." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 10.02.2022.	
WS2153 **OPDIVO-** **EMEA/H/C/003985/WS2153/0111** **Yervoy-EMEA/H/C/002213/WS2153/0093** Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Paula Boudewina van Hennik, Lead PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.2 and 6.6 of the SmPC to change the infusion time for ipilimumab when used as monotherapy or in combination with nivolumab in the melanoma indications; the Package Leaflet for Yervoy is updated accordingly. The RMP versions 34.0 for Yervoy and 26.0 for Opdivo have also been submitted. In addition, an administrative update in Annex II of Yervoy is introduced." Request for Supplementary Information adopted on 11.11.2021.	

B.5.4. PRAC assessed procedures

PRAC Led **Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0114** GlaxoSmithkline Biologicals SA, Rapporteur: Christophe Focke, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Karin Janssen van Doorn, "Submission of the final report from study EPI-HPV-048 listed as a category 3 study in the RMP. This surveillance study is part of the two-phase national HPV surveillance programme that was initiated in the UK by the Health Protection Agency in order to evaluate the impact of HPV vaccination on HPV type replacement. The study aimed to assess the prevalence of type-specific HPV deoxyribonucleic acid (DNA) in young women in England since HPV immunisation using Cervarix was introduced. In addition, the MAH has included for information the protocol of study EPI-HPV-099 to address the safety concern "Impact and effectiveness against anal lesions and cancer. The RMP version 25 has also been submitted." Request for Supplementary Information adopted on 10.02.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led	Request for supplementary information adopted

Enbrel - etanercept - EMEA/H/C/000262/II/0244 Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "C.I.13: Submission of the final report from study B1801310 (BIKER), listed as a category 3 study in the RMP. This is an observational Post-Authorisation Safety Study (PASS) of Etanercept and Methotrexate in the treatment of Juvenile Idiopathic Arthritis (JIA) using data obtained from participants in the German Biologics JIA Registry (BIKER) to monitor long-term safety and effectiveness of etanercept in the treatment of JIA in regular clinical practice." Request for Supplementary Information adopted on 10.02.2022, 02.09.2021.	with a specific timetable.
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 10.02.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Nplate - romiplostim - EMEA/H/C/000942/II/0083** Amgen Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of the final report from study 20070797 listed as a category 3 study in the RMP. This is an observational study assessing the long-term safety of romiplostim treatment in real-life clinical practice in three Nordic countries. The RMP version 21.0 has also been submitted." Request for Supplementary Information adopted on 10.02.2022.	Request for supplementary information adopted with a specific timetable.

PRAC Led **Opsumit - macitentan - EMEA/H/C/002697/II/0042, Orphan** Janssen-Cilag International N.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Update of the Risk management plan to v12.2 and consequential update of the Annex II and the patient alert card in the labelling based on the outcome of the PRAC assessment of EMEA/H/C/PSUSA/00010115/202010 : - The controlled distribution system and Prescriber Kit (SmPC, prescribing check list and HCP brochure) is being removed as additional risk minimization measures (aRMM) in the RMP and in the product information Annex II.D. Only the patient card is remaining as an aRMM. - Off-label use is being removed from the list of safety concerns. - "Elderly patients aged over 75 years", "Patients with moderate to severe hepatic impairment" and "Patients with severe renal impairment and/ or undergoing dialysis" are being removed as missing information. - The MAH has also taken the opportunity to include in the RMP Annex 4, the updated Specific Follow-up Questionnaires Forms (pregnancies, menstrual disorders, and ovarian cysts) due to revision of internal company template." Opinion adopted on 10.02.2022. Request for Supplementary Information adopted on 28.10.2021.	Positive Opinion adopted by consensus on 10.02.2022.
PRAC Led **Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0022** Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 2.3 to include clinical safety data from study mRNA-1273 P203 (NCT04649151), a Phase 2/3, randomised, observer-blind, placebo-controlled study evaluating the safety, reactogenicity, and effectiveness of the mRNA-1273 vaccine in healthy adolescents aged ≥ 12 to < 18 years." Opinion adopted on 10.02.2022. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 10.02.2022.

on 02.12.2021, 28.10.2021, 02.09.2021.	
PRAC Led **Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0028** Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 2.3 to include myocarditis and pericarditis as an important identified risk, as requested by PRAC as an outcome of the myocarditis and pericarditis signal assessment procedure." Opinion adopted on 10.02.2022. Request for Supplementary Information adopted on 02.12.2021, 28.10.2021, 02.09.2021.	Positive Opinion adopted by consensus on 10.02.2022.
PRAC Led **Stelara - ustekinumab - EMEA/H/C/000958/II/0091** Janssen-Cilag International N.V., Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, "Submission of the final safety registry report of CNTO1275PSO4007 "Pregnancy Research Initiative: Exposure to ustekinumab during pregnancy: A review and analysis of birth outcomes from the Swedish, Danish and Finnish medical birth registers." Consequently, the RMP version 22.1 has been updated." Request for Supplementary Information adopted on 10.02.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Vargatef - nintedanib - EMEA/H/C/002569/II/0044** Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Georgia Gkegka, PRAC-CHMP liaison: Konstantina Alexopoulou, "Submission of an updated RMP version 10.0 in order to remove safety concerns that were classified as important identified risks, important potential risks and missing information, based on cumulative post-marketing experience. The MAH is also proposing an update of the ATC code, an update of post-marketing exposure, the removal of adverse event follow-up forms and an update of search strategies." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 10.02.2022.	
PRAC Led **Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0038** AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Christophe Focke, "Submission of the final report from study MS1222-0003 ''Assessment of anti-PF4 antibodies prior to, and following, vaccination with AZD1222" listed as a category 3 study in the RMP. This is a study where sera of vaccinated individuals in study D8110C00001 are tested to elucidate whether vaccination with Vaxzevria leads to increased levels of circulating anti-PF4 antibodies, a key component of the hypothesised mechanism underlying thrombosis with thrombocytopenia syndrome (TTS)." Request for Supplementary Information adopted on 10.02.2022, 28.10.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **WS2078** **Lixiana-EMEA/H/C/002629/WS2078/0034** **Roteas-EMEA/H/C/004339/WS2078/0020** Daiichi Sankyo Europe GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Nathalie Gault, PRAC-CHMP liaison: Alexandre Moreau, "C.I.13: Submission of the final report from study ETNA-VTE-EUROPE (DSE-EDO-05-14-EU), listed as a category 3 study in the RMP. This is a Non-Interventional Study on Edoxaban Treatment in Routine Clinical Practice in Patients with Venous Thromboembolism in Europe. The RMP version 12.0 has also been submitted." Request for Supplementary Information adopted on 14.10.2021.	
PRAC Led **WS2151** **Aflunov-EMEA/H/C/002094/WS2151/0071** **Foclivia-EMEA/H/C/001208/WS2151/0068** Seqirus S.r.l, Lead Rapporteur: Armando Genazzani, Lead PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Armando Genazzani, "Submission of an updated RMP version 3.9 in order to align safety concerns for	Request for supplementary information adopted with a specific timetable.

both products AFLUNOV and FOCLIVIA. Module on 'Epidemiology of the indication and target population' and section on 'use in pregnancy and lactation' are updated. Some potential risks have been reclassified following the definition as per GVP Module V rev.2. Reference to adverse drug reaction follow-up forms for routine pharmacovigilance activity are removed." Request for Supplementary Information adopted on 10.02.2022, 28.10.2021.	
PRAC Led **WS2191** **Incresync-** **EMEA/H/C/002178/WS2191/0040** **Vipdomet-** **EMEA/H/C/002654/WS2191/0036** **Vipidia-EMEA/H/C/002182/WS2191/0029** Takeda Pharma A/S, Lead PRAC Rapporteur: Menno van der Elst, "Submission of a consolidated RMP version 11 for Vipidia, Vipdomet and Incresync in order to: - Update the RMPs for Alogliptin, Alogliptin/Pioglitazone fixed dose combination (FDC) and Alogliptin/Metformin fixed dose combination (FDC) to consolidate within a single RMP as committed within the PSUR procedure (PSUSA/00010061/202104). - Following review of cumulative safety data, removal of a number of safety concerns is done based on GVP Module V, Risk Management Systems (revision 2) guidelines. - Remove the target follow-up Questionnaires of Severe Hypersensitivity and skin reactions, Pancreatitis, Hepatic events and follow-up gastrointestinal events and infections from Alogliptin and Alo/Met RMPs. - Reflect the removal of the inverted black triangle as agreed as part of the alogliptin renewal procedure (EMEA/H/C/002178/R/0023) for Alogliptin and the FDC Alogliptin/Metformin. The black triangle was already removed from the FDC Alogliptin/Pioglitazone RMP as part of the Type II variation (EMEA/H/C/002178/II/0029)." Request for Supplementary Information adopted on 10.02.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **WS2192** **Dovato-EMEA/H/C/004909/WS2192/0026**	Positive Opinion adopted by consensus on 10.02.2022.

Juluca-EMEA/H/C/004427/WS2192/0040 **Tivicay-EMEA/H/C/002753/WS2192/0075** **Triumeq-EMEA/H/C/002754/WS2192/0099** ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Ingrid Wang, "Update of section 4.8 of the SmPC to add "completed suicide" to the list of adverse drug reactions (ADRs) with frequency "rare" in the dolutegravir (Tivicay), dolutegravir/ abacavir/lamivudine (Triumeq) and dolutegravir/lamivudine (Dovato) following the finalisation of PSUSA procedure EMEA/H/C/PSUSA/00010075/202101 (reporting period 17 Jan 2020 to 16 Jan 2021) based on reports of completed suicide from participants exposed to Doletugravir containing regimen in ViiV Healthcare-sponsored clinical trials. As the changes impact all Doletugravir containing products, the MAH did a worksharing procedure to include Juluca (Dolutegravir/Rilpivirine) product in accordance with Article 20 (worksharing procedure) of Commission Regulation (EC) 1234/2008. The Package Leaflet are updated accordingly." Opinion adopted on 10.02.2022.	
PRAC Led **WS2196** **Glyxambi-EMEA/H/C/003833/WS2196/0042** **Jardiance-EMEA/H/C/002677/WS2196/0063** **Synjardy-EMEA/H/C/003770/WS2196/0060** Boehringer Ingelheim International GmbH, Lead PRAC Rapporteur: Eva A. Segovia, "Update of section 4.4 of the SmPC to delete the warning on 'lower limb amputations' as a consequence of the results from the final meta-analysis report of PASS 1245.171 'A meta-analysis of amputation risk in empagliflozin studies (1245.25, 1245.110, 1245.121)' (included as a category 3 study in the RMP). The Package Leaflet has been updated accordingly. Updated RMP versions have also been submitted; version 17 for Jardiance, version 11 for Synjardy and version 6 for Glyxambi." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 10.02.2022.

B.5.5. CHMP-CAT assessed procedures

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0049/G, Orphan, ATMP Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang	
WS2194 **Tecartus-** **EMEA/H/C/005102/WS2194/0018** **Yescarta-** **EMEA/H/C/004480/WS2194/0048** Kite Pharma EU B.V., Lead Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus Request for Supplementary Information adopted on 10.02.2022.	Request for supplementary information adopted with a specific timetable.
WS2197 **Tecartus-** **EMEA/H/C/005102/WS2197/0017** **Yescarta-** **EMEA/H/C/004480/WS2197/0047** Kite Pharma EU B.V., Lead Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus	

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

PRAC Led **Yescarta - axicabtagene ciloleucel - EMEA/H/C/004480/II/0040, Orphan, ATMP** Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final study report for the non-interventional study KT-EU-471-0116 (Quantitative Testing of Healthcare Provider Knowledge about Yescarta (axicabtagene ciloleucel) Risk Minimisation Measures) in fulfilment of an additional pharmacovigilance activity (category 3) listed in the EU Risk Management Plan for Yescarta."

Request for Supplementary Information adopted on 10.09.2021.	

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

WS2136 **Esperoct-** **EMEA/H/C/004883/WS2136/0009** **NovoEight-** **EMEA/H/C/002719/WS2136/0039** Novo Nordisk A/S, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 03.02.2022.	Request for supplementary information adopted with a specific timetable.
WS2148/G **Hexacima-** **EMEA/H/C/002702/WS2148/0122/G** **Hexyon-** **EMEA/H/C/002796/WS2148/0126/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 10.02.2022. Request for Supplementary Information adopted on 09.12.2021.	Positive Opinion adopted by consensus on 10.02.2022.
WS2168 **Lyrica-EMEA/H/C/000546/WS2168/0114** **Pregabalin Pfizer-** **EMEA/H/C/003880/WS2168/0043** Upjohn EESV, Lead Rapporteur: Johann Lodewijk Hillege, "To update SmPC sections 4.4 and 4.8 to reflect new data on suicidal ideation following the review of the data provided in LEG 007 and 054. The package leaflet has been updated accordingly." Request for Supplementary Information adopted on 17.02.2022.	Request for supplementary information adopted with a specific timetable.
WS2171 **Glyxambi-** **EMEA/H/C/003833/WS2171/0040** **Synjardy-** **EMEA/H/C/003770/WS2171/0058** Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "To update section 4.8 of the SmPC and section 4 of the PL to include the side effect 'constipation' in order to align with the Jardiance PI following approval of EMEA/H/C/002677/II/0055." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 03.02.2022, 02.12.2021.	
WS2200 **Glyxambi-** **EMEA/H/C/003833/WS2200/0041** **Synjardy-** **EMEA/H/C/003770/WS2200/0059** Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "To update sections 4.2, 4.4 and 5.1 of the SmPC to propose a modification of the eGFR threshold in the EU PIs for the fixed dose combinations containing empagliflozin, for Synjardy (empagliflozin/metformin) and Glyxambi (empagliflozin/linagliptin) to allow for use of these empagliflozin containing products in patients with T2DM and high cardiovascular risk and an eGFR of ≥30 ml/min/1.73 m2. This is in line with the changed eGFR threshold for Jardiance (empagliflozin) which received a Positive Opinion on 16 Sep 2021 for the assessment of variation EMEA/H/C/002677/II/0057. Additionally, some editorial changes are also proposed in the revised Synjardy and Glyxambi Product Information. Furthermore, only for Synjardy, Annex A is also suggested to be updated with minor editorial changes. Finally, the MAH took the opportunity to submit some Minor Linguistic Changes to Synjardy and Glyxambi Product Information for several countries, as detailed below: - Glyxambi: SV, ES, FR, PL, HU and HR. - Synjardy: FR, DE, SV, PL, MT, ET, IT, ES, NL, FI and HR." Opinion adopted on 10.02.2022.	Positive Opinion adopted by consensus on 10.02.2022.
WS2203 **Kinzalmono-** **EMEA/H/C/000211/WS2203/0117** **Micardis-** **EMEA/H/C/000209/WS2203/0121** **Pritor-EMEA/H/C/000210/WS2203/0130** Boehringer Ingelheim International GmbH, Lead Rapporteur: Armando Genazzani, "To introduce several minor linguistic and editorial changes in the PI in all the EEA languages in alignment with the English PI, following the EMA recommendation to perform a full linguistic review of the PI in all EEA languages. In addition, the MAH has implemented the	

updated QRD template version 10.2 in all EEA languages including the English PI, for the products Pritor and Kinzalmono.”	
WS2207 **Copalia HCT-** **EMEA/H/C/001159/WS2207/0096** **Dafiro HCT-** **EMEA/H/C/001160/WS2207/0098** **Exforge HCT-** **EMEA/H/C/001068/WS2207/0095** Novartis Europharm Limited, Lead Rapporteur: Thalia Marie Estrup Blicher, “To bring the annexes in line with the current QRD template v10.2. In addition, the MAH has taken the opportunity to update the local contact details for the UK (Northern Ireland).” Opinion adopted on 03.02.2022.	Positive Opinion adopted by consensus on 03.02.2022.
WS2213/G **Aprovel-** **EMEA/H/C/000141/WS2213/0189/G** **Karvea-** **EMEA/H/C/000142/WS2213/0191/G** sanofi-aventis groupe, Lead Rapporteur: Maria Concepcion Prieto Yerro	

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

Plenadren - hydrocortisone - **EMEA/H/C/002185/II/0034** Takeda Pharmaceuticals International AG, Rapporteur: Kristina Dunder, “Update of section 4.8 of the SmPC to add bradycardias a new ADR with frequency unknown.” Request for Supplementary Information adopted on 28.10.2021.	Withdrawn on 10.02.2022
Nordimet - methotrexate - **EMEA/H/C/003983/II/0021/G** Nordic Group B.V., Rapporteur: Bruno Sepodes Request for Supplementary Information adopted on 13.01.2022.	Withdrawn on 03.02.2022

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

PRAC Led **Otezla - apremilast - EMEA/H/C/003746/II/0038** Amgen Europe B.V., Rapporteur: Peter Kiely, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "C.I.13 - Submission of the final study report (CSR) from PsOBest Registry, listed as a category 3 study in the RMP. This is an observational study to assess the long-term safety and effectiveness of apremilast in routine clinical practice in Germany. The RMP version 14.0 has also been submitted." Request for Supplementary Information adopted on 30.09.2021.	Request for an extension to the clock stop to respond to the RSI adopted in September 2021.
HEPLISAV B - hepatitis B surface antigen - EMEA/H/C/005063/II/0010 Dynavax GmbH, Rapporteur: Filip Josephson Request for Supplementary Information adopted on 14.10.2021.	Request for an extension to the clock stop to respond to the RSI adopted in October 2021.
PRAC Led **VPRIV - velaglucerase alfa - EMEA/H/C/001249/II/0049, Orphan** Takeda Pharmaceuticals International AG, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of final physician data study results for PASS study "Evaluation of the Effectiveness of Risk Minimisation Measures: A Survey among Health Care Professionals and Patient/Caregivers to Assess their Knowledge and Attitudes on Prescribing and Home Administration Conditions of Velaglucerase Alpha (VPRIV) in 6 European Countries" (EUPASS 14255)" Request for Supplementary Information adopted on 02.12.2021, 08.07.2021, 11.02.2021, 26.11.2020.	Request for an extension to the clock stop to respond to the RSI adopted in December 2021.

Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0031 AstraZeneca AB, Rapporteur: Sol Ruiz, "Submission of the final study report for MS1222-0002 "In Vitro Assay to Determine Release of Spike Protein From Transduced Cells" to fulfil the imposed study as reflected in Annex II of the product information and the RMP. As a result, Annex II of the product information is being updated to remove this study. The MAH is taking the opportunity to provide two additional studies linked to support the investigation on the platelet activation: the final study report for MS1222-0001 "Computational Prediction of Spike Protein Interaction with Platelet Factor 4 (PF4)" which is the first report requested within the required studies for "in vitro interaction of AZD1222 or spike protein with PF4 and/or platelets" as reflected in the RMP; and the study report for 520447 "Investigative Vaccine Study in the Mouse" to evaluate spike protein levels and haematology parameters." Request for Supplementary Information adopted on 13.01.2022, 23.09.2021.	Request for an extension to the clock stop to respond to the RSI adopted in January 2022.

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

nirsevimab - EMEA/H/C/005304 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	**Accelerated review**
in vitro diagnostic medical device - EMEA/H/D/006078 detection of PD-L1 protein	

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

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

asciminib - EMEA/H/C/005605, Orphan
Novartis Europharm Limited, treatment of Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP)
List of Questions adopted on 11.11.2021.

lenacapavir - EMEA/H/C/005638
treatment of human immunodeficiency virus type 1 (HIV-1) infection
List of Questions adopted on 16.12.2021.

Procysbi - mercaptamine - EMEA/H/C/002465/X/0035, Orphan
Chiesi Farmaceutici S.p.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Extension application to introduce a new pharmaceutical form associated with two new strengths (75 and 300 mg gastro-resistant granules). The RMP (version 7.2) is updated in accordance."
List of Questions adopted on 11.11.2021.

ranibizumab - EMEA/H/C/005019
The treatment of neovascular (wet) age-related macular degeneration (AMD), visual impairment due to diabetic macular oedema (DME), proliferative diabetic retinopathy (PDR), visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO) and visual impairment due to choroidal neovascularisation (CNV)
List of Questions adopted on 11.11.2021.

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

The RMP (version 6.0) has also been submitted."
List of Questions adopted on 27.01.2022.

valoctocogene roxaparvovec - EMEA/H/C/005830, Orphan, ATMP
BioMarin International Limited, treatment of severe haemophilia A
List of Questions adopted on 05.11.2021.

efgartigimod alfa - EMEA/H/C/005849, Orphan
Argenx, treatment of generalized Myasthenia Gravis (gMG)
List of Questions adopted on 16.12.2021.

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

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

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/R/0014, Orphan, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang, PRAC Rapporteur: Annika Folin

Alecensa - alectinib - EMEA/H/C/004164/R/0039
Roche Registration GmbH, Rapporteur: Filip Josephson, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Jana Lukacisinova

Dovprela - pretomanid - EMEA/H/C/005167/R/0010, Orphan
Mylan IRE Healthcare Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Liana Gross-Martirosyan

Elebrato Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004781/R/0026
GlaxoSmithKline Trading Services Limited, Duplicate, Duplicate of Trelegy Ellipta, Rapporteur: Peter Kiely, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Annika Folin

Hepcludex - bulevirtide - EMEA/H/C/004854/R/0013, Orphan

Gilead Sciences Ireland Unlimited Company, Rapporteur: Filip Josephson, PRAC Rapporteur: Adam Przybylkowski

Idefirix - imlifidase - EMEA/H/C/004849/R/0007, Orphan
Hansa Biopharma AB, Rapporteur: Martina Weise, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst

Nyxoid - naloxone - EMEA/H/C/004325/R/0014
Mundipharma Corporation (Ireland) Limited, Rapporteur: Bruno Sepodes, Co-Rapporteur: Elita Poplavska, PRAC Rapporteur: Liana Gross-Martirosyan

Ontruzant - trastuzumab - EMEA/H/C/004323/R/0040
Samsung Bioepis NL B.V., Rapporteur: Karin Janssen van Doorn, Co-Rapporteur: Elita Poplavska, PRAC Rapporteur: Brigitte Keller-Stanislawski

Ritonavir Mylan - ritonavir - EMEA/H/C/004549/R/0015
Mylan Pharmaceuticals Limited, Generic, Generic of Norvir, Rapporteur: John Joseph Borg, PRAC Rapporteur: Liana Gross-Martirosyan

Tacforius - tacrolimus - EMEA/H/C/004435/R/0010
Teva B.V., Generic, Generic of Advagraf, Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Ronan Grimes

Translarna - ataluren - EMEA/H/C/002720/R/0067, Orphan
PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan

Trelegy Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004363/R/0023
GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Annika Folin

Tremfya - guselkumab - EMEA/H/C/004271/R/0033
Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, Co-Rapporteur: Peter Kiely,

PRAC Rapporteur: Brigitte Keller-Stanislawski

VeraSeal - human fibrinogen / human thrombin - EMEA/H/C/004446/R/0018
Instituto Grifols, S.A., Rapporteur: Andrea Laslop, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Amelia Cupelli

Zejula - niraparib - EMEA/H/C/004249/R/0034, Orphan
GlaxoSmithKline (Ireland) Limited, Rapporteur: Ingrid Wang, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Jan Neuhauser

Zubsolv - buprenorphine / naloxone - EMEA/H/C/004407/R/0019
Accord Healthcare S.L.U., Rapporteur: Peter Kiely, Co-Rapporteur: Tomas Radimersky, PRAC Rapporteur: Martin Huber

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

Brukinsa - zanubrutinib - EMEA/H/C/004978/II/0003
BeiGene Ireland Ltd, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Johanna Lähteenvuo, PRAC Rapporteur: Menno van der Elst,
"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."

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

Roche Registration GmbH, Rapporteur: Peter Kiely, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, "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."

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"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)

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

BLINCYTO - blinatumomab - EMEA/H/C/003731/II/0045, Orphan

Amgen Europe B.V., Rapporteur: Alexandre

Moreau	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0108/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	See also B.5.1
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0109/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0112/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0115/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COVID-19 Vaccine Janssen - adenovirus type 26 encoding the sars-cov-2 spike glycoprotein - EMEA/H/C/005737/II/0041/G Janssen-Cilag International N.V., Rapporteur: Christophe Focke	
Drovelis - drospirenone / estetrol - EMEA/H/C/005336/II/0006/G Chemical Works of Gedeon Richter Plc. (Gedeon Richter Plc.), Rapporteur: Kristina Dunder	
Dupixent - dupilumab - EMEA/H/C/004390/II/0059/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus	
Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0113/G AstraZeneca AB, Rapporteur: Christophe Focke	
Jivi - damoctocog alfa pegol - EMEA/H/C/004054/II/0023 Bayer AG, Rapporteur: Thalia Marie Estrup Blicher	
Kanuma - sebelipase alfa - EMEA/H/C/004004/II/0036/G, Orphan Alexion Europe SAS, Rapporteur: Karin Janssen van Doorn	
Lydisilka - drospirenone / estetrol - EMEA/H/C/005382/II/0006/G	

Estetra SRL, Duplicate, Duplicate of Drovelis, Rapporteur: Kristina Dunder

MabThera - rituximab - EMEA/H/C/000165/II/0189/G
Roche Registration GmbH, Rapporteur: Sinan B. Sarac

Mekinist - trametinib - EMEA/H/C/002643/II/0053/G
Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik

MenQuadfi - meningococcal group a, c, w135 and y conjugate vaccine - EMEA/H/C/005084/II/0016/G
Sanofi Pasteur, Rapporteur: Andrea Laslop

Nityr - nitisinone - EMEA/H/C/004582/II/0011
Cycle Pharmaceuticals (Europe) Limited, Generic, Generic of Orfadin, Rapporteur: Peter Kiely

Nucala - mepolizumab - EMEA/H/C/003860/II/0049
GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely

Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (h5n1) (live attenuated, nasal) - EMEA/H/C/003963/II/0048/G
AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus

Paxlovid - (1r,2s,5s)-n-{(1s)-1-cyano-2-[(3s)-2-oxopyrrolidin-3-yl]ethyl}-6,6-dimethyl-3- [3-methyl-n-(trifluoroacetyl)-l-valyl]-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973/II/0001/G
Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race

Paxlovid - (1r,2s,5s)-n-{(1s)-1-cyano-2-[(3s)-2-oxopyrrolidin-3-yl]ethyl}-6,6-dimethyl-3- [3-methyl-n-(trifluoroacetyl)-l-valyl]-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973/II/0002
Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race

Paxlovid - (1r,2s,5s)-n-{(1s)-1-cyano-2-

[(3s)-2-oxopyrrolidin-3-yl]ethyl}-6,6-dimethyl-3- [3-methyl-n-(trifluoroacetyl)-l-valyl]-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973/II/0003/G
Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race

RoActemra - tocilizumab - EMEA/H/C/000955/II/0108
Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus

Soliris - eculizumab - EMEA/H/C/000791/II/0121, Orphan
Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa

Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0054/G
Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus

Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0171/G
GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder

Trulicity - dulaglutide - EMEA/H/C/002825/II/0062/G
Eli Lilly Nederland B.V., Rapporteur: Martina Weise

Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0064/G
AstraZeneca AB, Rapporteur: Sol Ruiz

Vyxeos liposomal - daunorubicin / cytarabine - EMEA/H/C/004282/II/0028/G, Orphan
Jazz Pharmaceuticals Ireland Limited, Rapporteur: Johanna Lähteenvuo

Wegovy - semaglutide - EMEA/H/C/005422/II/0001/G
Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege

Zinplava - bezlotoxumab - EMEA/H/C/004136/II/0031
Merck Sharp & Dohme B.V., Rapporteur: Jan

Mueller-Berghaus	
WS2193 **Cancidas-** **EMEA/H/C/000379/WS2193/0075** **Cubicin-EMEA/H/C/000637/WS2193/0081** **Invanz-EMEA/H/C/000389/WS2193/0065** **Ivemend-** **EMEA/H/C/000743/WS2193/0046** **Noxafil-EMEA/H/C/000610/WS2193/0069** **PREVYMIS-** **EMEA/H/C/004536/WS2193/0025** **Recarbrio-** **EMEA/H/C/004808/WS2193/0013** **Sivextro-** **EMEA/H/C/002846/WS2193/0044** **Temodal-** **EMEA/H/C/000229/WS2193/0096** **Zerbaxa-** **EMEA/H/C/003772/WS2193/0037** Merck Sharp & Dohme B.V., Lead Rapporteur: Filip Josephson	

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

Cibinqo - abrocitinib - **EMEA/H/C/005452/II/0002** Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder, "Update of section 4.5 of the SmPC based on results from Drug-Drug Interaction (DDI) study B7451061; A phase 1, randomized, crossover study to evaluate relative Bioavailability of abrocitinib Oral suspension and effect of an Acid-reducing agent on the Bioavailability of abrocitinib Commercial tablet and to assess The taste of abrocitinib oral Formulations in healthy adult Participants aged 18 to 55 years of age."	
COMIRNATY - tozinameran - **EMEA/H/C/005735/II/0111** BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC of Comirnaty 30 microgram/dose to lower the age of the booster dose from adults 18 years of age and older to adults and adolescents 12 years of age and older, based on real world evidence collected by the Ministry of Health of Israel. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to	See 9.1 and B.5.2

make minor editorial changes throughout the product information (SmPC and package leaflet)."

Cosentyx - secukinumab - EMEA/H/C/003729/II/0084

Novartis Europharm Limited, Rapporteur: Outi Mäki-Ikola, "Update of section 4.8 of the SmPC in order to add the new ADR "dyshidrotic eczema" with the frequency Uncommon based on post-marketing data. The section 4 of Package Leaflet is updated accordingly."

Cotellic - cobimetinib - EMEA/H/C/003960/II/0025

Roche Registration GmbH, Rapporteur: Filip Josephson, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC based on final results from study GO29665 (iMATRIX_cobimetinib) which corresponds to study 4 of PIP EMEA-C-001425-PIP01-13-M05. This is a phase I/II, multicentre, open-label, dose-escalation study of the safety, efficacy and pharmacokinetics of cobimetinib in paediatric and young adult patients with previously treated solid tumours. The section 2 of the Package Leaflet is updated accordingly. In addition, final results of the GO29665 study are submitted in line with Article 46 of Regulation (EC) No 1901/2006."

Edurant - rilpivirine - EMEA/H/C/002264/II/0040

Janssen-Cilag International N.V., Rapporteur: Paula Boudewina van Hennik, "Update of section 4.8 of the SmPC in order to remove several of the treatment emergent clinical laboratory abnormalities from the list of adverse drug reactions (ADRs). The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Hepcludex - bulevirtide - EMEA/H/C/004854/II/0011, Orphan

Gilead Sciences Ireland Unlimited Company, Rapporteur: Filip Josephson, "Update of section 4.4 of the SmPC in order to remove the existing warnings on 'Increase of bile salts' and 'Administration site reactions', and add them as ADRs in section 4.8 of the SmPC as well as the addition of a new ADR: hypersensitivity reactions (including

anaphylactic reaction) and editing existing ADRs following a safety review based on pooled data from clinical trials and post-marketing experience. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and to make it in line with the EU QRD template v10.2."

Kineret - anakinra - EMEA/H/C/000363/II/0087

Swedish Orphan Biovitrum AB (publ), Rapporteur: Thalia Marie Estrup Blicher, "C.I.13: Submission of the final report from study SAVE-MORE, as requested as part of procedure EMEA/H/C/000363/II/086. This is a prospective, double-blind, randomized, placebo-controlled study was to evaluate the efficacy and safety of the early start of anakinra treatment guided by suPAR in patients with LRTI by SARS-CoV-2 in improving the clinical state of COVID-19 patients over 28 days as measured by the ordinal scale of the 11-point WHO-CPS."

Luveris - lutropin alfa - EMEA/H/C/000292/II/0091

Merck Europe B.V., Rapporteur: Thalia Marie Estrup Blicher, "Update of sections 4.1, 4.2, 5.1 and 5.2 of the SmPC in order to update details regarding the definition of severe LH and FSH deficiency, to clarify follicular development as the treatment target and selection of the most adequate Medically Assisted Reproduction procedure for healthcare providers and to clarify the pharmacokinetic and pharmacodynamic properties of the two gonadotropins, in alignment with the variation EMEA/H/C/000714/II/0075 for Pergoveris, based on a systematic literature search and review.
The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0115

Pfizer Europe MA EEIG, Rapporteur: Ingrid Wang, "Update of section 5.1 of the SmPC, as requested by the CHMP following the conclusion of procedure P46/055, in order to include long-term antibody persistence data from study

MenACWY-TT-104: a phase III, randomised, open, controlled, multicentre, primary vaccination study to evaluate the immunogenicity and persistence of 1 and 2 doses of meningococcal conjugate vaccine MenACWY-TT in toddlers (after 1 month and up to 5 years) and to demonstrate non-inferiority of co-administration of MenACWY-TT and 13-valent pneumococcal conjugate vaccine prevenar 13 versus separate administration of the 2 vaccines. The Annex II has been updated accordingly."	
Revlimid - lenalidomide - EMEA/H/C/000717/II/0122 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Alexandre Moreau, "Update of section 4.2 of the SmPC to update the dosage for patients with impaired renal function (severe renal impairment and end stage renal disease) for the follicular lymphoma (FL) indication based on additional PK analysis. In addition, the MAH proposed to update the existing warning in section 4.4 of the SmPC to highlight that male patients should not donate semen or sperm during treatment and for at least seven days after the end of treatment in order to align with the Revlimid Annex IID requirements for the patient educational brochures and to align with similar wording in the Imnovid (pomaldiomide) and Thalidomide BMS (thalidomide) SmPCs. The Package Leaflet is updated accordingly."	
Ronapreve - casirivimab / imdevimab - EMEA/H/C/005814/II/0001 Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.1 and 5.1 of the SmPC in order to update information on the in vitro neutralisation activity of casirivimab/imdevimab against the SARS-CoV-2 B.1.1.529 (Omicron) variant."	See B.5.2
RYBREVANT - amivantamab - EMEA/H/C/005454/II/0001 Janssen-Cilag International N.V., Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to add hypokalaemia and hypomagnesaemia to the list of adverse drug reactions (ADRs), with the frequency common, based on an updated analysis of data submitted during the marketing authorisation procedure. The Package Leaflet is updated accordingly. In	

addition, the MAH proposed to update the current information in section 4.2 of the SmPC to improve clarity and provide more specific guidance. The MAH also took the opportunity to introduce editorial changes in section 4.8 of the SmPC."

Somavert - pegvisomant - EMEA/H/C/000409/II/0102

Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, "Update of section 5.1 of the SmPC in order to include details on insulin sensitivity based on the results of the ACROSTUDY (A6291010) and additional literature. In addition, the MAH took the opportunity to introduce editorial changes to the list of local representatives in the Package Leaflet."

Sprycel - dasatinib - EMEA/H/C/000709/II/0083

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Sinan B. Sarac, "Submission of the final report from study CA180226 PK substudy, as requested in X/0056/G procedure, and the population PK (PPK) analyses conducted to refine the PK characterisation of the dasatinib (BMS-354825) powder for oral suspension (PFOS) in paediatric patients with Philadelphia chromosome positive (Ph+) chronic phase chronic myeloid leukaemia (CP-CML) or Ph+ acute lymphoblastic leukaemia (ALL)."

Vocabria - cabotegravir - EMEA/H/C/004976/II/0011

ViiV Healthcare B.V., Rapporteur: Jean-Michel Race, "Submission of the final report from study 2021N477482_00. This is an in vitro study to assess the cabotegravir inducing potential on CYP1A2 and 2B6 mRNAs in human hepatocyte cells."

B.6.10. CHMP-PRAC assessed procedures

Cibinqo - abrocitinib - EMEA/H/C/005452/II/0001

Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of sections 4.4 and 4.8 of the SmPC based on updated safety data from the Full Cumulative Pool (April 2021 data cut) from the ongoing long-term extension study B7451015. The RMP version v1.0 has also been

submitted. In addition, MAH took the opportunity to implement editorial changes in the SmPC and to update the contact details of the local representatives in the Package Leaflet."

CRYSVITA - burosumab - EMEA/H/C/004275/II/0028, Orphan

Kyowa Kirin Holdings B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.8 and 5.1 of the SmPC in order to update the frequency of the adverse drug reactions, to split immunogenicity data into paediatric and adult populations and to update clinical efficacy in paediatric patients upon request by the CHMP, following PAM procedures P46/006, P46/007 and type II variations II/04 and II/10/G, based on the final results from studies UX023-CL201, UX023-CL205 and UX023-CL301.
In addition, the MAH proposes to delete the remaining specific obligation for study UX023-CL205 from the Annex II and requests the switch from a conditional MA to standard MA. The Package Leaflet was updated accordingly. The RMP version 5.0 has also been submitted."

Dapivirine Vaginal Ring 25 mg - dapivirine - EMEA/H/W/002168/II/0015/G

International Partnership for Microbicides Belgium AISBL, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Jan Neuhauser, "Submission of the four addenda from studies IPM 032, MTN-025, IPM 007 and MTN-015 listed as category 3 studies in the RMP. The data presented in the addenda are the results of retrospective next generation sequencing (NGS) and phenotype susceptibility testing on blood samples to further assess the potential development of nonnucleoside reverse transcriptase inhibitor (NNRTI) resistance in women with unrecognised or acute HIV-1 infection. The tested samples are all from women who were initially enrolled in the Phase III clinical trials IPM 027 and MTN-020 and then had the option to participate in the open-label extension (OLE) studies IPM 032 and MTN-025. If the women became infected with HIV during any of the trials, they could enrol in the observational studies IPM 007 and MTN-015. The RMP version 0.9 has also been submitted.

Additionally, the MAH would like to take the opportunity to update the EMA on other commitments outlined in the RMP as additional risk minimisation measures. These include the development of a Healthcare Professional Guide (HCP Guide) and a User Guide with agreed objectives and key messages."	
Dapivirine Vaginal Ring 25 mg - dapivirine - EMEA/H/W/002168/II/0016 International Partnership for Microbicides Belgium AISBL, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Jan Neuhauser, "Submission of an updated RMP version 0.9 and Annex II for Dapivirine in order to replace the current PAES: Phase IV, open label, multicentre efficacy trial in healthy HIV-negative young women age 18-25 years (IPM 055), listed as a category 1 study in the RMP, with the implementation study: Dapivirine vaginal ring implementation in a real-world setting in young women."	
Descovy - emtricitabine / tenofovir alafenamide - EMEA/H/C/004094/II/0057 Gilead Sciences Ireland UC, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ana Sofia Diniz Martins, "Submission of the clinical study report and supporting modular summaries for study GS-US-311-1269 'Phase 2/3, Open Label, Multi-Cohort Switch Study to Evaluate Emtricitabine/Tenofovir Alafenamide (F/TAF) in HIV 1 Infected Children and Adolescents Virologically Suppressed on a 2 NRTI Containing Regimen' in fulfilment of the milestone for the category 3 additional pharmacovigilance activity to address the safety concern of long-term safety information in adolescents (missing information) as detailed in the Descovy EU Risk Management Plan (RMP). The RMP version 6.1 has also been submitted."	
EXJADE - deferasirox - EMEA/H/C/000670/II/0082/G Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, "C.I.13: Submission of the final report from the Calypso study (CICL670F2202) listed as a category 3 study in the RMP. This is a randomized, open-label, multicentre, two arm, Phase II study to evaluate treatment compliance, efficacy and safety of deferasirox	

(granules) in paediatric patients with iron overload. The RMP version 20.0 has also been submitted.
C.I.11.b: Submission of an updated RMP version 20.0 with the following changes: to remove the risk of 'medication error' from the Exjade RMP and to remove the information related to the discontinuation of Exjade Dispersible Tablets in the EU."

Kisqali - ribociclib - EMEA/H/C/004213/II/0035

Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark, "Update of sections 4.4, 4.8 and 5.1 of the SmPC based on the final Overall Survival (OS) analysis from study A2301 (MONALEESA-2); a Phase III, randomized, double-blind, placebo-controlled, multicentre study of ribociclib in combination with letrozole in postmenopausal women with HR+, HER2–, locoregionally recurrent or metastatic breast cancer who had not received previous systemic therapy for advanced disease, and based on an updated pooled safety dataset (including the studies MONALEESA-2, MONALEESA-3 and MONALEESA-7). The Package Leaflet was updated accordingly.
The study is listed as a category 3 study in the RMP, and the submission of the final Study Report addresses MEA 004.
An updated RMP version 6.0 was also submitted."

Veklury - remdesivir - EMEA/H/C/005622/II/0034/G

Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, PRAC Rapporteur: Eva Jirsová, "Grouping variation to update sections 5.1 and 5.2 of the SmPC as a consequence of the submission of the final component of the Specific Obligation 012 agreed in the renewal of the CMA (EMEA/H/C/005622/R/0015) and listed in the Annex II of the Product Information. This submission includes the ACTT-1 final sequencing and phenotyping analysis and the full virology report including activity against variants. The Package Leaflet is updated accordingly. The RMP version 3.1 has also been submitted."

Xeljanz - tofacitinib - EMEA/H/C/004214/II/0046

Pfizer Europe MA EEIG, Rapporteur: Armando Genazzani, PRAC Rapporteur: Liana Gross-Martirosyan, "Update of section 5.3 of the SmPC in order to update safety information on reproductive and developmental toxicity based on final study results from An Oral (Gavage) Juvenile Toxicity Study of CP-690,550 in Sprague Dawley Rats (MEA 022) listed as a cat 3 study in the RMP.
The RMP version 23.1 has also been submitted. In addition, MAH is also taking this opportunity to update the contact details of the local representatives in the Package Leaflet."

Zepatier - elbasvir / grazoprevir - EMEA/H/C/004126/II/0034
Merck Sharp & Dohme B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ana Sofia Diniz Martins, "Submission of the final report from study MK-5172-017, listed as a category 3 study in the RMP. This is a Long-Term Follow-up Study to Evaluate the Durability of Virologic Response and/or Viral Resistance Patterns of Subjects with Chronic Hepatitis C Who Have Been Previously Treated with Zepatier in a Prior Clinical Trial. The submission of the study report addresses MEA 002.1. The RMP version 5.1 has also been submitted."

B.6.11. PRAC assessed procedures

PRAC Led
AJOVY - fremanezumab - EMEA/H/C/004833/II/0029
TEVA GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Kirsti Villikka, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of an updated RMP version 3.0 in line with the PI changes which were implemented following the assessment of PSUSA/202103 with regards to severe hypersensitivity reactions. The MAH has also taken the opportunity to update the PASS details according to the latest approved PASS protocols."

PRAC Led
Defitelio - defibrotide - EMEA/H/C/002393/II/0058/G, Orphan
Gentium S.r.l., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-

CHMP liaison: Kristina Dunder, "Grouped application including two type II variations as follows:
C.I.13: Submission of the final study report of the DEFIFrance registry: a national, post-registration observational study of the long-term safety and health outcome of patients treated with Defitelio, including patients with severe hepatic VOD after HSCT. This study is listed as a category 3 study in the RMP, and the submission of the study report addresses LEG/011.3. In addition, the MAH took the opportunity to provide two errata to the clinical study reports of studies #R09-1425 and #2006-05. Consequential changes to RMP version 9.2 have been implemented.
C.I.11: Submission of an updated RMP version 9.2 in order to remove reproductive toxicity as a potential risk."

PRAC Led

Hepcludex - bulevirtide - EMEA/H/C/004854/II/0012, Orphan

Gilead Sciences Ireland Unlimited Company, Rapporteur: Filip Josephson, PRAC Rapporteur: Adam Przybylkowski, PRAC-CHMP liaison: Ewa Balkowiec Iskra, "Submission of an updated RMP version 1.2 in order to replace the current non-interventional registry study, MYR-HDV, listed as a category 3 required additional pharmacovigilance activity in the currently RMP, with the interventional registry study GS-US-589-6206.
In addition, the MAH is also taking this opportunity to update the information on Epidemiology, Clinical Trial Exposure and Post-authorisation experience."

PRAC Led

Nucala - mepolizumab - EMEA/H/C/003860/II/0048

GlaxoSmithKline Trading Services Limited, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Submission of an updated RMP version 9 to reflect the proposal to stop the enrolment and to close the pregnancy registry "Mepolizumab Pregnancy Exposure Study 200870: a phase IV, prospective, observational, exposure cohort study of pregnancy outcomes in women (category 3 post authorisation measure in the RMP)". The application also includes details of

the proposed enhanced data collection for all pregnancies reported as an alternative.”	
PRAC Led **Rapamune - sirolimus -** **EMEA/H/C/000273/II/0184** Pfizer Europe MA EEIG, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, “Submission of the final report from non-interventional study B1741224, A Population Based Cohort Study to Monitor the Safety and Effectiveness of Sirolimus in Patients With Sporadic Lymphangioleiomyomatosis (S-LAM), designated as a category 3 PASS.”	
PRAC Led **WS2223/G** **Glyxambi-** **EMEA/H/C/003833/WS2223/0043/G** **Jardiance-** **EMEA/H/C/002677/WS2223/0066/G** **Synjardy-** **EMEA/H/C/003770/WS2223/0062/G** Boehringer Ingelheim International GmbH, Lead PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Blanca Garcia-Ochoa, “Grouping of two variations as follows: C.I.13: Submission of the final report from study PASS 1245.146 listed as a category 3 study in the RMP. This is ‘a 5-year enhanced pharmacovigilance surveillance initiative to survey and characterise spontaneous occurrence and experience of ketoacidotic events in patients treated with empagliflozin-containing products'. The RMP has been updated as a consequence. C.I.11 for RMP: Submission of an updated RMP in order to remove the following safety concerns: - Bone fracture, classified as an important potential risk and - Pregnancy/breast-feeding, classified as missing information. Updated RMP versions 18.0 for Jardiance, 12.0 for Synjardy and 7.0 for Glyxambi were submitted accordingly.”	
PRAC Led **WS2235** **Kisplyx-EMEA/H/C/004224/WS2235/0050** **Lenvima-** **EMEA/H/C/003727/WS2235/0046**	

Eisai GmbH, Lead PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, "Update of section 4.8 of the SmPC of Lenvima and Kisplyx in order to add colitis to the list of ADRs with frequency uncommon, following PRAC Signal assessment of colitis with lenvatinib (EPITT no: 19691). The Package Leaflets are updated accordingly."

B.6.12. CHMP-CAT assessed procedures

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0050, Orphan, ATMP
Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0052, Orphan, ATMP
Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

WS2202/G
Comtan- EMEA/H/C/000171/WS2202/0059/G
Comtess- EMEA/H/C/000170/WS2202/0062/G
Corbilta- EMEA/H/C/002785/WS2202/0028/G
Entacapone Orion- EMEA/H/C/002440/WS2202/0021/G
Levodopa/Carbidopa/Entacapone Orion- EMEA/H/C/002441/WS2202/0036/G
Stalevo- EMEA/H/C/000511/WS2202/0098/G
Orion Corporation, Lead Rapporteur: Outi Mäki-Ikola

WS2226/G
Aflunov- EMEA/H/C/002094/WS2226/0076/G
Foclivia- EMEA/H/C/001208/WS2226/0074/G

Seqirus S.r.l, Lead Rapporteur: Armando Genazzani

WS2230
Ebymect-
EMEA/H/C/004162/WS2230/0056
Xigduo-EMEA/H/C/002672/WS2230/0066
AstraZeneca AB, Lead Rapporteur: Kristina Dunder

WS2233
Hexacima-
EMEA/H/C/002702/WS2233/0127
Hexyon-
EMEA/H/C/002796/WS2233/0131
Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus

WS2234/G
Ebymect-
EMEA/H/C/004162/WS2234/0055/G
Edistride-
EMEA/H/C/004161/WS2234/0052/G
Forxiga-
EMEA/H/C/002322/WS2234/0073/G
Qtern-
EMEA/H/C/004057/WS2234/0034/G
Xigduo-
EMEA/H/C/002672/WS2234/0065/G
AstraZeneca AB, Lead Rapporteur: Johann Lodewijk Hillege

WS2236/G
Aflunov-
EMEA/H/C/002094/WS2236/0077/G
Foclivia-
EMEA/H/C/001208/WS2236/0075/G
Seqirus S.r.l, Lead Rapporteur: Armando Genazzani

WS2238
Hukyndra-
EMEA/H/C/005548/WS2238/0001
Libmyris-
EMEA/H/C/005947/WS2238/0001
STADA Arzneimittel AG, Lead Rapporteur: Outi Mäki-Ikola

WS2248/G
Aflunov-
EMEA/H/C/002094/WS2248/0078/G
Foclivia-

EMEA/H/C/001208/WS2248/0076/G
Seqirus S.r.l, Lead Rapporteur: Armando Genazzani

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

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

B.7.2. Monthly Line listing for Type I variations

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

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

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

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

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

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

E. Annex E - EMA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. Time-Tables – starting & ongoing procedures: For information

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

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

G. ANNEX G

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

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

G.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 21-24 February 2022 CHMP plenary:

G.2.2. List of procedures starting in February 2022 for March 2022 CHMP adoption of outcomes

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