31 May 2022
EMA/CHMP/214270/2022
Human Medicines Division

# Committee for medicinal products for human use (CHMP)

## Minutes for the meeting on 21-24 March 2022

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

**Disclaimers**

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

Of note, these minutes are a working document primarily designed for CHMP members and the work the Committee undertakes.

**Note on access to documents**

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

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# 1. Introduction

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

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

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the meeting, the Committee Secretariat announced the restricted involvement of some Committee members, alternates and experts for concerned agenda topics.

Participants were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared. Restrictions applicable to this meeting are captured in the list of participants included in the minutes.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

## 1.2. Adoption of agenda

CHMP agenda for 21-24 March 2022.

The CHMP adopted the agenda.

## 1.3. Adoption of the minutes

CHMP minutes for 21-14 February 2022.

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

The CHMP adopted the minutes of the February Plenary meeting as well as the minutes from the March PROM meeting.

# 2. Oral Explanations

## 2.1. Pre-authorisation procedure oral explanations

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

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

Scope: Oral explanation

**Action**: Oral explanation to be held on 22 March 2022 at 14:00

List of Outstanding Issues adopted on 27.01.2022, 11.11.2021. List of Questions adopted on 22.07.2021.

Participation of patient representatives.

An oral explanation was held on 22 March 2022. The presentation by the applicant focused on the clinical data in support of the application.

See 3.2

### 2.1.2. budesonide, micronised - Orphan - EMEA/H/C/005653

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

Scope: Possible oral explanation

**Action**: Oral explanation to be held on 23 March 2022 at 11:00

List of Outstanding Issues adopted on 27.01.2022. List of Questions adopted on 14.09.2021.

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

See 3.2

### 2.1.3. capmatinib - EMEA/H/C/004845

treatment of non-small cell lung cancer (NSCLC)

Scope: Oral explanation

**Action**: Oral explanation to be held on 23 March 2022 at 15:30

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

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

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

## 2.2. Re-examination procedure oral explanations

No items

## 2.3. Post-authorisation procedure oral explanations

### 2.3.1. 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 for the treatment of the following microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumours in adults with: -unresectable or metastatic colorectal cancer after previous fluoropyrimidine based combination therapy; -advanced or recurrent endometrial carcinoma, who have disease progression on or following prior treatment with a platinum containing therapy in any setting and who are not candidates for curative surgery or radiation; -unresectable or metastatic gastric, small intestine, or biliary cancer, who have disease progression on or following at least one 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 35) has been submitted."

Scope: Oral explanation

**Action**: Oral explanation to be held on 22 March 2022 at 16:00

Request for Supplementary Information adopted on 24.02.2022, 14.10.2021.

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

See 5.1

## 2.4. Referral procedure oral explanations

No items

# 3. Initial applications

## 3.1. Initial applications; Opinions

### 3.1.1. Amifampridine SERB - amifampridine - EMEA/H/C/005839

SERB SA; treatment of Lambert-Eaton Myasthenic Syndrome

Scope: Opinion

**Action**: For adoption

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

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

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

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

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

The summary of opinion was circulated for information.

### 3.1.2. Camcevi - leuprorelin - EMEA/H/C/005034

Accord Healthcare S.L.U.; indicated for the treatment of hormone dependent advanced prostate cancer

Scope: Opinion

**Action**: For adoption

Hybrid application (Article 10(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 27.01.2022. List of Questions adopted on 23.07.2020.

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

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

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

The summary of opinion was circulated for information.

### 3.1.3. Carvykti - ciltacabtagene autoleucel - PRIME - Orphan - ATMP - EMEA/H/C/005095

Janssen-Cilag International NV; treatment of multiple myeloma

Scope: Opinion

**Action**: For adoption

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

List of Outstanding Issues adopted on 10.12.2021. List of Questions adopted on 10.09.2021.

The CHMP was updated on discussions at the CAT.

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

The CHMP, based on the draft opinion prepared by the CAT, adopted a positive opinion

recommending the granting of a conditional marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

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

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

The CHMP noted the letter of recommendations dated 18 March 2022.

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report.

### 3.1.4. Evusheld - tixagevimab / cilgavimab - EMEA/H/C/005788

AstraZeneca AB, prophylaxis of COVID-19 in adults 18 years of age and older

Scope: Opinion

**Action**: For adoption

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

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

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

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

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

The CHMP noted the letter of recommendations dated 24 March 2022.

The summary of opinion was circulated for information.

### 3.1.5. Zolsketil pegylated liposomal - doxorubicin - EMEA/H/C/005320

Accord Healthcare S.L.U.; treatment of breast cancer, ovarian cancer, progressive multiple myeloma and AIDS-related Kaposi's sarcoma

Scope: Opinion

**Action**: For adoption

Hybrid application (Article 10(3) of Directive No 2001/83/EC)

List of Outstanding Issues adopted on 27.01.2022, 26.03.2020. List of Questions adopted on 17.10.2019.

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

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

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

The summary of opinion was circulated for information.

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

### 3.2.1. doxorubicin hydrochloride - EMEA/H/C/005330

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

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 28.05.2020.

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

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

### 3.2.2. ertapenem - EMEA/H/C/005815

treatment of bacterial infections and prophylaxis of surgical site infection following elective colorectal surgery

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 24.06.2021.

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

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

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

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

Scope: List of outstanding issues

**Action**: For adoption

List of Outstanding Issues adopted on 27.01.2022, 11.11.2021. List of Questions adopted on 22.07.2021.

See 2.1

Participation of patient representatives.

An oral explanation was held on 22 March 2022. The presentation by the applicant focused

on the clinical data in support of the application.

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

### 3.2.4. ganirelix - EMEA/H/C/005641

Prevention of premature luteinising hormone (LH) surges in women undergoing controlled ovarian hyperstimulation (COH) for assisted reproduction techniques (ART).

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 22.07.2021.

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

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

### 3.2.5. budesonide, micronised - Orphan - EMEA/H/C/005653

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

Scope: List of outstanding issues

**Action**: For adoption

List of Outstanding Issues adopted on 27.01.2022. List of Questions adopted on 14.09.2021.

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

See 2.1

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

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

### 3.2.6. mosunetuzumab - Orphan - EMEA/H/C/005680

Roche Registration GmbH; refractory follicular lymphoma (FL)

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 25.01.2022.

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

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

### 3.2.7. melphalan flufenamide - Orphan - EMEA/H/C/005681

Oncopeptides AB; treatment of multiple myeloma

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 16.09.2021.

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

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

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

### 3.2.8. mitapivat - Orphan - EMEA/H/C/005540

Agios Netherlands B.V.; treatment of pyruvate kinase deficiency

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 11.11.2021.

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

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

### 3.2.9. valoctocogene roxaparvovec - Orphan - ATMP - EMEA/H/C/005830

BioMarin International Limited; treatment of severe haemophilia A

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 05.11.2021.

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

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

### 3.2.10. eptacog beta (activated) - EMEA/H/C/005655

treatment and for the prevention of bleeding

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 24.06.2021.

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

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

### 3.2.11. sitagliptin / metformin hydrochloride - EMEA/H/C/005850

treatment of type 2 diabetes mellitus

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 16.09.2021.

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

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

### 3.2.12. sugammadex - EMEA/H/C/005760

Reversal of neuromuscular blockade induced by rocuronium or vecuronium

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 22.07.2021.

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

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

### 3.2.13. tezepelumab - EMEA/H/C/005588

add-on maintenance treatment in adults and adolescents 12 years and older with severe asthma

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 14.10.2021.

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

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

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

### 3.3.1. tabelecleucel - PRIME - Orphan - ATMP - EMEA/H/C/004577

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

Scope: List of questions

**Action**: For information

The CHMP was updated on discussions at the CAT. The Committee discussed the issues identified in this application.

The Committee endorsed the CHMP recommendation and scientific discussion together with the list of questions, as adopted by CAT.

### 3.3.2. abaloparatide - EMEA/H/C/005928

treatment of osteoporosis

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

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

### 3.3.3. spironolactone ph. eur. - EMEA/H/C/005535

Management of refractory oedema

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

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

### 3.3.4. miglustat - Orphan - EMEA/H/C/005695

Amicus Therapeutics Europe Limited; treatment of adults aged 18 years and older with a confirmed diagnosis of Pompe disease

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

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

### 3.3.5. pirfenidone - EMEA/H/C/005862

treatment of Idiopathic Pulmonary Fibrosis (IPF)

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

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

### 3.3.6. cipaglucosidase alfa - Orphan - EMEA/H/C/005703

Amicus Therapeutics Europe Limited; treatment of adults aged 18 years and older with a confirmed diagnosis of Pompe disease

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

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

### 3.3.7. sugammadex - EMEA/H/C/005935

reversal of neuromuscular blockade induced by rocuronium or vecuronium

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

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

### 3.3.8. infigratinib - Orphan - EMEA/H/C/005361

Helsinn Birex Pharmaceuticals Limited; treatment of cholangiocarcinoma

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

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

### 3.3.9. vadadustat - EMEA/H/C/005131

Treatment of anaemia

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

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

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

### 3.4.1. dengue tetravalent vaccine (live, attenuated) - Article 58 - EMEA/H/W/005362

prevention of dengue disease

Scope: Letter from the applicant dated 09 March 2022 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in November 2021.

**Action**: For adoption

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

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted in November 2021.

### 3.4.2. dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/005155

prevention of dengue disease

Scope: Letter from the applicant dated 09 March 2022 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in November 2021.

**Action**: For adoption

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

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of outstanding issues adopted in November 2021.

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

Y-Mabs Therapeutics A/S, treatment of neuroblastoma

Scope: Letter from the applicant dated 08 March 2022 requesting an extension to the clock stop to respond to the list of questions adopted in September 2021. The request was adopted by CHMP via written procedure on 10 March 2022.

**Action**: For information

List of Questions adopted on 16.09.2021.

The CHMP noted the request, which was adopted via written procedure on 10.03.2022.

### 3.4.4. dabigatran etexilate - EMEA/H/C/005639

prevention of venous thromboembolic events

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

**Action**: For adoption

List of Outstanding Issues adopted on 24.02.2022. List of Questions adopted on 12.11.2020.

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

### 3.4.5. bardoxolone methyl - Orphan - EMEA/H/C/005869

Reata Ireland Limited; treatment of chronic kidney disease

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

**Action**: For adoption

List of Questions adopted on 24.02.2022.

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

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

No items

## 3.6. Initial applications in the decision-making phase

No items

## 3.7. Withdrawals of initial marketing authorisation application

### 3.7.1. Miplyffa - arimoclomol - Orphan - EMEA/H/C/005203

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

Scope: Withdrawal of marketing authorisation application

**Action**: For information

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

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

The CHMP noted the withdrawal of marketing authorisation application.

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

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

### 4.1.1. Zejula - niraparib - Orphan - EMEA/H/C/004249/X/0029

GlaxoSmithKline (Ireland) Limited

Rapporteur: Ingrid Wang, PRAC Rapporteur: Jan Neuhauser

Scope: "Extension application to introduce a new pharmaceutical form (100 mg film-coated tablet). The RMP (version 5.1) is updated in accordance."

**Action**: For adoption

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

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

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

The summary of opinion was circulated for information.

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

### 4.2.1. Biktarvy - bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449/X/0040/G

Gilead Sciences Ireland UC

Rapporteur: Jean-Michel Race, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Extension application to introduce a new strength (30 mg/120 mg/15 mg). The extension application is grouped with a type II variation (C.I.6.a) to include a paediatric indication: use in patients 2 years of age and older and weighing at least 14 kg. Sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC and the Package Leaflet are updated to support the extended indication. The RMP (version 3.1) is updated in accordance."

**Action**: For adoption

List of Questions adopted on 14.10.2021.

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

The Committee adopted the CHMP recommendation and scientific discussion together with

the list of outstanding issues and a specific timetable.

### 4.2.2. Genvoya - elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004042/X/0079/G

Gilead Sciences Ireland UC

Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ilaria Baldelli

Scope: "Extension application to introduce a new strength (90 mg/90 mg/120 mg/6 mg film-coated tablets). The extension application is grouped with a type II variation (C.I.6.a) to include treatment of human immunodeficiency virus 1 (HIV 1) infection without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir in paediatric patients aged from 2 years and with body weight at least 14 kg. Sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and the Package Leaflet are updated to support the extended indication. The RMP (version 5.1) is updated in accordance."

**Action**: For adoption

List of Questions adopted on 11.11.2021.

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

The Committee adopted the CHMP recommendation and scientific discussion together with the list of outstanding issues and a specific timetable.

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

No items

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

No items

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

No items

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

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

### 5.1.1. Adtralza - tralokinumab - EMEA/H/C/005255/II/0002

LEO Pharma A/S

Rapporteur: Jayne Crowe

Scope: "Extension of indication to include treatment of adolescent patients (12-17 years) for Adtralza based on final study LP0162-1334 (ECZTRA 6): a multicentre, randomised, double-blind, placebo-controlled study in adolescent patients 12 to 17 years of age with moderate-to-severe atopic dermatitis to evaluate the efficacy and safety of tralokinumab monotherapy in this population group. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance."

**Action**: For adoption

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

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

### 5.1.2. 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 Cabometyx as monotherapy treatment of adult patients 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; 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 6.1 of the RMP has also been submitted."

**Action**: For adoption

Request for Supplementary Information adopted on 24.02.2022, 11.11.2021.

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

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

The summary of opinion was circulated for information.

The CHMP adopted the similarity assessment report.

### 5.1.3. Enhertu - trastuzumab deruxtecan - EMEA/H/C/005124/II/0014

Daiichi Sankyo Europe GmbH

Rapporteur: Thalia Marie Estrup Blicher, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of indication for Enhertu to include treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received one or more prior anti-HER2-based regimens; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.2 of the RMP has also been submitted.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

**Action**: For adoption

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

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

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

Roche Registration GmbH

Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Annika Folin

Scope: "Extension of indication to include monotherapy treatment of adult and paediatric patients 12 years of age and older with locally advanced or metastatic RET-mutant medullary thyroid cancer for Gavreto; based on the efficacy and safety data obtained from the pivotal study BO42863 (ARROW). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. Furthermore, some minor changes to the PI have been implemented in line with the latest Anticancer Guidelines Recommendations. Extension of indication to include monotherapy treatment of adult and paediatric patients 12 years of age and older with locally advanced or metastatic RET fusion-positive thyroid cancer for Gavreto; based on the efficacy and safety data obtained from the pivotal study BO42863 (ARROW). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

**Action**: For adoption

The Committee discussed the issues identified in this application, concerning clinical aspects and the request for 1 year of market protection.

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

### 5.1.5. Imbruvica - ibrutinib - EMEA/H/C/003791/II/0070

Janssen-Cilag International N.V.

Rapporteur: Filip Josephson, Co-Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of the existing CLL indication to include combination treatment with venetoclax for previously untreated patients based on efficacy and safety data from phase 3 study GLOW and phase 2 study CAPTIVATE. The SmPC is revised to reflect the information on the combination with venetoclax. The PL is updated accordingly. The RMP version 18.4 has been submitted. Justification to support one-year extension of the marketing protection period is included in the submission.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

**Action**: For adoption

The Committee discussed the issues identified in this application, concerning clinical aspects and the request for 1 year of market protection.

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

### 5.1.6. Jakavi - ruxolitinib - EMEA/H/C/002464/II/0053

Novartis Europharm Limited

Rapporteur: Filip Josephson, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Annika Folin

Scope: "Extension of indication to include treatment of patients with GvHD aged 12 years and older who have inadequate response to corticosteroids or other systemic therapies for Jakavi; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 13.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representative for The Netherlands in the Package Leaflet."

**Action**: For adoption

Request for Supplementary Information adopted on 16.12.2021, 24.06.2021.

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

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

The CHMP noted the letter of recommendations dated 23 March 2022.

The summary of opinion was circulated for information.

### 5.1.7. 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 for the treatment of the following microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumours in adults with: -unresectable or metastatic colorectal cancer after previous fluoropyrimidine based combination therapy; -advanced or recurrent endometrial carcinoma, who have disease progression on or following prior treatment with a platinum containing therapy in any setting and who are not candidates for curative surgery or

radiation; -unresectable or metastatic gastric, small intestine, or biliary cancer, who have disease progression on or following at least one 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 35) has been submitted."

**Action:** For adoption

Request for Supplementary Information adopted on 24.02.2022, 14.10.2021.

See 2.3

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

The Committee adopted a positive opinion by majority (29 positive out of 31 votes) together with the CHMP Assessment Report and translation timetable.

The divergent position (Johann Lodewijk Hillege, Outi Maki-Ikola) was appended to the opinion.

The summary of opinion was circulated for information.

### 5.1.8. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0117

Merck Sharp & Dohme B.V.

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

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

**Action**: For adoption

Request for Supplementary Information adopted on 27.01.2022.

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

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

The summary of opinion was circulated for information.

### 5.1.9. Kymriah - tisagenlecleucel - Orphan - ATMP - EMEA/H/C/004090/II/0044

Novartis Europharm Limited

Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include treatment of adult patients with follicular lymphoma (FL) after two or more lines of therapy who are refractory or relapsed during or within 6 months after completion of anti-CD20 antibody maintenance or relapsed after

autologous haematopoietic stem cell transplantation (HSCT) for Kymriah. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and corresponding sections in the Package Leaflet are updated accordingly. The RMP has been updated to version 4.0 to align with the indication extension. Lastly, the minor editorial corrections are made throughout the SmPC and package leaflet to align with the current QRD template version 10.2.", 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 10.12.2021.

The CHMP was updated on discussions at the CAT. The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee, based on the draft opinion prepared by the CAT, adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The summary of opinion was circulated for information.

## 5.1.10. Nexpovio - selinexor - EMEA/H/C/005127/II/0001/G

Karyopharm Europe GmbH

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

Scope: "Group of variations including an extension of indication for Nexpovio in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy and a quality variation for the addition of a new pack size to align with the dose modification guidance for the new indication. Sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 6.5 of the SmPC are updated to reflect the new indication and the new pack size. Annex II is updated to reflect the completion of the Specific Obligation. The Labelling and Package Leaflet are amended accordingly. The RMP (v 1.1) is amended consequently."

**Action**: For adoption

Request for Supplementary Information adopted on 16.12.2021, 22.07.2021.

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

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

## 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 fulfils SOB003 thus supporting the switch from CMA to full MA. Annexes I, II, IIIB are revised. The RMP is also updated."

**Action**: For adoption

Request for Supplementary Information adopted on 24.02.2022.

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

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

The summary of opinion was circulated for information.

### 5.1.12. Tecartus - autologous peripheral blood T cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - Orphan - ATMP - EMEA/H/C/005102/II/0008/G

Kite Pharma EU B.V.

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

Scope: "Group of variations including an extension of indication to include treatment of adult patients with relapsed or refractory (r/r) B-cell acute lymphoblastic leukaemia (B-ALL) for Tecartus and a type IB variation. As a consequence, sections 2.2, 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 1.1 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template." 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 10.09.2021.

The CHMP was updated on discussions at the CAT. The Committee discussed the issues identified in this application, concerning clinical aspects.

The Committee endorsed a 2nd request for supplementary information with a specific timetable, as adopted by CAT.

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

### 5.1.13. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0064

Roche Registration GmbH

Rapporteur: Thalia Marie Estrup Blicher, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "C.I.6 (Extension of indication)
Extension of indication to include adjuvant treatment of non-small cell lung cancer (NSCLC) following resection and platinum-based chemotherapy for adult patients whose tumours have PD-L1 expression on ≥ 1% of tumour cells (TC) for Tecentriq as monotherapy based on the results from the pivotal phase III study GO29527 (IMpower010); as a consequence,

sections 4.1, 4.2, 4.4, 4.8 and 5.1 of both the Tecentriq 840 mg concentrate for solution for infusion SmPC and the Tecentriq 1,200 mg concentrate for solution for infusion SmPC are updated. Minor editorial changes have been made throughout the SmPC. The Package Leaflets are updated in accordance. Version 21.0 of the RMP has also been submitted."

**Action**: For adoption

Request for Supplementary Information adopted on 14.10.2021.

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

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

## 5.1.14. Ultomiris - ravulizumab - EMEA/H/C/004954/II/0026

Alexion Europe SAS

Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension of indication to include treatment of adult patients with generalised myasthenia gravis (gMG). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC and corresponding sections in the Package Leaflet are updated accordingly. The RMP has been updated to version 4.0 to align with the indication extension. Lastly, minor editorial corrections are made throughout the SmPC and package leaflet. The Applicant also requested 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)."

**Action**: For adoption

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

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

## 5.1.15. Vyxeos liposomal - daunorubicin / cytarabine - Orphan - EMEA/H/C/004282/II/0018/G

Jazz Pharmaceuticals Ireland Limited

Rapporteur: Johanna Lähteenvuo, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC to include relevant information in paediatric patients based on results from the paediatric clinical study AAML1421. The Package leaflet is updated accordingly."

**Action**: For adoption

Request for Supplementary Information adopted on 11.11.2021, 20.05.2021.

The CHMP was reminded that the applicant withdrew the extension of indication part from the scope of this variation, instead proposing inclusion of relevant paediatric data in the product information based on results from study AAML1421.

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

addressed.

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

### 5.1.16. WS2150
DuoPlavin - clopidogrel / acetylsalicylic acid - EMEA/H/C/001143/WS2150/0060
Iscover - clopidogrel - EMEA/H/C/000175/WS2150/0146
Plavix - clopidogrel - EMEA/H/C/000174/WS2150/0145

sanofi-aventis groupe

Lead Rapporteur: Bruno Sepodes, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of indication to include clopidogrel in combination with acetylsalicylic acid in ST segment elevation acute myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI); as a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. Version 1.5 of the RMP has also been submitted. In addition, an editorial update has been made to the labelling."

**Action**: For adoption

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

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

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

### 5.2.1. Olumiant - baricitinib - EMEA/H/C/004085/II/0028

Eli Lilly Nederland B.V.

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Christophe Focke, PRAC Rapporteur: Adam Przybylkowski

Scope: "C.I.6 - Extension of indication to include treatment of coronavirus disease 2019 (COVID 19) in hospitalised adult and paediatric patients aged 10 years and older who require low-flow oxygen or non-invasive ventilation/high flow oxygen for Olumiant; as a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Annex II and the Package Leaflet are updated in accordance. Version 11.1 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)

Letter from the applicant dated 07 March 2022 requesting an extension to the clock stop to respond to the request of supplementary information adopted in October 2021. The request was adopted by CHMP via written procedure on 11 March 2022.

**Action**: For information

Request for Supplementary Information adopted on 14.10.2021, 22.07.2021.

The CHMP noted the clock-stop extension which was adopted via written procedure on 11

March 2022.

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

Daiichi Sankyo Europe GmbH

Rapporteur: Thalia Marie Estrup Blicher, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of indication to include monotherapy treatment of adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior anti-HER2-based regimen for Enhertu based on final results from studies DS8201 A J202 (DESTINY Gastric01) and DS8201-A-U205 (DESTINY Gastric02); as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, changes regarding the dosing recommendation for corticosteroid treatment and the protection of the infusion bag from light have been introduced. Version 1.1 of the RMP has also been submitted.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

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

**Action:** For adoption

Request for Supplementary Information adopted on 27.01.2022.

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

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

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

Biogen Netherlands B.V.

Re-examination Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Martin Huber

Scope: "C.I.6 (Extension of indication) type II Art.29 Extension of indication to include treatment of relapsing remitting multiple sclerosis (RRMS) in paediatric patients from 10 years of age and over; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.3 are updated. The Package Leaflet is updated in accordance.
The MAH is requesting an extension of the market protection of one additional year in line with the guidance on elements required to support the significant clinical benefit in comparison with existing therapies of a new therapeutic indication in accordance with Article 14(11) of Regulation (EC) 726/2004.
Version 11.4 of the RMP has also been submitted to update the RMP (parts I-IV) based on study 109MS306 data supporting the request for a paediatric indication and the applicant took the opportunity to update the RMP with the most updated data (Part II modules SIV, SV and SVII). " Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

**Action**: For adoption

Opinion adopted on 27.01.2022. Request for Supplementary Information adopted on 16.12.2021, 16.09.2021.

The CHMP appointed Daniela Philadelphy as a re-examination rapporteur.

The CHMP adopted the re-examination timetable.

# 6. Medical devices

## 6.1. Ancillary medicinal substances - initial consultation

No items

## 6.2. Ancillary medicinal substances – post-consultation update

No items

## 6.3. Companion diagnostics – initial consultation

### 6.3.1. in vitro diagnostic medical device - EMEA/H/D/006065

In vitro quantitative determination of anti-Müllerian hormone (AMH) in human serum and plasma

Scope: Request for Supplementary Information

**Action:** For adoption

The Committee discussed the issues identified in this application, concerning the companion diagnostics classification.

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

## 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. Glofitamab - Orphan - H0005751

Roche Registration GmbH; indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphomas (DLBCL), high grade B cell lymphoma (HGBCL) and primary mediastinal large B-cell lymphoma (PMBCL), after two or more lines of systemic therapy.

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

**Action:** For adoption

The CHMP did not agree to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

## 8.2. Priority Medicines (PRIME)

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

### 8.2.1. List of applications received

**Action:** For information

The CHMP noted the list of applications received.

### 8.2.2. Recommendation for PRIME eligibility

**Action:** For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 2 recommendations for eligibility to PRIME: 2 were denied.

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

# 9. Post-authorisation issues

## 9.1. Post-authorisation issues

### 9.1.1. Defitelio - defibrotide – Orphan - EMEA/H/C/002393/II/0056

Gentium S.r.l.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Submission of the final report from study 15-007 listed as a specific obligation in the Annex II of the Product Information. This is a phase 3, randomised, adaptive study (15-007) of Defibrotide vs. best supportive care in the prevention of hepatic venoocclusive disease in adult and paediatric patients undergoing hematopoietic stem cell transplant (HSCT). The RMP version 9 has also been submitted.
The MAH has also taken the opportunity to align the PI to the latest QRD template 10.2 which replaces the United Kingdom with United Kingdom (Northern Ireland) in the PIL.
In addition, the MAH is correcting the following errata during the linguistic review of the PI: correction of the paragraph number for Regulation (EC) No 726.2004 which was cited incorrectly in Annex II of the French PI and formatting updates to Norwegian and Swedish language PIs."

**Action:** For adoption

Request for Supplementary Information adopted on 10.03.2022, 28.10.2021, 08.07.2021.

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

The Committee agreed to update the request for supplementary information adopted on 10.03.2022.

### 9.1.2. Raxone - idebenone – Orphan - EMEA/H/C/003834/II/0031

Santhera Pharmaceuticals (Deutschland) GmbH

Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli

Scope: "Update of sections 4.2, 4.4, 4.9 and 5.1 of the SmPC based on the final study report from the PAROS study SNT-IV-003 (SOB003; listed as a cat 2 study in the RMP): "A non-interventional study of clinical experience in patients prescribed Raxone for the treatment of Leber's Hereditary Optic Neuropathy (LHON)". Annex II is updated in accordance. A revised RMP version 1.14 was also submitted."

**Action:** For adoption

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

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

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

Orexigen Therapeutics Ireland Limited

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

Scope: "Submission of updated study design and protocol synopsis for CVOT-2 study, a category 1 study listed in Annex II.D (ANX/001.7) undertaken to assess the effect of naltrexone extended release (ER) / bupropion ER on the occurrence of major adverse cardiovascular events (MACE), as requested in the CHMP AR for ANX/001.6. The Annex II and the RMP version 13 are updated accordingly."

**Action:** For adoption

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

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

### 9.1.4. Veklury - remdesivir - EMEA/H/C/005622/R/0031

Gilead Sciences Ireland UC

Rapporteur: Janet Koenig, PRAC Rapporteur: Eva Jirsová

Scope: Renewal of conditional marketing authorisation

**Action:** For adoption

Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.

The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional.

### 9.1.5. Piqray - alpelisib - EMEA/H/C/004804/II/0008/G

Novartis Europharm Limited

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

Scope: "Update of section 5.1 of the SmPC based on final results from study CBYL719C2301 (SOLAR-1) listed as a PAES in the Annex II; this is a phase III, randomized, double-blind, placebo controlled study of alpelisib in combination with fulvestrant for men and postmenopausal women with hormone receptor positive, HER2-negative advanced breast cancer which progressed on or after aromatase inhibitor treatment; the Annex II is updated accordingly. In addition, the MAH is updating the ATC code in the SmPC. The RMP version 5.0 has also been submitted."

**Action:** For adoption

Request for Supplementary Information adopted on 28.10.2021.

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

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

### 9.1.6. Rubraca - rucaparib - EMEA/H/C/004272/II/0029

Clovis Oncology Ireland Limited

Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Annika Folin

Scope: "Update of sections 4.4, 4.8 and 5.1 of the SmPC based on final results from study CO-338-043 (ARIEL4); this is a phase 3, multicentre, open-label, randomised study evaluating the efficacy and safety of rucaparib versus chemotherapy for treatment of relapsed ovarian cancer listed as a specific obligation in the Annex II; the Package Leaflet is updated accordingly. The RMP version 6.1 has also been submitted. With this variation

application, the MAH requests for the Rubraca marketing authorisation to no longer be subject to specific obligations. The SmPC, Annex II and PL are updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes and bring the PI in line with the latest QRD template version 10.2 Rev.1."

**Action:** For adoption

Request for Supplementary Information adopted on 11.11.2021.

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

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

The CHMP agreed to seek PRAC advice.

### 9.1.7. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0115

Merck Sharp & Dohme B.V.

Rapporteur: Armando Genazzani

Scope: "Update of section 5.1 of the SmPC in order to update efficacy information based on final results from study KEYNOTE-426 listed as imposed PAES in the Annex II; this is a Phase III Randomized, Open-label Study to Evaluate Efficacy and Safety of Pembrolizumab (MK-3475) in combination with Axitinib versus Sunitinib Monotherapy as a First-line Treatment for Locally Advanced or Metastatic Renal Cell Carcinoma (mRCC)."

**Action:** For adoption

Request for Supplementary Information adopted on 02.12.2021.

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

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

### 9.1.8. Adcetris - brentuximab vedotin – orphan - EMEA/H/C/002455/II/0099

Takeda Pharma A/S

Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst

Scope: "Update of sections 4.8 and 5.1 of the SmPC, based on final results from study C25006, a multi-centre open-label, phase 4 study of 50 patients with r/r sALCL undertaken to further evaluate the efficacy and safety of brentuximab vedotin as a single agent in adult patients who had previously received at least 1 multiagent chemotherapy regimen. This study was listed as an interventional category 2 PASS in the RMP (SOB 010). In addition, the MAH took the opportunity to request the granting of a marketing authorisation not subject to specific obligations and valid for five years, in accordance with Article 14-a(8) of Regulation (EC) No 726/2004, thereby deleting SOB 010 from the annex II and of the reference to the conditional marketing authorisation from annex II and the package leaflet. The revised RMP version 16.1 has also been submitted. An editorial update under section 5.1 of the SmPC (update of the ATC code) has been implemented.

In addition, the CHMP, having considered the application as set out in the assessment report and having reviewed the data submitted by the marketing authorisation holder including the evidence concerning compliance with specific obligations, is of the opinion that the risk-benefit balance of the above mentioned medicinal product remains favourable, that all specific obligations laid down in Annex II have been fulfilled and that comprehensive data supports a favourable benefit-risk balance of the above mentioned medicinal product. Therefore, pursuant to Article 14-a(8) of Regulation (EC) No 726/2004, the CHMP recommends by consensus the granting of a marketing authorisation in accordance with Article 14(1) of Regulation (EC) No 726/2004 for the above mentioned medicinal product for which the draft Summary of Product Characteristics is set out in Annex I."

**Action:** For adoption

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

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

### 9.1.9. 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

Scope: Renewal of Marketing Authorisation

Request for Supplementary Information adopted on 18.02.2022.

The CHMP was updated on discussions at the CAT.

Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.

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

## 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

### 10.2.1. Presence of nitrosamine impurities in human medicinal products containing chemically synthesised active pharmaceutical ingredients EMEA/H/A-5(3)/1490

MAHs: various

Referral Rapporteur: Martina Weise, Referral Co-Rapporteur: Kristina Dunder

Scope: Update on implementation of Article 5(3)

**Action**: For information

The CHMP noted the update. The members received an overview of the identified risks of presence of nitrosamines for centrally authorised products and market surveillance activities. Prioritisation criteria were proposed and an updated question-and-answer document presented. Furthermore, a public communication to raise awareness of the structure-based risk for active substance derived nitrosamines, was introduced.

## 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

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

**Action**: For information

The CHMP noted the information.

# 12. Inspections

## 12.1. GMP inspections

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

## 12.2. GCP inspections

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

## 12.3. Pharmacovigilance inspections

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

## 12.4. GLP inspections

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

# 13. Innovation Task Force

## 13.1. Minutes of Innovation Task Force

No items

## 13.2. Innovation Task Force briefing meetings

No items

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

No items

## 13.4. Nanomedicines activities

No items

# 14. Organisational, regulatory and methodological matters

## 14.1. Mandate and organisation of the CHMP

### 14.1.1. CHMP Co-rapporteur critique

Experience of the implementation of Co-Rapporteur critique in initial marketing authorisation applications. Follow-up on the February PROM meeting.

**Action:** For information

The CHMP noted the update.

## 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 March 2022

**Action:** For adoption

The CHMP adopted the EURD list.

### 14.2.2. Paediatric Committee (PDCO)

PIPs reaching D30 at March 2022 PDCO

**Action:** For information

The CHMP noted the information.

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

### 14.3.1. Biologics Working Party (BWP)

Chair: Sol Ruiz

Reports from BWP March 2022 meeting to CHMP for adoption:

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

**Action:** For adoption

The CHMP adopted the BWP reports.

### 14.3.2. Scientific Advice Working Party (SAWP)

Chair: Paolo Foggi

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

**Action:** For information

The CHMP noted the report.

Scientific advice letters:

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

### 14.3.3. Ad-hoc Influenza Working Group

Scope: EU Strain selection for the Influenza Vaccines for the Season 2022/2023: Report from the Ad Hoc Influenza working group to the BWP

**Action:** For adoption

Scope: EU Recommendation for the Seasonal Influenza Vaccine Composition for the Season 2022/2023

**Action:** For adoption

The CHMP adopted the EU strain selection report and the EU recommendation for the Seasonal Influenza Vaccine Composition for the Season 2022/2023.

### 14.3.4. Oncology Working Party (ONCWP)

Scope: Nomination of Chair, Vice-Chair and new member following the resignation of Sinan B. Sarac.

**Action:** For adoption

The CHMP endorsed the proposed new Oncology WP member.

### 14.3.5. Recommendation for the membership of Working Parties

Confirmation of membership of the following working parties:

Central Nervous System WP
Cardiovascular WP
Rheumatology and Immunology WP
Vaccine WP
Infectious Diseases WP
Haematology WP
Methodology WP
Non-clinical WP
J3Rs WP

**Action:** For adoption

The CHMP adopted the lists of membership of the above mentioned working parties.

The CHMP noted the call for an additional member with expertise in the respiratory field for the Rheumatology and Immunology Working Party.

### 14.3.6. Appointment of the chair and vice-chair of the Oncology Scientific Advice Group

Formal appointment of the chair and vice-chair of the SAG Oncology following the elections.

**Action:** For endorsement

The CHMP endorsed Lothar Bergmann as chair and Tarec El Galaly as vice-chair of the SAG Oncology.

## 14.4. Cooperation within the EU regulatory network

No items

## 14.5. Cooperation with International Regulators

No items

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

No items

## 14.7. CHMP work plan

No items

## 14.8. Planning and reporting

### 14.8.1. Update of the Business Pipeline report for the human scientific committees

2022 initial marketing authorisation application submissions with eligibility request to central procedure

**Action:** For information

The CHMP noted the information.

## 14.9. Others

### 14.9.1. Pharma Strategy

Revision of the Pharmaceutical legislation: update

**Action:** For discussion

The CHMP noted the update.

# 15. Any other business

## 15.1. AOB topic

### 15.1.1. Update on COVID-19

**Action:** For information

The CHMP noted the information.

### 15.1.2. Diabetes guideline

Update on revision of the diabetes guideline following the meeting of the drafting group

**Action:** For discussion

The CHMP noted the update.

## List of participants

List of participants including any restrictions with respect to involvement of members/alternates/experts following evaluation of declared interests for the 21-24 March 2022 CHMP meeting.

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Harald Enzmann | Chair | Germany | No interests declared | |
| Andrea Laslop | Member | Austria | No interests declared | |
| Daniela Philadelphy | Alternate | Austria | No interests declared | |
| Christophe Focke | Member | Belgium | No restrictions applicable to this meeting | |
| Karin Janssen van Doorn | Alternate | Belgium | No interests declared | |
| Velislava Todorova | Alternate | Bulgaria | No interests declared | |
| Margareta Bego | Member | Croatia | No interests declared | |
| Selma Arapovic Dzakula | Alternate | Croatia | No interests declared | |
| Helena Panayiotopoulou | Member | Cyprus | No interests declared | |
| Ondřej Slanař | Member | Czechia | No restrictions applicable to this meeting | |
| Tomas Radimersky | Alternate | Czechia | No interests declared | |
| Thalia Marie Estrup Blicher | Alternate | Denmark | No participation in discussion, final deliberations and voting | Piqray - alpelisib - EMEA/H/C/004804/II/0008/G |
| Alar Irs | Member | Estonia | No restrictions applicable to this meeting | |
| Edward Laane | Alternate | Estonia | No restrictions applicable to this meeting | |
| Outi Mäki-Ikola | Member | Finland | No restrictions applicable to this meeting | |
| Johanna Lähteenvuo | Alternate | Finland | No interests declared | |
| Alexandre Moreau | Member | France | No interests declared | |
| Jean-Michel Race | Alternate | France | No interests declared | |
| Martina Weise | Member | Germany | No restrictions applicable to this meeting | |
| Janet Koenig | Alternate | Germany | No interests declared | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Konstantina Alexopoulou | Member | Greece | No interests declared | |
| Anastasia Mountaki | Alternate | Greece | No interests declared | |
| Robert Porszasz | Member | Hungary | No interests declared | |
| Agnes Gyurasics | Alternate | Hungary | No interests declared | |
| Jan Sjöberg | Alternate | Iceland | No interests declared | |
| Jayne Crowe | Member | Ireland | No interests declared | |
| Peter Kiely | Alternate | Ireland | No interests declared | |
| Armando Genazzani | Member | Italy | No interests declared | |
| Maria Grazia Evandri | Alternate | Italy | No interests declared | |
| Elita Poplavska | Member | Latvia | No interests declared | |
| Romaldas Mačiulaitis | Member | Lithuania | No participation in final deliberations and voting | COVID-19 vaccines |
| Silvijus Abramavicius | Alternate | Lithuania | No restrictions applicable to this meeting | |
| Martine Trauffler | Member | Luxembourg | No interests declared | |
| Carola de Beaufort | Alternate | Luxembourg | No interests declared | |
| John Joseph Borg | Member | Malta | No interests declared | |
| Johann Lodewijk Hillege | Member | Netherlands | No interests declared | |
| Paula Boudewina van Hennik | Alternate | Netherlands | No interests declared | |
| Ingrid Wang | Member | Norway | No interests declared | |
| Eva Skovlund | Alternate | Norway | No interests declared | |
| Ewa Balkowiec Iskra | Member | Poland | No interests declared | |
| Bruno Sepodes | Member (Vice-Chair) | Portugal | No interests declared | |
| Fatima Ventura | Alternate | Portugal | No participation in final deliberations and voting | COVID-19 vaccines |
| Simona Badoi | Member | Romania | No interests declared | |
| Dana Gabriela Marin | Alternate | Romania | No interests declared | |
| Francisek Drafi | Member | Slovakia | No interests declared | |
| Dorota Distlerova | Alternate | Slovakia | No interests declared | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Nevenka Trsinar Brodt | Alternate | Slovenia | No interests declared | |
| Maria Concepcion Prieto Yerro | Member | Spain | No interests declared | |
| Blanca Garcia-Ochoa | Alternate | Spain | No interests declared | |
| Kristina Dunder | Member | Sweden | No interests declared | |
| Filip Josephson | Alternate | Sweden | No interests declared | |
| Christian Gartner | Co-opted member | Austria | No interests declared | |
| Carla Torre | Co-opted member | Portugal | No interests declared | |
| Jan Mueller-Berghaus | Co-opted member | Germany | No interests declared | |
| Blanka Hirschlerova | Co-opted member | Czechia | No interests declared | |
| Sol Ruiz | Co-opted member | Spain | No interests declared | |
| Vincent Gazin | Expert - via WebEx* | France | No interests declared | |
| Maija Tarkkanen | Expert - via WebEx* | Finland | No interests declared | |
| Paolo Foggi | Expert - via WebEx* | Italy | No interests declared | |
| Joerg Zinserling | Expert - via WebEx* | Germany | No interests declared | |
| Clemens Mittmann | Expert - via WebEx* | Germany | No interests declared | |
| Mario Miguel Coelho da Silva Rosa | Expert - via WebEx* | Portugal | No interests declared | |
| Andre Elferink | Expert - via WebEx* | Netherlands | No interests declared | |
| Anna Vikerfors | Expert - via WebEx* | Sweden | No interests declared | |
| Nora Cascante Estepa | Expert - via WebEx* | Germany | No interests declared | |
| Wilmar Igl | Expert - via WebEx* | Sweden | No interests declared | |
| Kairi Rooma | Expert - via WebEx* | Estonia | No interests declared | |
| Paula Contreras Alarcón | Expert - via WebEx* | Spain | No restrictions applicable to this meeting | |
| Maria Victoria Tudanca Pacios | Expert - via Webex* | Spain | No restrictions applicable to this meeting | |
| Mas Parra Paloma | Expert - via WebEx* | Spain | No restrictions applicable to this meeting | |
| Carolina Prieto Fernandez | Expert - via WebEx* | Spain | No interests declared | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Lucia Lopez-Anglada Fernandez | Expert - via WebEx* | Spain | No interests declared | |
| Macarena Gajardo | Expert - via WebEx* | Spain | No interests declared | |
| Johannes Petrus Theodorus Span | Expert - via WebEx* | Netherlands | No interests declared | |
| Jacobus Romme | Expert - via WebEx* | Netherlands | No interests declared | |
| Jacoba (Jacqueline) van Kuijk | Expert - via WebEx* | Netherlands | No interests declared | |
| Ineke Havinga | Expert - via WebEx* | Netherlands | No interests declared | |
| Susanne Breedijk-van den Ende | Expert - via WebEx* | Netherlands | No interests declared | |
| Nancy Postma | Expert - via WebEx* | Netherlands | No interests declared | |
| Laura Rodwell | Expert - via WebEx* | Netherlands | No interests declared | |
| Jessica Harskamp | Expert - via WebEx* | Netherlands | No interests declared | |
| Adrianus Van Gompel | Expert - via WebEx* | Netherlands | No interests declared | |
| Ieva Auseja | Expert - via WebEx* | Latvia | No interests declared | |
| Vita Gulevska | Expert - via WebEx* | Latvia | No interests declared | |
| Thomas Hinz | Expert - via WebEx* | Germany | No interests declared | |
| Dominique Gaston | Expert - via WebEx* | Germany | No interests declared | |
| Zuzana Jedlickova | Expert - via WebEx* | Germany | No interests declared | |
| Susanne Mueller-Egert | Expert - via WebEx* | Germany | No interests declared | |
| Hilke Zander | Expert - via WebEx* | Germany | No interests declared | |
| Gaby Wangorsch | Expert - via WebEx* | Germany | No interests declared | |
| Maren Richter | Expert - via WebEx* | Germany | No restrictions applicable to this meeting | |
| Matea Cartolano | Expert - via WebEx* | Germany | No interests declared | |
| Lukas Malte Aguirre Davila | Expert - via WebEx* | Germany | No interests declared | |
| Claudia Reichmann | Expert - via WebEx* | Germany | No interests declared | |
| Michal Zwiewka | Expert - via WebEx* | Germany | No interests declared | |
| Anne Hasle Buur | Expert - via WebEx* | Denmark | No interests declared | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Deirdre Mannion | Expert - via WebEx* | Denmark | No restrictions applicable to this meeting | |
| Kristin Skougaard | Expert - via WebEx* | Denmark | No interests declared | |
| Theis Moeslund Jensen | Expert - via WebEx* | Denmark | No restrictions applicable to this meeting | |
| Meera Varma | Expert - via WebEx* | Denmark | No restrictions applicable to this meeting | |
| Line Praest Lauridsen | Expert - via WebEx* | Denmark | No restrictions applicable to this meeting | |
| Mette Tranholm | Expert - via WebEx* | Denmark | No interests declared | |
| Sine Buhl Naess-Schmidt | Expert - via WebEx* | Denmark | No restrictions applicable to this meeting | |
| Anne-Marie Dalseg | Expert - via WebEx* | Denmark | No interests declared | |
| Ebru Karakoc Madsen | Expert - via WebEx* | Denmark | No restrictions applicable to this meeting | |
| Lene Weber Vestermark | Expert - via WebEx* | Denmark | No interests declared | |
| Mette Linnert Jensen | Expert - via WebEx* | Denmark | No interests declared | |
| Doris Johanna Hovgaard | Expert - via WebEx* | Denmark | No interests declared | |
| Aaron Emmanuel Sosa Mejia | Expert - via WebEx* | Denmark | No interests declared | |
| Emilie Birch Kristensen | Expert - via WebEx* | Denmark | No restrictions applicable to this meeting | |
| Marcel Maliepaard | Expert - via WebEx* | Netherlands | No interests declared | |
| Jana Klimasová | Expert - via WebEx* | Slovakia | No interests declared | |
| Anna Kubandová | Expert - via WebEx* | Slovakia | No interests declared | |
| Peter Sisovsky | Expert - via WebEx* | Slovakia | No interests declared | |
| Jana Schweigertova | Expert - via WebEx* | Slovakia | No interests declared | |
| Eva Malikova | Expert - via WebEx* | Slovakia | No interests declared | |
| Nathalie Dumarcet | Expert - via WebEx* | France | No interests declared | |
| Cecile Dop | Expert - via WebEx* | France | No restrictions applicable to this meeting | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Stephanie Jambon | Expert - via WebEx* | France | No interests declared | |
| Norontsoa Rasolondramanitra | Expert - via WebEx* | France | No interests declared | |
| Olga Kholmanskikh | Expert - via WebEx* | Belgium | No interests declared | |
| Violette Dirix | Expert - via WebEx* | Belgium | No interests declared | |
| Edwige Haelterman Brenneisen | Expert - via WebEx* | Belgium | No interests declared | |
| Valerie Lescrainier | Expert - via WebEx* | Belgium | No interests declared | |
| Adriana Ammassari | Expert - via WebEx* | Italy | No interests declared | |
| Luca Santi | Expert - via WebEx* | Italy | No restrictions applicable to this meeting | |
| Martina Perini | Expert - via WebEx* | Italy | No restrictions applicable to this meeting | |
| Cristina Migali | Expert - via WebEx* | Italy | No interests declared | |
| Sara Galluzzo | Expert - via WebEx* | Italy | No interests declared | |
| Michela Piezzo | Expert - via WebEx* | Italy | No interests declared | |
| Alexandru Mihail Simion | Expert - via WebEx* | Belgium | No interests declared | |
| Joelle Warlin | Expert - via WebEx* | Belgium | No interests declared | |
| Kimberly Vanthuyne | Expert - via WebEx* | Belgium | No interests declared | |
| Roel Van Loock | Expert - via WebEx* | Belgium | No interests declared | |
| Flora Musuamba Tshinanu | Expert - via WebEx* | Belgium | No restrictions applicable to this meeting | |
| Gabriella Passacquale | Expert - via WebEx* | Italy | No interests declared | |
| Antonella Isgrò | Expert - via WebEx* | Italy | No interests declared | |
| Maria Di Marzo | Expert - via WebEx* | Italy | No interests declared | |
| Rune Kjeken | Expert - via WebEx* | Norway | No restrictions applicable to this meeting | |
| Maja Sommerfelt Grønvold | Expert - via WebEx* | Norway | No interests declared | |
| Charlotte Anderberg | Expert - via WebEx* | Sweden | No restrictions applicable to this meeting | |
| Ulla Wändel Liminga | Expert - via WebEx* | Sweden | No interests declared | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| | Expert - via WebEx* | Patient Representative | No interests declared | |
| | Expert - via WebEx* | Patient Representative | No interests declared | |
| | Expert - via WebEx* | Patient Representative | No interests declared | |
| Sabine Mayrhofer | Expert - via WebEx* | Germany | No interests declared | |
| Irene Bachmann | Expert - via WebEx* | Germany | No interests declared | |
| Anette Kristine Stark | Expert - via WebEx* | Denmark | No interests declared | |
| Sandrine Chiappini | Expert - via WebEx* | France | No interests declared | |
| Ingrid Lund | Expert - via WebEx* | Norway | No interests declared | |
| Martin Walter | Expert - via WebEx* | Austria | No interests declared | |
| Elisabeth Wischnitzki | Expert - via WebEx* | Austria | No interests declared | |
| Harald Bernsteiner | Expert - via WebEx* | Austria | No interests declared | |
| Brigitte Mueller | Expert - via WebEx* | Austria | No interests declared | |
| Miram Hinterleitner | Expert - via WebEx* | Austria | No interests declared | |
| Elisabeth Fuerst | Expert - via WebEx* | Austria | No interests declared | |
| Jan Joseph | Expert - via WebEx* | Austria | No interests declared | |
| Ilona G. Reischl | Expert - via WebEx* | Austria | No interests declared | |
| Philipp Janesch | Expert - via WebEx* | Austria | No interests declared | |
| Carin Bergquist | Expert - via WebEx* | Sweden | No interests declared | |
| Linda Dalin | Expert - via WebEx* | Sweden | No interests declared | |
| Violaine Closson Carella | Expert - via WebEx* | France | No interests declared | |
| Martina Schuessler-Lenz | Expert - via WebEx* | Germany | No interests declared | |
| Heidi Meyer | Expert - via WebEx* | Germany | No interests declared | |
| Jörg Engelbergs | Expert - via WebEx* | Germany | No interests declared | |
| Elina Rönnemaa | Expert - via WebEx* | Sweden | No interests declared | |
| Elisabeth Johanne Rook | Expert - via WebEx* | Netherlands | No interests declared | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Claus Bang Pedersen | Expert - via WebEx* | Denmark | no part in discussions, final deliberations and voting | Adtralza - tralokinumab - EMEA/H/C/005255/II/0002 |
| Elisabeth Penninga | Expert - via WebEx* | Denmark | No interests declared | |
| Iftekhar Khan | Expert - via WebEx* | Ireland | No interests declared | |
| Jelena Katic | Expert - via WebEx* | Germany | No interests declared | |
| Martin Huber | Expert - via WebEx* | Germany | No interests declared | |
| Pierre Demolis | Expert - via WebEx* | France | No interests declared | |
| Carla Herberts | Expert - via WebEx* | Netherlands | No interests declared | |
| Anna Cunney | Expert - via telephone* | Ireland | No interests declared | |
| Meeting run with the help of EMA staff | | | | |

*Experts were evaluated against the product(s) they have been invited to talk about

## 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)*

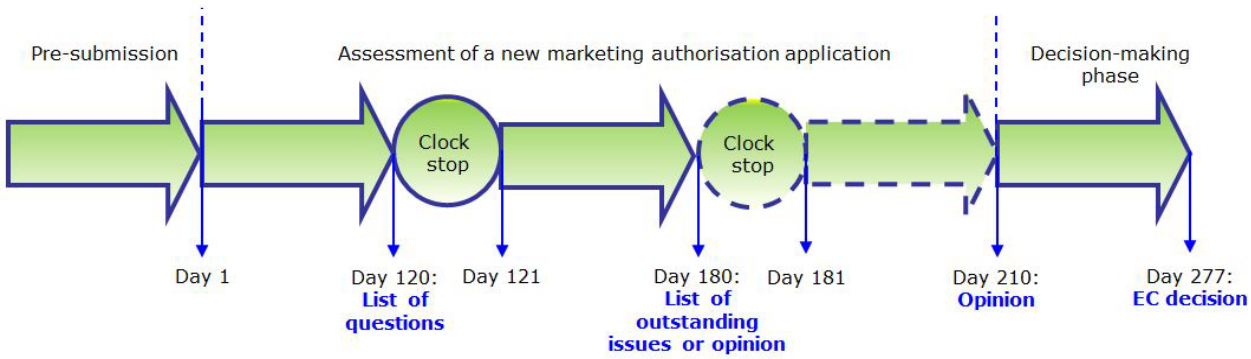
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

31 May 2022
EMA/CHMP/172920/2022

# Annex to 21-24 March 2022 CHMP Minutes

Pre-submission and post-authorisations issues

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## A. PRE-SUBMISSION ISSUES

### A.1. ELIGIBILITY REQUESTS

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

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

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|---|---|
| Final Outcome of Rapporteurship allocation for March 2022: **For adoption** | Adopted |

### A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

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

## B. POST-AUTHORISATION PROCEDURES OUTCOMES

### B.1. Annual re-assessment outcomes

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

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|---|---|
| **Myalepta - metreleptin - EMEA/H/C/004218/S/0023, Orphan**<br>Amryt Pharmaceuticals DAC, Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Adam Przybylkowski<br>Request for Supplementary Information adopted on 27.01.2022. | Positive Opinion adopted by consensus together with the CHMP assessment report.<br>The Marketing Authorisation remains under exceptional circumstances. |
| **Orphacol - cholic acid - EMEA/H/C/001250/S/0042, Orphan**<br>Laboratoires CTRS, Rapporteur: Anastasia Mountaki, PRAC Rapporteur: Sofia Trantza | Positive Opinion adopted by consensus together with the CHMP assessment report.<br>The Marketing Authorisation remains under exceptional circumstances. |
| **Raxone - idebenone - EMEA/H/C/003834/S/0029, Orphan**<br>Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli<br>Request for Supplementary Information adopted on 24.03.2022, 27.01.2022. | Request for supplementary information adopted with a specific timetable. |
| **Vyndaqel - tafamidis - EMEA/H/C/002294/S/0076, Orphan**<br>Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Tiphaine Vaillant<br>Request for Supplementary Information adopted | Positive Opinion adopted by consensus together with the CHMP assessment report.<br>The Marketing Authorisation remains under exceptional circumstances. |

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| on 24.02.2022. | |

## B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

### B.2.2. Renewals of Marketing Authorisations for unlimited validity

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| **Efavirenz/Emtricitabine/Tenofovir disoproxil Mylan - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/004240/R/0019**<br>Mylan Pharmaceuticals Limited, Generic, Generic of Atripla (SRD), Rapporteur: Bruno Sepodes, PRAC Rapporteur: Martin Huber | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br><br>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. |
| **Efavirenz/Emtricitabine/Tenofovir disoproxil Zentiva - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/004250/R/0025**<br>Zentiva k.s., Generic, Generic of Atripla (SRD), Rapporteur: Tomas Radimersky, PRAC Rapporteur: Martin Huber<br>Request for Supplementary Information adopted on 27.01.2022. | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br><br>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. |
| **Fotivda - tivozanib - EMEA/H/C/004131/R/0021**<br>EUSA Pharma (Netherlands) B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Rugile Pilviniene<br>Request for Supplementary Information adopted on 24.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **LUTATHERA - lutetium (177lu) oxodotreotide - EMEA/H/C/004123/R/0032, Orphan**<br>Advanced Accelerator Applications, Rapporteur: Janet Koenig, Co-Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Adam Przybylkowski<br>Request for Supplementary Information adopted on 24.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **Rydapt - midostaurin - EMEA/H/C/004095/R/0023, Orphan**<br>Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Ingrid Wang, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br><br>Based on the review of the available information, the CHMP was of the opinion that |

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| Request for Supplementary Information adopted on 24.02.2022. | the renewal of the marketing authorisation can be granted with unlimited validity. |
| **Symtuza - darunavir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004391/R/0040**<br>Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Ana Sofia Diniz Martins | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br><br>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. |

### B.2.3. Renewals of Conditional Marketing Authorisations

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| **LIBTAYO - cemiplimab - EMEA/H/C/004844/R/0029**<br>Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Menno van der Elst<br>Request for Supplementary Information adopted on 24.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **Nexpovio - selinexor - EMEA/H/C/005127/R/0005**<br>Karyopharm Europe GmbH, Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Menno van der Elst | Positive Opinion adopted by consensus together with the CHMP assessment report.<br>The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.<br>The Marketing Authorisation remains conditional. |
| **Rozlytrek - entrectinib - EMEA/H/C/004936/R/0007**<br>Roche Registration GmbH, Rapporteur: Armando Genazzani, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br><br>The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.<br><br>The Marketing Authorisation remains conditional. |
| **Veklury - remdesivir - EMEA/H/C/005622/R/0031**<br>Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, PRAC Rapporteur: Eva Jirsová | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br><br>The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted. The Marketing Authorisation remains conditional.<br><br>See 9.1 |
| **Zolgensma - onasemnogene abeparvovec - EMEA/H/C/004750/R/0021, Orphan,** | Positive Opinion adopted by consensus together with the CHMP assessment report and |

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| **ATMP**<br>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<br>Request for Supplementary Information adopted on 18.02.2022. | translation timetable.<br><br>Based on the review of the available information, the CHMP was of the opinion that the risk-benefit balance remains favourable and that all specific obligations have been fulfilled, therefore the CHMP recommended granting of a Marketing Authorisation not subject to specific obligations.<br><br>See 9.1 |

## B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

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| **Signal detection**<br><br>PRAC recommendations on signals adopted at the PRAC meeting held on 07-10 March 2022<br>PRAC: | |
| **Signal of vitiligo**<br><br>Lemtrada – alemtuzumab<br><br>Rapporteur: Thalia Marie Estrup Blicher, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark<br>PRAC recommendation on a variation<br>**Action:** For adoption | Adopted |
| **Signal of drug interaction with cannabidiol leading to calcineurin inhibitors and mTOR inhibitors serum levels increased and toxicity**<br><br>Epidyolex, Advagraf, Envarsus, Modigraf, Tacforius, Afinitor, Votubia, Rapamune, Torisel - Cannabidiol, calcineurin inhibitors: ciclosporin; tacrolimus, mammalian target of rapamycin (mTOR) inhibitors: everolimus, sirolimus, temsirolimus<br>CHMP Rapporteurs: multiple, PRAC Rapporteur: Ronan Grimes<br>PRAC recommendation on a variation<br>**Action:** For adoption | Adopted |

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| **Signal of capillary Leak Syndrome**<br><br>Spikevax - Elasomeran, COVID-19 mRNA vaccine (nucleoside modified)<br><br>Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Hans Christian Siersted<br>PRAC recommendation on a variation<br>**Action:** For adoption | Adopted |
| PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its March 2022 meeting: | |
| **EMEA/H/C/PSUSA/00000962/202107**<br>(desloratadine)<br>CAPS:<br>**Aerius** (EMEA/H/C/000313) (desloratadine), Organon N.V., Rapporteur: Christophe Focke<br>**Azomyr** (EMEA/H/C/000310) (desloratadine), Organon N.V., Rapporteur: Christophe Focke<br>**Dasselta** (EMEA/H/C/002310) (desloratadine), KRKA, d.d., Novo mesto, Rapporteur: Agnes Gyurasics<br>**Desloratadine Actavis** (EMEA/H/C/002435) (desloratadine), Actavis Group PTC ehf, Rapporteur: Agnes Gyurasics<br>**Desloratadine ratiopharm** (EMEA/H/C/002404) (desloratadine), ratiopharm GmbH, Rapporteur: Christophe Focke<br>**Desloratadine Teva** (EMEA/H/C/002419) (desloratadine), Teva B.V., Rapporteur: Agnes Gyurasics<br>**Neoclarityn** (EMEA/H/C/000314) (desloratadine), Organon N.V., Rapporteur: Christophe Focke<br>NAPS:<br>**NAPs** - EU<br>PRAC Rapporteur: Jean-Michel Dogné, "16/07/2016 To: 15/07/2021" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the medicinal products containing the above referred active substance(s), concerning the following change(s):<br>Update of section 4.8 of the SmPC and section 4 of the Package Leaflet:<br>- to add the adverse reaction "depressed mood" with a frequency unknown<br>- to add the adverse reaction "eye dryness" with a frequency unknown |
| **EMEA/H/C/PSUSA/00000963/202107**<br>(desloratadine / pseudoephedrine)<br>CAPS:<br>**Aerinaze** (EMEA/H/C/000772) (desloratadine / pseudoephedrine sulphate), Organon N.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Jean-Michel Dogné, "15/07/2016 To: 15/07/2021" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br>Update of section 4.8 of the Summary of Product Characteristics to add the adverse reaction "depressed mood" with a frequency unknown. |

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| | The Package leaflet is updated accordingly. |
| **EMEA/H/C/PSUSA/00002127/202108**<br>(natalizumab)<br>CAPS:<br>**Tysabri** (EMEA/H/C/000603) (natalizumab), Biogen Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "07/08/2020 To: 07/08/2021" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br>Update of section 4.6 of the SmPC to inform about the risk of anaemia in infants born to women exposed to natalizumab during pregnancy and the need to monitor the haemoglobin levels. |
| **EMEA/H/C/PSUSA/00010730/202108**<br>(tezacaftor / ivacaftor)<br>CAPS:<br>**Symkevi** (EMEA/H/C/004682) (tezacaftor / ivacaftor), Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, "12/02/2021 To: 12/08/2021" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended recommends by consensus the variation to the terms of the marketing authorisation(s) for the above-mentioned medicinal product(s), concerning the following change(s):<br>Update of section 4.4 of the Summary of Product Characteristics to add the warning of Elevated transaminase and hepatic injury. The Package leaflet is updated accordingly. |
| **EMEA/H/C/PSUSA/00010823/202108**<br>(upadacitinib)<br>CAPS:<br>**RINVOQ** (EMEA/H/C/004760) (upadacitinib), AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce, "15/02/2021 To: 15/08/2021" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above-mentioned medicinal product(s), concerning the following change(s):<br>Update of section 4.8 of the SmPC to add the adverse reaction urinary tract infection with a frequency common. The Package leaflet is updated accordingly. |
| **EMEA/H/C/PSUSA/00010869/202108**<br>(belantamab mafodotin)<br>CAPS:<br>**Blenrep** (EMEA/H/C/004935) (belantamab mafodotin), GlaxoSmithKline (Ireland) Limited, Rapporteur: Johanna Lähteenvuo, PRAC Rapporteur: Annika Folin, "05/02/2021 To: 04/08/2021" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br>In view of available data on pneumonitis from spontaneous reports including in one case a |

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| | reasonable temporal relationship and absence of other causal explanations and in view of a non-clinical signal and plausible mechanism of action, the PRAC considers a causal relationship between belantamab mafodotin and pneumonitis is at least a reasonable possibility. Therefore, changes to the wording in section 4.4 are proposed by deleting "although a causal association has not been established" and in addition to update section 4.8 with 'pneumonitis' as an ADR. |

**B.4. EPARs / WPARs**

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| **Amversio - betaine anhydrous - EMEA/H/C/005637**<br>SERB SA, treatment of homocystinuria, Generic, Generic of Cystadane, Generic application (Article 10(1) of Directive No 2001/83/EC) | For information only. Comments can be sent to the PL in case necessary. |
| **Dimethyl fumarate Mylan - dimethyl fumarate - EMEA/H/C/005956**<br>Mylan Ireland Limited, treatment of multiple sclerosis, Generic, Generic of TECFIDERA, Generic application (Article 10(1) of Directive No 2001/83/EC) | For information only. Comments can be sent to the PL in case necessary. |
| **Dimethyl fumarate Neuraxpharm - dimethyl fumarate - EMEA/H/C/006039**<br>Laboratorios Lesvi S.L., treatment of multiple sclerosis, Generic, Duplicate, Generic of TECFIDERA, Duplicate of Dimethyl fumarate Polpharma, Generic application (Article 10(1) of Directive No 2001/83/EC) | For information only. Comments can be sent to the PL in case necessary. |
| **Dimethyl fumarate Polpharma - dimethyl fumarate - EMEA/H/C/005955**<br>Zakłady Farmaceutyczne Polpharma S.A., treatment of multiple sclerosis, Generic, Generic of TECFIDERA, Generic application (Article 10(1) of Directive No 2001/83/EC) | For information only. Comments can be sent to the PL in case necessary. |
| **Inpremzia - insulin human (rDNA) - EMEA/H/C/005331**<br>Baxter Holding B.V., treatment of patients with diabetes mellitus who require intravenous insulin, 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. |
| **IPIQUE - bevacizumab - EMEA/H/C/005433**<br>Rotterdam Biologics B.V., indicated in adults for the treatment of neovascular macular | For information only. Comments can be sent to the PL in case necessary. |

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| degeneration associated with aging and diabetes., Well-established use application (Article 10a of Directive No 2001/83/EC) | |
| **Kapruvia - difelikefalin - EMEA/H/C/005612**<br>Vifor Fresenius Medical Care Renal Pharma France, treatment of pruritus, 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. |
| **KIMMTRAK - tebentafusp - EMEA/H/C/004929, Orphan**<br>Immunocore Ireland Limited, treatment of uveal melanoma, 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. |
| **MIPLYFFA (WD) - arimoclomol - EMEA/H/C/005203, Orphan**<br>Orphazyme A/S, treatment of Niemann-Pick disease type C (NPC), New active substance (Article 8(3) of Directive No 2001/83/EC)<br>**WPAR** | For information only. Comments can be sent to the PL in case necessary. |
| **Orgovyx - relugolix - EMEA/H/C/005353**<br>Myovant Sciences Ireland Limited, treatment of adult patients with advanced prostate cancer., New active substance (Article 8(3) of Directive No 2001/83/EC) | For information only. Comments can be sent to the PL in case necessary. |
| **Padcev - enfortumab vedotin - EMEA/H/C/005392**<br>Astellas Pharma Europe B.V., treatment of locally advanced (LA) or metastatic urothelial cancer (mUC), 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. |
| **PreHevbri - hepatitis B surface antigen - EMEA/H/C/005466**<br>VBI Vaccines B.V., indicated for the prevention of infection caused by all known subtypes of the hepatitis B virus in adults., Known active substance (Article 8(3) of Directive No 2001/83/EC) | For information only. Comments can be sent to the PL in case necessary. |
| **QUVIVIQ - daridorexant - EMEA/H/C/005634**<br>Idorsia Pharmaceuticals Deutschland GmbH, treatment of insomnia, 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. |
| **Sitagliptin Accord - sitagliptin - EMEA/H/C/005598**<br>Accord Healthcare S.L.U., treatment of type 2 | For information only. Comments can be sent to the PL in case necessary. |

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| diabetes mellitus, Generic, Generic of Januvia, Generic application (Article 10(1) of Directive No 2001/83/EC) | |
| **Truvelog Mix 30 - insulin aspart - EMEA/H/C/005635**<br>sanofi-aventis groupe, treatment of diabetes mellitus, 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. |
| **Vydura - rimegepant - EMEA/H/C/005725**<br>Biohaven Pharmaceutical Ireland DAC, management of migraine, New active substance (Article 8(3) of Directive No 2001/83/EC) | For information only. Comments can be sent to the PL in case necessary. |

### B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

Scopes related to Chemistry, Manufacturing, and Controls cannot be released at the present time as these contain commercially confidential information.

#### B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

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| **ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0030/G**<br>Baxalta Innovations GmbH, Rapporteur: Andrea Laslop<br>Opinion adopted on 17.03.2022. | Positive Opinion adopted by consensus on 17.03.2022. |
| **Alymsys - bevacizumab - EMEA/H/C/005286/II/0007/G**<br>Mabxience Research SL, Rapporteur: Christian Gartner<br>Request for Supplementary Information adopted on 17.02.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Apidra - insulin glulisine - EMEA/H/C/000557/II/0088/G**<br>Sanofi-Aventis Deutschland GmbH, Rapporteur: Thalia Marie Estrup Blicher<br>Opinion adopted on 10.03.2022.<br>Request for Supplementary Information adopted on 03.02.2022. | Positive Opinion adopted by consensus on 10.03.2022. |
| **Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0158**<br>Amgen Europe B.V., Rapporteur: Martina Weise<br>Opinion adopted on 17.03.2022.<br>Request for Supplementary Information adopted on 13.01.2022. | Positive Opinion adopted by consensus on 17.03.2022. |
| **Bimzelx - bimekizumab -** | Request for supplementary information adopted |

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| **EMEA/H/C/005316/II/0003/G**<br>UCB Pharma S.A., Rapporteur: Peter Kiely<br>Request for Supplementary Information adopted on 24.03.2022, 13.01.2022. | with a specific timetable. |
| **Bimzelx - bimekizumab - EMEA/H/C/005316/II/0004**<br>UCB Pharma S.A., Rapporteur: Peter Kiely<br>Opinion adopted on 10.03.2022.<br>Request for Supplementary Information adopted on 20.01.2022. | Positive Opinion adopted by consensus on 10.03.2022. |
| **Cerezyme - imiglucerase - EMEA/H/C/000157/II/0123/G**<br>Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege<br>Opinion adopted on 03.03.2022.<br>Request for Supplementary Information adopted on 13.01.2022, 14.10.2021. | Positive Opinion adopted by consensus on 03.03.2022. |
| **COMIRNATY - tozinameran - EMEA/H/C/005735/II/0105**<br>BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson<br>Opinion adopted on 24.03.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **COMIRNATY - tozinameran - EMEA/H/C/005735/II/0109/G**<br>BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson<br>Opinion adopted on 10.03.2022. | Positive Opinion adopted by consensus on 10.03.2022. |
| **COMIRNATY - tozinameran - EMEA/H/C/005735/II/0112/G**<br>BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson<br>Opinion adopted on 24.03.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **COMIRNATY - tozinameran - EMEA/H/C/005735/II/0115/G**<br>BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson<br>Opinion adopted on 03.03.2022. | Positive Opinion adopted by consensus on 03.03.2022. |
| **COMIRNATY - tozinameran - EMEA/H/C/005735/II/0121/G**<br>BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson<br>Opinion adopted on 23.03.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **COVID-19 Vaccine Janssen - adenovirus type 26 encoding the sars-cov-2 spike glycoprotein - EMEA/H/C/005737/II/0040**<br>Janssen-Cilag International N.V., Rapporteur: | Positive Opinion adopted by consensus on 17.03.2022. |

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| Christophe Focke<br>Opinion adopted on 17.03.2022. | |
| **Elaprase - idursulfase - EMEA/H/C/000700/II/0095**<br>Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege<br>Request for Supplementary Information adopted on 24.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **Enbrel - etanercept - EMEA/H/C/000262/II/0243/G**<br>Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 03.02.2022, 02.09.2021. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Enhertu - trastuzumab deruxtecan - EMEA/H/C/005124/II/0010**<br>Daiichi Sankyo Europe GmbH, Rapporteur: Sinan B. Sarac<br>Opinion adopted on 03.03.2022.<br>Request for Supplementary Information adopted on 16.12.2021, 28.10.2021. | Positive Opinion adopted by consensus on 03.03.2022. |
| **Erbitux - cetuximab - EMEA/H/C/000558/II/0092**<br>Merck Europe B.V., Rapporteur: Filip Josephson<br>Opinion adopted on 03.03.2022.<br>Request for Supplementary Information adopted on 13.01.2022. | Positive Opinion adopted by consensus on 03.03.2022. |
| **Febuxostat Mylan - febuxostat - EMEA/H/C/004374/II/0012**<br>Mylan Pharmaceuticals Limited, Generic, Generic of Adenuric, Rapporteur: Elita Poplavska<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 27.01.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0025/G**<br>Seqirus Netherlands B.V., Rapporteur: Sol Ruiz<br>Opinion adopted on 24.03.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Fulphila - pegfilgrastim - EMEA/H/C/004915/II/0029**<br>Viatris Limited, Rapporteur: Martina Weise<br>Request for Supplementary Information adopted on 17.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **Hemlibra - emicizumab -** | Request for supplementary information adopted |

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| **EMEA/H/C/004406/II/0029/G**<br>Roche Registration GmbH, Rapporteur: Alexandre Moreau<br>Request for Supplementary Information adopted on 17.03.2022. | with a specific timetable. |
| **Hepsera - adefovir dipivoxil - EMEA/H/C/000485/II/0087**<br>Gilead Sciences Ireland UC, Rapporteur: Jean-Michel Race<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 13.01.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Ilumetri - tildrakizumab - EMEA/H/C/004514/II/0029/G**<br>Almirall S.A, Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 17.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **Leqvio - inclisiran - EMEA/H/C/005333/II/0008**<br>Novartis Europharm Limited, Rapporteur: Martina Weise<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 27.01.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0023/G, Orphan**<br>Pfizer Europe MA EEIG, Rapporteur: Thalia Marie Estrup Blicher<br>Opinion adopted on 10.03.2022.<br>Request for Supplementary Information adopted on 27.01.2022. | Positive Opinion adopted by consensus on 10.03.2022. |
| **Natpar - parathyroid hormone - EMEA/H/C/003861/II/0033/G, Orphan**<br>Takeda Pharmaceuticals International AG, Rapporteur: Karin Janssen van Doorn<br>Request for Supplementary Information adopted on 17.03.2022, 02.12.2021. | Request for supplementary information adopted with a specific timetable. |
| **Natpar - parathyroid hormone - EMEA/H/C/003861/II/0035, Orphan**<br>Takeda Pharmaceuticals International AG, Rapporteur: Karin Janssen van Doorn<br>Opinion adopted on 10.03.2022.<br>Request for Supplementary Information adopted on 13.01.2022. | Positive Opinion adopted by consensus on 10.03.2022. |
| **NUVAXOVID - sars-cov-2, spike protein, recombinant, expressed in sf9 cells derived from spodoptera frugiperda -** | Positive Opinion adopted by consensus on 24.03.2022. |

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| **EMEA/H/C/005808/II/0004**<br>Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege<br>Opinion adopted on 24.03.2022. | |
| **Odomzo - sonidegib - EMEA/H/C/002839/II/0041**<br>Sun Pharmaceutical Industries Europe B.V., Rapporteur: Paula Boudewina van Hennik | Request for supplementary information adopted with a specific timetable. |
| **Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0027**<br>Alexion Europe SAS, Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 17.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **Paxlovid - (1r,2s,5s)-n-((1s)-1-cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2s)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973/II/0001/G**<br>Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race<br>Request for Supplementary Information adopted on 17.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **Paxlovid - (1r,2s,5s)-n-((1s)-1-cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2s)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973/II/0002**<br>Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race<br>Opinion adopted on 17.03.2022. | Positive Opinion adopted by consensus on 17.03.2022. |
| **Paxlovid - (1r,2s,5s)-n-((1s)-1-cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2s)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973/II/0003/G**<br>Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race<br>Request for Supplementary Information adopted on 17.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **Pedea - ibuprofen - EMEA/H/C/000549/II/0030**<br>Recordati Rare Diseases, Rapporteur: Jayne Crowe | Request for supplementary information adopted with a specific timetable. |

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| Request for Supplementary Information adopted on 17.03.2022. | |
| **Polivy - polatuzumab vedotin - EMEA/H/C/004870/II/0014/G, Orphan**<br>Roche Registration GmbH, Rapporteur: Alexandre Moreau<br>Opinion adopted on 17.03.2022.<br>Request for Supplementary Information adopted on 03.02.2022. | Positive Opinion adopted by consensus on 17.03.2022. |
| **Regkirona - regdanvimab - EMEA/H/C/005854/II/0002**<br>Celltrion Healthcare Hungary Kft., Rapporteur: Filip Josephson<br>Opinion adopted on 24.03.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Ruconest - conestat alfa - EMEA/H/C/001223/II/0071**<br>Pharming Group N.V, Rapporteur: Andrea Laslop<br>Request for Supplementary Information adopted on 17.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **Spectrila - asparaginase - EMEA/H/C/002661/II/0026**<br>medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Andrea Laslop<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 25.11.2021. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Spikevax - elasomeran - EMEA/H/C/005791/II/0038/G**<br>Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 17.02.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Spikevax - elasomeran - EMEA/H/C/005791/II/0050**<br>Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 24.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **Spikevax - elasomeran - EMEA/H/C/005791/II/0054/G**<br>Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 10.03.2022. | Positive Opinion adopted by consensus on 10.03.2022. |
| **Supemtek - quadrivalent influenza vaccine** | Request for supplementary information adopted |

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| **(recombinant, prepared in cell culture) - EMEA/H/C/005159/II/0007/G**<br>Sanofi Pasteur, Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 10.03.2022. | with a specific timetable. |
| **Toviaz - fesoterodine - EMEA/H/C/000723/II/0065/G**<br>Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro<br>Opinion adopted on 03.03.2022.<br>Request for Supplementary Information adopted on 20.01.2022. | Positive Opinion adopted by consensus on 03.03.2022. |
| **TRODELVY - sacituzumab govitecan - EMEA/H/C/005182/II/0002/G**<br>Gilead Sciences Ireland UC, Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 17.03.2022. | Positive Opinion adopted by consensus on 17.03.2022. |
| **TRODELVY - sacituzumab govitecan - EMEA/H/C/005182/II/0003**<br>Gilead Sciences Ireland UC, Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 17.03.2022. | Positive Opinion adopted by consensus on 17.03.2022. |
| **Trulicity - dulaglutide - EMEA/H/C/002825/II/0062/G**<br>Eli Lilly Nederland B.V., Rapporteur: Martina Weise<br>Opinion adopted on 17.03.2022. | Positive Opinion adopted by consensus on 17.03.2022. |
| **Tysabri - natalizumab - EMEA/H/C/000603/II/0132**<br>Biogen Netherlands B.V., Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 17.03.2022. | 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/0095**<br>MCM Vaccine B.V., Rapporteur: Christophe Focke<br>Opinion adopted on 17.03.2022. | Positive Opinion adopted by consensus on 17.03.2022. |
| **Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0062**<br>AstraZeneca AB, Rapporteur: Sol Ruiz<br>Request for Supplementary Information adopted | Request for supplementary information adopted with a specific timetable. |

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| on 24.03.2022. | |
| **Xolair - omalizumab - EMEA/H/C/000606/II/0114**<br>Novartis Europharm Limited, Rapporteur: Kristina Dunder<br>Request for Supplementary Information adopted on 24.03.2022, 13.01.2022. | Request for supplementary information adopted with a specific timetable. |
| **ZABDENO - ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005337/II/0009/G**<br>Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege<br>Request for Supplementary Information adopted on 17.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **WS2159/G**<br>**Prolia- EMEA/H/C/001120/WS2159/0095/G**<br>**XGEVA- EMEA/H/C/002173/WS2159/0079/G**<br>Amgen Europe B.V., Lead Rapporteur: Kristina Dunder<br>Request for Supplementary Information adopted on 17.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **WS2218/G**<br>**Advate- EMEA/H/C/000520/WS2218/0115/G**<br>**ADYNOVI- EMEA/H/C/004195/WS2218/0029/G**<br>Baxalta Innovations GmbH, Lead Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 17.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **WS2225/G**<br>**Abseamed- EMEA/H/C/000727/WS2225/0097/G**<br>**Binocrit- EMEA/H/C/000725/WS2225/0096/G**<br>**Epoetin alfa Hexal- EMEA/H/C/000726/WS2225/0096/G**<br>Sandoz GmbH, Lead Rapporteur: Alexandre Moreau<br>Request for Supplementary Information adopted on 17.03.2022. | Request for supplementary information adopted with a specific timetable. |

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

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| **Bimzelx - bimekizumab - EMEA/H/C/005316/II/0002** | Positive Opinion adopted by consensus on |

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| UCB Pharma S.A., Rapporteur: Peter Kiely, "C.I.4 - Update of section 5.1 of the SmPC in order to update efficacy information based on interim results from study PS0015; this is a multicentre, randomized, double-blind, active comparator controlled, parallel group study to evaluate the efficacy and safety of bimekizumab compared with secukinumab in adult study participants with moderate to severe plaque psoriasis. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2."<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 16.12.2021. | 24.03.2022. |
| **Brilique - ticagrelor - EMEA/H/C/001241/II/0054**<br>AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning and new adverse drug reactions on bradyarrhythmia and AV blocks based on a review of all currently available information, including clinical trial data, post- marketing reports, and plausible mechanism."<br>Opinion adopted on 03.03.2022.<br>Request for Supplementary Information adopted on 14.10.2021. | Positive Opinion adopted by consensus on 03.03.2022. |
| **Cyramza - ramucirumab - EMEA/H/C/002829/II/0043**<br>Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik, "Update of section 4.4 of the SmPC in order to add a new warning on heart failure following a detailed cumulative review of post-marketing data. The Package Leaflet and Labelling are updated accordingly. In addition, the MAH took the opportunity to update the package leaflet to include hypothyroidism as a common side effect."<br>Request for Supplementary Information adopted on 24.03.2022, 16.12.2021. | Request for supplementary information adopted with a specific timetable. |
| **Dapivirine Vaginal Ring 25 mg - dapivirine - EMEA/H/W/002168/II/0014/G**<br>International Partnership for Microbicides Belgium AISBL, Rapporteur: Paula Boudewina van Hennik, "C.I.13: Submission of the study report from study MTN-020 (Version 2.0). This is a multicentre, randomized, double-blind, placebo-controlled Phase III safety and | Request for supplementary information adopted with a specific timetable. |

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| effectiveness trial of a vaginal matrix ring containing dapivirine for the prevention of HIV-1 infection in women.<br>C.I.13: Submission of the Clinical Virology Report (Version 4.0). This report describes virologic characterisation of virus from HIV-1 seroconversion events during double-blind, placebo-controlled, randomized, multicentre Phase III clinical trials evaluating the safety and efficacy of Dapivirine Vaginal Ring."<br>Request for Supplementary Information adopted on 24.03.2022, 13.01.2022. | |
| **Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0053**<br>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."<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 17.02.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Iclusig - ponatinib - EMEA/H/C/002695/II/0061, Orphan**<br>Incyte Biosciences Distribution B.V., Rapporteur: Filip Josephson, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC based on results from the OPTIC study (AP24534-14-203) listed as a specific obligation in the Annex II. This is a randomised, open-label, Phase 2 trial of ponatinib in patients with chronic myeloid leukaemia to characterise the efficacy and safety of ponatibib over a range of doses; the Package Leaflet is updated accordingly."<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 13.01.2022, 14.10.2021. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Keytruda - pembrolizumab - EMEA/H/C/003820/II/0115**<br>Merck Sharp & Dohme B.V., Rapporteur: | Positive Opinion adopted by consensus on 24.03.2022. |

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| Armando Genazzani, "Update of section 5.1 of the SmPC in order to update efficacy information based on final results from study KEYNOTE-426 listed as imposed PAES in the Annex II; this is a Phase III Randomized, Open-label Study to Evaluate Efficacy and Safety of Pembrolizumab (MK-3475) in combination with Axitinib versus Sunitinib Monotherapy as a First-line Treatment for Locally Advanced or Metastatic Renal Cell Carcinoma (mRCC). In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet."<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 02.12.2021. | See 9.1 |
| **Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0060**<br>GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus, "Submission of the final study report from study Malaria-073, a Phase III, randomized, open-label, controlled and multicentre study that addressed two safety concerns listed in the RMP: immunogenicity when co-administered with yellow fever and measles vaccines, and cross-immunisation against human catalase. The submission of the study addresses MEA 004."<br>Opinion adopted on 17.03.2022. | Positive Opinion adopted by consensus on 17.03.2022. |
| **Orphacol - cholic acid - EMEA/H/C/001250/II/0044, Orphan**<br>Laboratoires CTRS, Rapporteur: Anastasia Mountaki, "Update of sections 4.3 and 4.5 of the SmPC in order to extend the currently existing contra-indication with phenobarbital in order to include primidone based on scientific literature. The Package Leaflet is updated accordingly. In addition, the MAH is also taking this opportunity to submit a combined SmPC for both dosages, 50 mg and 250 mg and to introduce editorial changes and update the contact details of the local representatives in the Package Leaflet."<br>Request for Supplementary Information adopted on 24.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **Orphacol - cholic acid - EMEA/H/C/001250/II/0045, Orphan** | Request for supplementary information adopted with a specific timetable. |

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| Laboratoires CTRS, Rapporteur: Anastasia Mountaki, "Update of section 4.5 of the SmPC in order to update the existing information regarding concomitant use of cholic acid (the active substance of Orphacol) and ursodeoxycholic acid based on scientific literature. The Package Leaflet is updated accordingly."<br>Request for Supplementary Information adopted on 24.03.2022. | |
| **QINLOCK - ripretinib - EMEA/H/C/005614/II/0002, Orphan**<br>Deciphera Pharmaceuticals (Netherlands) B.V., Rapporteur: Filip Josephson, "Submission of the final report from study XT218029 (DP-4851: ABC Transporter Substrate Potential in Cells). This submission fulfils the PAM commitment "New in vitro experiment to study whether ripretinib is a substrate of BCRP, which follows the design outlined in appendix 3 of the DDI GL - October 2021-REC."<br>Opinion adopted on 10.03.2022. | Positive Opinion adopted by consensus on 10.03.2022. |
| **Retsevmo - selpercatinib - EMEA/H/C/005375/II/0010**<br>Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, "Update of sections 4.2 and 5.3 of the SmPC in order to reflect the need to monitor open growth plates in adolescent patients based on the results from a non-clinical juvenile toxicity study LOXO-292-TOX-028. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to correct figures in section 5.1 of the SmPC."<br>Request for Supplementary Information adopted on 24.03.2022, 16.12.2021. | Request for supplementary information adopted with a specific timetable. |
| **Ronapreve - casirivimab / imdevimab - EMEA/H/C/005814/II/0001**<br>Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.1, 4.4 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."<br>Opinion adopted on 04.03.2022.<br>Request for Supplementary Information adopted on 10.02.2022. | Positive Opinion adopted by consensus on 04.03.2022. |
| **Tivicay - dolutegravir - EMEA/H/C/002753/II/0077** | Positive Opinion adopted by consensus on 17.03.2022. |

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| ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Following the recommendation (REC) requested during the procedure EMA/H/C/2753/X/58G, the MAH submits the manuscript of the ODYSSEY study which contains efficacy and long-term safety results to 96 weeks for Tivicay tablets. This study is an open-label, multicentre, randomized (1:1), non-inferiority, Phase II/III, 96-week, 2-arm clinical trial to compare the efficacy and toxicity of dolutegravir (DTG) plus 2 NRTIs vs. standard of care in HIV infected children aged less than 18 years who are starting first-line ART (ODYSSEY A) or switching to second-line ART (ODYSSEY B).<br>Based on the results, no amendments to the product information for DTG (Tivicay) are considered warranted and therefore, no updated SmPC is provided as part of this application."<br>Opinion adopted on 17.03.2022. | |
| **Toviaz - fesoterodine - EMEA/H/C/000723/II/0063**<br>Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro, "C.I.3<br>Update of sections 4.2, 5.1 and 5.2 of the SmPC with the results from study A0221047, to evaluate the safety and efficacy of fesoterodine in subjects aged 6 to 17 years with neurogenic detrusor overactivity. The change was suggested in the outcome of the EMEA/H/C/000723/P46/030.1.<br>The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.1."<br>Request for Supplementary Information adopted on 03.03.2022, 14.10.2021. | Request for supplementary information adopted with a specific timetable. |
| **Trogarzo - ibalizumab - EMEA/H/C/004961/II/0018**<br>Theratechnologies Europe Limited, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC in order to add additional efficacy data based on results from study TMB-311, a multicentre, expanded access phase 3 study providing post-hoc long-term data on patients from study TMB-301."<br>Request for Supplementary Information adopted on 24.03.2022. | Request for supplementary information adopted with a specific timetable. |

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| **VITRAKVI - larotrectinib - EMEA/H/C/004919/II/0021**<br>Bayer AG, Rapporteur: Filip Josephson, "Update of section 5.2 of the SmPC in order to reflect the outcome of an updated analysis of the population pharmacokinetic (PopPk) model based on additional PK sampling in patients aged 1 month to 6 years from study LOXO-TRK-15003 (SCOUT) imposed as a specific obligation (SOB). The MAH is also proposing to delete this SOB from Annex II. The MAH took the opportunity of this variation to introduce corrections to section 4.8 of the SmPC and to Annex II."<br>Request for Supplementary Information adopted on 17.03.2022, 02.12.2021. | Request for supplementary information adopted with a specific timetable. |
| **Xarelto - rivaroxaban - EMEA/H/C/000944/II/0093**<br>Bayer AG, Rapporteur: Kristina Dunder, "Update of section 5.1 and subsequent changes in sections 4.2 and 4.8. based on final results from study 18226 (UNIVERSE); this is a prospective, open-label, active controlled, multicentre, 2-part study, designed to evaluate the single- and multiple-dose pharmacokinetic properties of rivaroxaban (Part A), and to evaluate the safety and efficacy of rivaroxaban when used for thromboprophylaxis for 12 months compared with acetylsalicylic acid (Part B) in children 2 to 8 years of age with single ventricle physiology who had the Fontan procedure.<br>In addition, the MAH took the opportunity to introduce editorial changes to sections 4.8 and 4.9 of the SmPC."<br>Request for Supplementary Information adopted on 24.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **Xtandi - enzalutamide - EMEA/H/C/002639/II/0058**<br>Astellas Pharma Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 4.5 in order to add information regarding drug-drug interaction based on final results from study 9785-CL-0018 - A Phase 1 Open-label Study to Evaluate the Effect of Multiple Doses of Enzalutamide on the Pharmacokinetics of Substrates of P-glycoprotein (Digoxin) and Breast Cancer Resistant Protein (Rosuvastatin) in Male Subjects with Prostate Cancer. Additionally, the MAH has taken the opportunity | Positive Opinion adopted by consensus on 17.03.2022. |

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| to make an update to the information about the excipients in section 4.4 of the SmPC, to introduce editorial changes in the SmPC and in the Package Leaflet, and to update the list of local representatives in the Package Leaflet."<br>Opinion adopted on 17.03.2022. | |
| **WS2174**<br>**Hexacima-**<br>**EMEA/H/C/002702/WS2174/0123**<br>**Hexyon-**<br>**EMEA/H/C/002796/WS2174/0127**<br>Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus, "Update of section 4.5 of the SmPC in order to add drug-drug interaction information regarding the co-administration of Hexyon / Hexacima with varicella vaccines based on a re-analysis of the A3L15 clinical trial varicella serological data, submitted in the initial CTD dossier. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to correct some typo errors in the SmPC and PL."<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 20.01.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **WS2183**<br>**Infanrix hexa-**<br>**EMEA/H/C/000296/WS2183/0310**<br>GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke, "Update of section 2 of the SmPC of Infanrix Hexa and other 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 Package Leaflet is updated accordingly. 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."<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 03.02.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **WS2224**<br>**Eucreas-**<br>**EMEA/H/C/000807/WS2224/0094** | Request for supplementary information adopted with a specific timetable. |

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| **Galvus-EMEA/H/C/000771/WS2224/0075 Icandra-EMEA/H/C/001050/WS2224/0097 Jalra-EMEA/H/C/001048/WS2224/0077 Xiliarx-EMEA/H/C/001051/WS2224/0075 Zomarist-EMEA/H/C/001049/WS2224/0096**<br>Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to update the list of ADRs and update the ADR table in line with the EC SmPC guideline (2009). The Package Leaflet is updated accordingly."<br>Request for Supplementary Information adopted on 17.03.2022. | |

### B.5.3. CHMP-PRAC assessed procedures

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| **ADCETRIS - brentuximab vedotin - EMEA/H/C/002455/II/0099, Orphan**<br>Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.8 and 5.1 of the SmPC, based on final results from study C25006, a multi-centre open-label, phase 4 study of 50 patients with r/r sALCL undertaken to further evaluate the efficacy and safety of brentuximab vedotin as a single agent in adult patients who had previously received at least 1 multiagent chemotherapy regimen. This study was listed as an interventional category 2 PASS in the RMP (SOB 010). In addition, the MAH took the opportunity to request the granting of a marketing authorisation not subject to specific obligations and valid for five years, in accordance with Article 14-a(8) of Regulation (EC) No 726/2004, thereby deleting SOB 010 from the annex II and of the reference to the conditional marketing authorisation from annex II and the package leaflet. The revised RMP version 16.1 has also been submitted. An editorial update under section 5.1 of the SmPC (update of the ATC code) has been implemented.<br>In addition, the CHMP, having considered the application as set out in the appended assessment report and having reviewed the data submitted by the marketing authorisation holder including the evidence concerning compliance with specific obligations, is of the | Positive Opinion adopted by consensus on 24.03.2022.<br><br>See 9.1 |

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| opinion that the risk-benefit balance of the above mentioned medicinal product remains favourable, that all specific obligations laid down in Annex II have been fulfilled and that comprehensive data supports a favourable benefit-risk balance of the above mentioned medicinal product. Therefore, pursuant to Article 14-a(8) of Regulation (EC) No 726/2004, the CHMP recommends by consensus the granting of a marketing authorisation in accordance with Article 14(1) of Regulation (EC) No 726/2004 for the above mentioned medicinal product for which the draft Summary of Product Characteristics is set out in Annex I."<br>Opinion adopted on 24.03.2022. | |
| **Afstyla - lonoctocog alfa - EMEA/H/C/004075/II/0042**<br>CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sonja Hrabcik, "Update of section 5.1 of the SmPC in order to update efficacy and safety information based on final results from study 3001 listed as a category 3 study in the RMP; this is an open label, multicentre extension study to assess the Safety and Efficacy of Afstyla in subjects with severe Hemophilia A. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 6.0 has also been submitted."<br>Request for Supplementary Information adopted on 10.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **ASPAVELI - pegcetacoplan - EMEA/H/C/005553/II/0002, Orphan**<br>Swedish Orphan Biovitrum AB (publ), Rapporteur: Alexandre Moreau, PRAC Rapporteur: Kimmo Jaakkola, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC based on final results from study APL2-302 (Pegasus) listed as a category 3 study in the RMP; this is a global, Phase 3, prospective, randomised, multicentre, open-label, active-comparator–controlled study in 80 subjects. The objective was to confirm treatment efficacy and safety of pegcetacoplan monotherapy for the treatment of Paroxysmal Nocturnal Hemoglobinuria (PNH). The submission of this study addresses MEA 001.The Package Leaflet is updated accordingly. The RMP version 0.5 has also been submitted." | Request for supplementary information adopted with a specific timetable. |

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| Request for Supplementary Information adopted on 24.03.2022. | |
| **Defitelio - defibrotide - EMEA/H/C/002393/II/0056, Orphan**<br>Gentium S.r.l., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from study 15-007 listed as a specific obligation in the Annex II of the Product Information. This is a phase 3, randomised, adaptive study (15-007) of Defibrotide vs. best supportive care in the prevention of hepatic venoocclusive disease in adult and paediatric patients undergoing hematopoietic stem cell transplant (HSCT). The RMP version 9 has also been submitted.<br>The MAH has also taken the opportunity to align the PI to the latest QRD template 10.2 which replaces the United Kingdom with United Kingdom (Northern Ireland) in the PIL.<br>In addition, the MAH is correcting the following errata during the linguistic review of the PI: correction of the paragraph number for Regulation (EC) No 726.2004 which was cited incorrectly in Annex II of the French PI and formatting updates to Norwegian and Swedish language PIs."<br>Request for Supplementary Information adopted on 10.03.2022, 28.10.2021, 08.07.2021. | Request for supplementary information adopted with a specific timetable.<br><br>See 9.1 |
| **Dexdor - dexmedetomidine - EMEA/H/C/002268/II/0035**<br>Orion Corporation, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.4 of the SmPC in order to add a new warning on mortality in ICU patients $\leqslant$ 65 years old, based on results from study SPICE III (randomised controlled trial) and following the assessment of the post-authorisation measure LEG 16.4. PRAC also recommended corresponding PIL wording (as no MAH proposal received). In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. RMP version 9, proposed DHPC and communication plan have also been submitted."<br>Request for Supplementary Information adopted on 24.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **Esperoct - turoctocog alfa pegol - EMEA/H/C/004883/II/0010, Orphan**<br>Novo Nordisk A/S, Rapporteur: Andrea Laslop, | Request for supplementary information adopted with a specific timetable. |

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| PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.4 and 4.8 of the SmPC to add a new warning and update the list of ADRs based on a validated safety signal concerning a lack of factor VIII activity in patients switching from a similar factor VIII product to Esperoct. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and to align it with the latest QRD template version 10.2. The RMP version 2.0 has also been submitted."<br>Request for Supplementary Information adopted on 24.03.2022. | |
| **Fintepla - fenfluramine - EMEA/H/C/003933/II/0010/G, Orphan**<br>Zogenix ROI Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, "- Update of section 5.3 of the SmPC in order to update the non-clinical information following the study 20147822 (A 6-month Carcinogenicity Study of Fenfluramine Hydrochloride in Mice).<br>- Update of section 5.3 in order to update the non-clinical information following the study 8001993 (A 2-year Oral Gavage Carcinogenicity Study of Fenfluramine Hydrochloride in Rats).<br>- Submission of the final report of study 20147821 (Dose range finding study for 20147822).<br>- Submission of the final report of study 20166554 (Dose range finding study for 20147822).<br>- Submission of the final report of study 2021006-Z001-01 (In-vitro Evaluation of Potential Melanin Binding by Fenfluramine and Norfenfluramine).<br>An RMP version 3.1 has also been submitted."<br>Request for Supplementary Information adopted on 10.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **Fintepla - fenfluramine - EMEA/H/C/003933/II/0011/G, Orphan**<br>Zogenix ROI Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, "- Update of sections 4.2 and 5.2 of the SmPC to include the relevant information regarding patients with renal impairment following the study 1902 (Pharmacokinetic study of fenfluramine hydrochloride in subjects with varying degrees of impaired and normal renal | Request for supplementary information adopted with a specific timetable. |

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| function)<br>- Update of sections 4.4 and 4.5 of the SmPC in order to reflect the relevant information on CYP1A2 or CYP2B6 or CYP2D6 inducers following the study 1904 (Pharmacokinetic drug-drug interaction study of fenfluramine hydrochloride with and without fluvoxamine (CYP1A2 inhibitor), paroxetine (CYP2D6 inhibitor) and rifampin (CYP2B6 inducer) in healthy subjects).<br>An RMP version 2.2 has also been submitted."<br>Request for Supplementary Information adopted on 10.03.2022. | |
| **GIVLAARI - givosiran - EMEA/H/C/004775/II/0006, Orphan**<br>Alnylam Netherlands B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Martin Huber, "Type II C.I.4: Update of SmPC section 4.8 to add 'blood homocysteine increase' as a new ADR and update to SmPC section 4.4 to add a related warning. The package leaflet is being updated accordingly. RMPv1.1 is also being submitted: consequences of blood homocysteine increase is being added as a new important potential risk, the clinical and post-marketing exposure is being updated and the due dates for ALN-AS1-002 and ALN-AS1-003 final study reports are being postponed.<br>In addition, the MAH took the opportunity to make editorial changes to the Product Information in other EU languages and to update the contact number of the local representatives for Malta and Cyprus."<br>Request for Supplementary Information adopted on 10.03.2022, 13.01.2022, 28.10.2021, 02.09.2021. | Request for supplementary information adopted with a specific timetable. |
| **LUTATHERA - lutetium (177lu) oxodotreotide - EMEA/H/C/004123/II/0030, Orphan**<br>Advanced Accelerator Applications, Rapporteur: Janet Koenig, PRAC Rapporteur: Adam Przybylkowski, "Update of the SmPC sections 4.4, 4.8 and 5.1 based on the pivotal Phase III study, NETTER-1. Additionally, updates are proposed in the PI to correct some information based on currently approved data. The PL is updated accordingly. The RMP v. 2.0 has been submitted. The MAH took also the opportunity to update the details of local representatives in the PL." | Positive Opinion adopted by consensus on 24.03.2022. |

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| Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 16.12.2021. | |
| **MabThera - rituximab - EMEA/H/C/000165/II/0188**<br>Roche Registration GmbH, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Anette Kirstine Stark, "Submission of the final report from study MA28150 (RITAZAREM) entitled Rituximab versus azathioprine as therapy for maintenance of remission for anti-neutrophilcytoplasm antibody-associated vasculitis listed as an interventional category 3 study in the RMP.<br>The RMP version 23.0 has also been submitted."<br>Opinion adopted on 24.03.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Mekinist - trametinib - EMEA/H/C/002643/II/0051**<br>Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: David Olsen, "Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations in hepatic impairment and update pharmacokinetic information based on final results from study MEC116354 listed as a category 3 study in the RMP; this is a Phase I Trial of Single Agent Trametinib (GSK1120212) in Advanced Cancer Patients with Hepatic Dysfunction. The RMP version 18 has also been submitted."<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 16.12.2021. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Myalepta - metreleptin - EMEA/H/C/004218/II/0025, Orphan**<br>Amryt Pharmaceuticals DAC, Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Adam Przybylkowski, "Submission of an updated RMP version 2.1. The applicant is proposing an alternative study to the currently agreed protocol for Specific Obligation SOB002 (AEGR-734-002) due to the challenges of implementing the existing protocol. Annex II is being updated accordingly.<br>MAH took the opportunity to update the RMP in line with the outcome of previous procedures and to include editorial changes."<br>Request for Supplementary Information adopted | Request for supplementary information adopted with a specific timetable. |

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| on 24.03.2022. | |
| **Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0024, Orphan**<br>Pfizer Europe MA EEIG, Rapporteur: Thalia Marie Estrup Blicher, 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 Leukaemia. 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."<br>Request for Supplementary Information adopted on 18.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0056**<br>Orexigen Therapeutics Ireland Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, "Submission of updated study design and protocol synopsis for CVOT-2 study, a category 1 study listed in Annex II.D (ANX/001.7) undertaken to assess the effect of naltrexone extended release (ER) / bupropion ER on the occurrence of major adverse cardiovascular events (MACE), as requested in the CHMP AR for ANX/001.6. The Annex II and the RMP version 13 are updated accordingly."<br>Request for Supplementary Information adopted on 24.03.2022. | Request for supplementary information adopted with a specific timetable.<br><br>See 9.1 |
| **Pemazyre - pemigatinib - EMEA/H/C/005266/II/0005, Orphan**<br>Incyte Biosciences Distribution B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4, 4.8 and 5.1 of the SmPC based on the final results from study INCB054828 (FIGHT-202) listed as a specific obligation in the Annex II (SOB/002); this is a phase 2 study investigating the efficacy and safety of pemigatinib in adults with advanced/metastatic or surgically unresectable cholangiocarcinoma including FGFR2 translocations who failed | Request for supplementary information adopted with a specific timetable. |

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| previous therapy. The Annex II has been updated accordingly. RMP version 2.0 has also been submitted."<br>Request for Supplementary Information adopted on 24.03.2022. | |
| **Piqray - alpelisib - EMEA/H/C/004804/II/0008/G**<br>Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst, "Update of section 5.1 of the SmPC based on final results from study CBYL719C2301 (SOLAR-1) listed as a PAES in the Annex II; this is a phase III, randomized, double-blind, placebo controlled study of alpelisib in combination with fulvestrant for men and postmenopausal women with hormone receptor positive, HER2-negative advanced breast cancer which progressed on or after aromatase inhibitor treatment; the Annex II is updated accordingly. In addition, the MAH is updating the ATC code in the SmPC. The RMP version 5.0 has also been submitted."<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 28.10.2021. | Positive Opinion adopted by consensus on 24.03.2022.<br><br>See 9.1 |
| **Prolia - denosumab - EMEA/H/C/001120/II/0093**<br>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 representative in the Package Leaflet and to implement minor editorial changes in the Labelling."<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 24.02.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Raxone - idebenone -** | Request for supplementary information adopted |

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| **EMEA/H/C/003834/II/0031, Orphan**<br>Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli, "Update of sections 4.2, 4.4, 4.9 and 5.1 of the SmPC based on the final study report from the PAROS study SNT-IV-003 (SOB003; listed as a cat 2 study in the RMP): "A non-interventional study of clinical experience in patients prescribed Raxone for the treatment of Leber's Hereditary Optic Neuropathy (LHON)". Annex II is updated in accordance. A revised RMP version 1.14 was also submitted."<br>Request for Supplementary Information adopted on 24.03.2022. | with a specific timetable.<br><br>See 9.1 |
| **Replagal - agalsidase alfa - EMEA/H/C/000369/II/0117**<br>Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, "Update of sections 4.2 and 6.6 of the SmPC in order to add self-administration by a trained patient and/or a caregiver as a new method of administration. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. The RMP version 0.1 has also been submitted."<br>Request for Supplementary Information adopted on 24.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **RINVOQ - upadacitinib - EMEA/H/C/004760/II/0015/G**<br>AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce, "Grouping of 2 variations:<br>C.I.4 - Update of sections 4.8 to add neutropenia and 5.1 of the SmPC in order to update efficacy information of Rinvoq in Ankylosing Spondylitis (AS) patients who are biologic DMARD inadequate responders (bDMARD-IR) based on interim results from study M19-944 study 1; this is a Phase 3, randomized, double-blind, study evaluating the long-term safety, tolerability, and efficacy of upadacitinib 15 mg QD in subjects with active AS who have an inadequate response (IR) to bDMARD.<br>C.I.4 - Update of section 5.1 of the SmPC in order to include long-term (through week 104) | Request for supplementary information adopted with a specific timetable. |

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| data in AS patients who are naïve to previous treatment with a bDMARD based on interim results from study M16-098; this is a Multicentre, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Safety and Efficacy of Upadacitinib in Subjects with Active Ankylosing Spondylitis;<br>The RMP version 7.0 has also been submitted.<br>In addition, the MAH took the opportunity to introduce minor editorial changes in the product information."<br>Request for Supplementary Information adopted on 24.03.2022. | |
| **Rubraca - rucaparib - EMEA/H/C/004272/II/0029**<br>Clovis Oncology Ireland Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Annika Folin, "Update of sections 4.4, 4.8 and 5.1 of the SmPC based on final results from study CO-338-043 (ARIEL4); this is a phase 3, multicentre, open-label, randomised study evaluating the efficacy and safety of rucaparib versus chemotherapy for treatment of relapsed ovarian cancer listed as a specific obligation in the Annex II; the Package Leaflet is updated accordingly. The RMP version 6.1 has also been submitted. With this variation application, the MAH requests for the Rubraca marketing authorisation to no longer be subject to specific obligations. The SmPC, Annex II and PL are updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes and bring the PI in line with the latest QRD template version 10.2 Rev.1."<br>Request for Supplementary Information adopted on 24.03.2022, 11.11.2021. | Request for supplementary information adopted with a specific timetable.<br><br>See 9.1 |
| **Rydapt - midostaurin - EMEA/H/C/004095/II/0024, Orphan**<br>Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "C.I.11.b Submission of the final report from study CPKC412E2301 listed as an obligation in the Annex II of the Product Information. This is a Phase III study to investigate the efficacy in elderly patients. A final pharmacogenomic report is also provided to fulfil MEA004. The Annex II and the RMP (submitted version 7.0) are updated accordingly." | Request for supplementary information adopted with a specific timetable. |

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| Request for Supplementary Information adopted on 10.03.2022. | |
| **Ryeqo - relugolix / estradiol / norethisterone acetate - EMEA/H/C/005267/II/0006**<br>Gedeon Richter Plc., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Martin Huber, "Submission of the final report from study MVT-601-035 listed as a category 3 study in the RMP. This is an international phase III double-blind, placebo-controlled, randomised withdrawal study of relugolix co-administered with estradiol and norethisterone in women with heavy menstrual bleeding associated with uterine fibroids to evaluate the efficacy and safety of long-term use of this medicinal product. The RMP version 1.0 has also been submitted."<br>Request for Supplementary Information adopted on 10.03.2022. | Request for supplementary information adopted with a specific timetable. |
| **WAYLIVRA - volanesorsen - EMEA/H/C/004538/II/0017/G, Orphan**<br>Akcea Therapeutics Ireland Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber, "C.I.4: Update of sections 4.8 and 5.1 of the SmPC based on the final results from study (ISIS 304801 CS7), a multicentre open label extension study of Volanesorsen administered subcutaneously to patients with Familial Chylomicronemia Syndrome. The Package Leaflet has been updated accordingly. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI in order to align with the QRD template and to introduce minor linguistic update to Annex III of the product information to support product launch.<br>C.I.11b. for RMP: Submission of an updated RMP version 2.1 based on the clinical study report addendum: A randomized, double blind, placebo-controlled Phase 3 study of ISIS 304801 administered subcutaneously to patients with Familial Chylomicronemia Syndrome (ISIS 304801 CS6 (APPROACH).<br>C.I.11b. for RMP: Submission of an updated RMP version 2.1 in order to update section V.2 Additional Risk Minimisation Measures in the RMP to reflect a change in the distribution methodology of the educational materials (from | Request for supplementary information adopted with a specific timetable. |

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| a centralised model to a localised model of distribution) and to clarify what is meant by the prescriber kit.<br>C.I.13: Submission of the final report from study ISIS 304801 (CS17). This is a Phase 2/3 double blind, randomized, placebo-controlled study, with an open label extension of ISIS 304801 administered subcutaneously to patients with familial partial lipodystrophy. The RMP version 2.1 has also been submitted."<br>Request for Supplementary Information adopted on 10.03.2022. | |
| **Xtandi - enzalutamide - EMEA/H/C/002639/II/0057**<br>Astellas Pharma Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "C.I.4<br>Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to reflect the updated safety and efficacy data from the final analysis of the 9785-CCL-0335 (ARCHES) study, a phase 3 randomized, double-blind, placebo-controlled study that evaluated the safety and efficacy of enzalutamide plus androgen deprivation therapy (ADT) vs placebo plus ADT in men with mHSPC; the Package Leaflet is updated accordingly. The RMP version 17.0 has also been submitted. In addition, the MAH took the opportunity to make minor editorial changes to section 4.8 and section 5.1 of the SmPC."<br>Opinion adopted on 10.03.2022. | Positive Opinion adopted by consensus on 10.03.2022. |

### B.5.4. PRAC assessed procedures

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| PRAC Led<br>**COMIRNATY - tozinameran - EMEA/H/C/005735/II/0087**<br>BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of the RMP version 5.0 to include data from the booster/third dose, including data in patients who have undergone a solid organ transplantation, following the outcome of procedures EMEA/H/C/005735/II/0062 (third dose in immunocompromise as part of the primary vaccination) and EMEA/H/C/005735/II/0067 (booster dose).<br>The MAH took the opportunity to update the RMP regarding the discontinuation of enrolment in | Positive Opinion adopted by consensus on 10.03.2022. |

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| study C4591015 (*Phase 2/3 study to evaluate the safety, tolerability, and immunogenicity in healthy pregnant women 18 years of age and older*) and the CSR milestones; and to include the ongoing non-interventional study C4591022 (*Pfizer-BioNTech COVID-19 Vaccine Exposure during Pregnancy: A Non-Interventional Post-Approval Safety Study of Pregnancy and Infant Outcomes in the Organization of Teratology Information Specialists (OTIS)/MotherToBaby Pregnancy Registry*) to address the missing information *Use in pregnancy*.<br>The MAH also updated the RMP in compliance with the outcome of the Signal of Multisystem inflammatory syndrome (MIS) for COVID-19 vaccines (EPITT ref 19732).<br>In addition, the MAH consolidated in RMP version 5.0 the updates made in the RMP as part of the approved procedure EMEA/H/C/005735/X/0077."<br>Opinion adopted on 10.03.2022.<br>Request for Supplementary Information adopted on 13.01.2022. | |
| PRAC Led<br>**Cyramza - ramucirumab - EMEA/H/C/002829/II/0047**<br>Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from study I4T-MC-JVDD listed as a category 3 study in the RMP for Cyramza, entitled 'Safety and Effectiveness of Ramucirumab in Patients with Advanced Gastric Cancer in the European Union and North America: A Prospective Observational Registry (Study I4T-MC-JVDD)' (Related to MEA 001.1). The RMP version 10.1 has also been submitted."<br>Opinion adopted on 10.03.2022. | Positive Opinion adopted by consensus on 10.03.2022. |
| PRAC Led<br>**Hemlibra - emicizumab - EMEA/H/C/004406/II/0025**<br>Roche Registration GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Armando Genazzani, "Update of sections 4.4, 4.8 and 5.1 of the Product information concerning immunogenicity and loss of efficacy due to anti-emicizumab antibodies. The RMP (v.4.1) is proposed to be updated accordingly." | Positive Opinion adopted by consensus on 10.03.2022. |

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| Opinion adopted on 10.03.2022.<br>Request for Supplementary Information adopted on 13.01.2022, 02.12.2021, 02.09.2021. | |
| PRAC Led<br>**Hemlibra - emicizumab - EMEA/H/C/004406/II/0028**<br>Roche Registration GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Armando Genazzani, "Submission of the final study report for BO40853 (Hemlibra Survey to Prescribers and Patients/Carers to Evaluate Awareness, Knowledge, and Compliance to Additional Risk Minimisation Measures, listed as a category 3 study in the RMP). An updated RMP (version 4.0) is presented in support of this application."<br>Opinion adopted on 10.03.2022.<br>Request for Supplementary Information adopted on 13.01.2022, 02.12.2021. | Positive Opinion adopted by consensus on 10.03.2022. |
| PRAC Led<br>**Inflectra - infliximab - EMEA/H/C/002778/II/0105**<br>Pfizer Europe MA EEIG, Duplicate, Duplicate of Remsima, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of the final report from study CT-P13 4.2; An Observational, Prospective Cohort Study to Evaluate Safety and Efficacy of Inflectra in Patients with Rheumatoid Arthritis (study report excluding the joint analysis of patients in the PERSIST study). The submission of the study report addresses MEA 007.6."<br>Opinion adopted on 10.03.2022. | Positive Opinion adopted by consensus on 10.03.2022. |
| PRAC Led<br>**Kuvan - sapropterin - EMEA/H/C/000943/II/0073**<br>BioMarin International Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Submission of the final report from study BMN 162-501 KAMPER (formerly EMR700773-001) listed as a category 3 study in the RMP. This is an observational drug registry to assess the long-term safety in subjects treated with Kuvan. The submission of this study addresses the PAM MEA 020. The RMP version 15.1 has also been submitted."<br>Request for Supplementary Information adopted | Request for supplementary information adopted with a specific timetable. |

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| on 10.03.2022. | |
| PRAC Led<br>**Latuda - lurasidone - EMEA/H/C/002713/II/0037**<br>Aziende Chimiche Riunite Angelini Francesco A.C.R.A.F. S.p.A., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "Submission of an updated RMP version 9.1, to implement the PASS study outcome (EMEA/H/C/002713/II/0033), to remove from the list of safety concerns all important identified risks, all important potential risks, and to remove missing information on 'elderly patients', 'patients with cardiac impairment', and 'long-term safety'; and to discontinue the use of targeted adverse event follow-up questionnaire for angioedema."<br>Opinion adopted on 10.03.2022. | Positive Opinion adopted by consensus on 10.03.2022. |
| PRAC Led<br>**Moventig - naloxegol - EMEA/H/C/002810/II/0038**<br>Kyowa Kirin Holdings B.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Submission of an updated RMP version 7.2 proposing the cancellation of the cat. 3 study (D3820R00009: An Observational Drug Utilisation PASS of Moventig in selected European populations), following the assessment of MEA 006.11"<br>Request for Supplementary Information adopted on 10.03.2022. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**PecFent - fentanyl - EMEA/H/C/001164/II/0054**<br>Kyowa Kirin Holdings B.V., Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of an updated RMP (version 7.1) in line with the outcome of the last PSUR single assessment (PSUSA) procedure (PSUSA 00001369/202004) finalised in January 2021 in order to update the key messages of the educational materials in line with Instanyl (fentanyl). As a result, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated accordingly. Finally, the MAH took the opportunity to bring the RMP in | Request for supplementary information adopted with a specific timetable. |

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| line with revision 2 of GVP module V on 'Risk management systems' and the product information in line with the latest quality review of documents (QRD) template (version 10.2). The requested variation proposed amendments to the Annex II and to the Risk Management Plan (RMP)."<br>Request for Supplementary Information adopted on 10.03.2022, 28.10.2021. | |
| PRAC Led<br>**Praluent - alirocumab - EMEA/H/C/003882/II/0068**<br>sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC, based on the final results from category 3 study OBS14697; a non-interventional, retrospective drug utilisation study that was designed to assess in Europe the effectiveness of the dosing recommendation and to describe patterns of alirocumab utilisation in real world clinical practice. In addition, the MAH took the opportunity to implement editorial changes in the SmPC and package leaflet. The submission of the study report addresses the Post-Authorisation Measure MEA/FSR 019.8."<br>Request for Supplementary Information adopted on 10.03.2022. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**Remsima - infliximab - EMEA/H/C/002576/II/0111**<br>Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of the final report from study CT-P13 4.2; An Observational, Prospective Cohort Study to Evaluate Safety and Efficacy of Remsima in Patients with Rheumatoid Arthritis (study report excluding the joint analysis of patients in the PERSIST study)."<br>Opinion adopted on 10.03.2022. | Positive Opinion adopted by consensus on 10.03.2022. |
| PRAC Led<br>**Tegsedi - inotersen - EMEA/H/C/004782/II/0026, Orphan**<br>Akcea Therapeutics Ireland Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Updated RMP version 3.1 removes | Positive Opinion adopted by consensus on 10.03.2022. |

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| carcinogenicity in rats as missing information, adds a targeted questionnaire as routine pharmacovigilance measure and a patient alert card as additional risk minimisation for liver transplant rejection. Adds 'injection site reactions' and 'immunogenicity' as risks not considered important for inclusion in the summary of safety concerns (SVII.1.) and updates the patient alert card with additional warnings on hepatic monitoring and ocular toxicity. Further sections of the RMP are updated."<br>Opinion adopted on 10.03.2022.<br>Request for Supplementary Information adopted on 13.01.2022. | |
| PRAC Led<br>**XALKORI - crizotinib - EMEA/H/C/002489/II/0075**<br>Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final report for non-interventional PASS cat 3 study A8081062, a descriptive study of potential sight threatening event and severe visual loss following exposure to crizotinib (related to MEA 024)."<br>Request for Supplementary Information adopted on 10.03.2022. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**Zepatier - elbasvir / grazoprevir - EMEA/H/C/004126/II/0033**<br>Merck Sharp & Dohme B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "Submission of the final report from study B20-146 listed as a category 3 study in the RMP. This is a non-imposed joint post-authorisation safety study to evaluate the risk of de novo hepatocellular carcinoma in patients with compensated cirrhosis treated with direct-acting antivirals for chronic hepatitis C (HCC De Novo PASS)."<br>Request for Supplementary Information adopted on 10.03.2022. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**WS2210**<br>**Dovato-EMEA/H/C/004909/WS2210/0028**<br>**Juluca-EMEA/H/C/004427/WS2210/0041**<br>**Tivicay-EMEA/H/C/002753/WS2210/0076** | Positive Opinion adopted by consensus on 10.03.2022. |

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| **Triumeq-**<br>**EMEA/H/C/002754/WS2210/0100**<br>ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Ingrid Wang, "Following the finalisation of procedure EMEA/H/C/WS1810 concerning submission of EuroSIDA (category 3 PASS) study, this Type II worksharing variation was proposed to address the removal of three important risks (Dolutegravir Hypersensitivity reactions, Hepatobiliary reactions and Serious rash) from all four dolutegravir-containing product EU-RMPs; Tivicay (dolutegravir), Triumeq (dolutegravir/abacavir/lamivudine), Dovato (dolutegravir/lamivudine) and Juluca (dolutegravir/rilpivirine) - i.e. deletion of safety concerns.<br>In addition, the MAH took the opportunity to propose a harmonisation of the risks across all four dolutegravir-containing product EU-RMPs and other minor updates (including study details and epidemiology data).<br>The requested worksharing procedure proposed amendments to the Risk Management Plan (RMP)."<br>Opinion adopted on 10.03.2022. | |
| PRAC Led<br>**WS2212**<br>**Effentora-**<br>**EMEA/H/C/000833/WS2212/0060**<br>Teva B.V., Lead Rapporteur: Janet Koenig, Lead PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of an updated RMP version 5.1 in order to reformat the RMP according to the revised guidance on GVP Module V (revision 2) and to implement PRAC comments arising from previous assessments as follows:<br>- Revision of the list of safety concerns;<br>- Implementation of key messages in educational materials adopted by PRAC for Instanyl;<br>- Revision of Annex 6 to include verbatim the text adopted by PRAC for Instanyl as presented in Annex 2 of the PRAC PSUSA AR;<br>- Revision of the use of digital access to educational material;<br>- Explanation of the role of the Health Products Regulatory Authority (HPRA)'s CAPA being no | Request for supplementary information adopted with a specific timetable. |

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| longer found to be a trigger of the current RMP update.<br>The 'additional risk minimisation measures' in the Annex II of the product information have been updated accordingly."<br>Request for Supplementary Information adopted on 10.03.2022. | |
| PRAC Led<br>**WS2214**<br>**Duloxetine Mylan-EMEA/H/C/003981/WS2214/0029**<br>Mylan Pharmaceuticals Limited, Generic, Generic of Cymbalta, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "To update the RMP in order to align with the originator. The MAH has taken the opportunity to amend the RMP template GVP Module V Rev.2, where required, and to achieve one RMP covering multiple different marketing authorisation procedures containing the same active substance for which Mylan has an approved RMP. The RMP is also updated with the results of a follow-up questionnaire pertaining to suicidality as recommended in the Renewal EMEA/H/C/003981/R/0021."<br>Opinion adopted on 10.03.2022. | Positive Opinion adopted by consensus on 10.03.2022. |
| PRAC Led<br>**WS2216**<br>**Exviera-EMEA/H/C/003837/WS2216/0052**<br>**Maviret-EMEA/H/C/004430/WS2216/0049**<br>**Viekirax-EMEA/H/C/003839/WS2216/0064**<br>AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "Submission of the final report from study B20-146 listed as a category 3 study in the RMP. This is a non-imposed joint post-authorisation safety study to evaluate the risk of de novo hepatocellular carcinoma in patients with compensated cirrhosis treated with direct-acting antivirals for chronic hepatitis C (HCC De Novo PASS)."<br>Request for Supplementary Information adopted on 10.03.2022. | Request for supplementary information adopted with a specific timetable. |
| PRAC Led<br>**WS2222** | Request for supplementary information adopted with a specific timetable. |

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| **Epclusa-**<br>**EMEA/H/C/004210/WS2222/0064**<br>**Harvoni-**<br>**EMEA/H/C/003850/WS2222/0104**<br>**Sovaldi-EMEA/H/C/002798/WS2222/0077**<br>**Vosevi-EMEA/H/C/004350/WS2222/0054**<br>Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "Submission of the final report from study B20-146 listed as a category 3 study in the RMP. This is a non-imposed joint post-authorisation safety study to evaluate the risk of de novo hepatocellular carcinoma in patients with compensated cirrhosis treated with direct-acting antivirals for chronic hepatitis C (HCC De Novo PASS)."<br>Request for Supplementary Information adopted on 10.03.2022. | |

### B.5.5. CHMP-CAT assessed procedures

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| **Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0048, ATMP**<br>Amgen Europe B.V., Rapporteur: Maija Tarkkanen, CHMP Coordinator: Johanna Lähteenvuo, "Update of section 4.4 of the SmPC in order to add a new warning about the potential risk of hepatic haemorrhage with the transcutaneous intrahepatic route of administration of talimogene laherparepvec. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."<br>Opinion adopted on 24.03.2022, 18.03.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Tecartus - brexucabtagene autoleucel - EMEA/H/C/005102/II/0016, Orphan, ATMP**<br>Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus<br>Opinion adopted on 24.03.2022, 18.03.2022.<br>Request for Supplementary Information adopted on 21.01.2022. | Positive Opinion adopted by consensus on 24.03.2022. |
| **Zolgensma - onasemnogene abeparvovec - EMEA/H/C/004750/II/0020/G, Orphan, ATMP**<br>Novartis Gene Therapies EU Limited, Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege | Request for supplementary information adopted with a specific timetable. |

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| Request for Supplementary Information adopted on 18.03.2022, 10.12.2021. | |
| **Zolgensma - onasemnogene abeparvovec - EMEA/H/C/004750/II/0024, Orphan, ATMP**<br>Novartis Gene Therapies EU Limited, Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege,<br>Request for Supplementary Information adopted on 18.03.2022. | Request for supplementary information adopted with a specific timetable. |

### B.5.6. CHMP-PRAC-CAT assessed procedures

### B.5.7. PRAC assessed ATMP procedures

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| **Strimvelis - autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - EMEA/H/C/003854/II/0033, Orphan, ATMP**<br>Orchard Therapeutics (Netherlands) BV, Rapporteur: Sol Ruiz, CHMP Coordinator: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst, "Submission of the final report from study STRIM-001 "Evaluation of referring healthcare providers' and parents'/carers' understanding of specific risks associated with Strimvelis treatment" listed as a category 3 study in the RMP. The RMP version 6.1 has also been submitted."<br>Request for Supplementary Information adopted on 18.03.2022. | Request for supplementary information adopted with a specific timetable. |

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

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| **WS2171**<br>**Glyxambi-**<br>**EMEA/H/C/003833/WS2171/0040**<br>**Synjardy-**<br>**EMEA/H/C/003770/WS2171/0058**<br>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. | Positive Opinion adopted by consensus on 24.03.2022. |

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| In addition, the following ADR have been updated in section 4.8:<br>- for Glyxambi: 'Necrotising fasciitis of the perineum (Fournier´s gangrene)' from 'not known' to 'rare'; 'Volume depletion', to add a footnote to indicate that studies with empagliflozin in patients with heart failure showed a higher frequency of volume depletion ("very common") in patients with heart failure where half of the patients had type 2 diabetes mellitus.<br>- for Synjardy: 'Necrotising fasciitis of the perineum (Fournier´s gangrene)' from 'not known' to 'rare'; 'Angioedema' from 'not known' to 'uncommon'; 'Volume depletion', to add a footnote to indicate that studies with empagliflozin in patients with heart failure showed a higher frequency of volume depletion ("very common") in patients with heart failure where half of the patients had type 2 diabetes mellitus."<br>Opinion adopted on 24.03.2022.<br>Request for Supplementary Information adopted on 03.02.2022, 02.12.2021. | |
| **WS2220/G**<br>**Cymbalta-**<br>**EMEA/H/C/000572/WS2220/0088/G**<br>**Duloxetine Lilly-**<br>**EMEA/H/C/004000/WS2220/0025/G**<br>**Yentreve-**<br>**EMEA/H/C/000545/WS2220/0073/G**<br>Eli Lilly Nederland B.V., Duplicate, Duplicate of Ariclaim (SRD), Yentreve, Lead Rapporteur: Maria Concepcion Prieto Yerro<br>Opinion adopted on 10.03.2022. | Positive Opinion adopted by consensus on 10.03.2022. |
| **WS2221/G**<br>**Eucreas-**<br>**EMEA/H/C/000807/WS2221/0093/G**<br>**Galvus-**<br>**EMEA/H/C/000771/WS2221/0074/G**<br>**Icandra-**<br>**EMEA/H/C/001050/WS2221/0096/G**<br>**Jalra-**<br>**EMEA/H/C/001048/WS2221/0076/G**<br>**Xiliarx-**<br>**EMEA/H/C/001051/WS2221/0074/G**<br>**Zomarist-**<br>**EMEA/H/C/001049/WS2221/0095/G**<br>Novartis Europharm Limited, Lead Rapporteur: | Positive Opinion adopted by consensus on 17.03.2022. |

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| Kristina Dunder<br>Opinion adopted on 17.03.2022. | |
| **WS2228**<br>**Eucreas-**<br>**EMEA/H/C/000807/WS2228/0095**<br>**Icandra-**<br>**EMEA/H/C/001050/WS2228/0098**<br>**Zomarist-**<br>**EMEA/H/C/001049/WS2228/0097**<br>Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder,<br>Opinion adopted on 24.03.2022. | Positive Opinion adopted by consensus on 24.03.2022. |

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

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| **WS2120**<br>**Nuwiq-EMEA/H/C/002813/WS2120/0045**<br>**Vihuma-**<br>**EMEA/H/C/004459/WS2120/0027**<br>Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 16.12.2021, 02.09.2021.<br>Withdrawal request submitted on 09.03.2022. | The MAH withdrew the procedure on 09.03.2022. |
| **Feraccru - ferric maltol -**<br>**EMEA/H/C/002733/II/0033**<br>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."<br>Request for Supplementary Information adopted on 03.02.2022, 21.10.2021, 22.07.2021.<br>Withdrawal request submitted on 01.03.2022. | The MAH withdrew the procedure on 01.03.2022. |

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

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| **Uptravi - selexipag - EMEA/H/C/003774/II/0034**<br>Janssen-Cilag International N.V., Rapporteur: Martina Weise, PRAC Rapporteur: Nathalie Gault, "Update of section 4.8 of the SmPC to add 'dyspepsia' as a new ADR with frequency 'common', and to include further information on the frequency of 'dyspepsia' and 'anaemia' specific to initial 2-step triple combination therapy, based on the studies AC-065A308 (TRITON) and AC-065A404 (TRACE). AC-065A308 (TRITON) study was a randomized, double-blind, placebo-controlled, parallel-group, Phase 3b, efficacy and safety study comparing triple oral combination therapy (selexipag, macitentan, tadalafil) with double oral combination therapy (placebo, macitentan, tadalafil) in newly diagnosed, treatment-naïve participants with PAH. The AC-065A404 (TRACE) study was a randomized, double-blind, placebo-controlled, parallel-group, exploratory Phase 4 study in participants with PAH to assess the effect of selexipag on daily life physical activity and participant's self-reported symptoms and their impacts. The package leaflet is updated accordingly. A revised RMP version 9.2 was provided as part of the application."<br>Request for Supplementary Information adopted on 02.12.2021. | Request by the applicant for an extension to the clock stop to respond to the RSI adopted in December 2021.<br><br>The CHMP agreed to the request by the applicant. |

### B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

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| **enalapril maleate ph. eur. - EMEA/H/C/005731, PUMA**<br>treatment of heart failure in children from birth to less than 18 years. | |
| **eculizumab - EMEA/H/C/005652**<br>treatment of paroxysmal nocturnal haemoglobinuria | |
| **dabigatran etexilate - EMEA/H/C/006023**<br>Prevention of venous thromboembolic events | |
| **tixagevimab / cilgavimab - EMEA/H/C/005788**<br>prophylaxis of COVID-19 in adults 18 years of | See also 3.1 |

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| age and older | |
| **etranacogene dezaparvovec - EMEA/H/C/004827, Orphan, ATMP**<br>CSL Behring GmbH, treatment of adults with Haemophilia B (congenital Factor IX deficiency) and with a preexisting neutralising anti-AAV5 antibody titre below 1:700 to reduce the frequency of bleeding episodes and the need for Factor IX replacement therapy | **Accelerated review** |
| **tislelizumab - EMEA/H/C/005919, Orphan**<br>Novartis Europharm Limited, treatment of adult patients with unresectable, recurrent, locally advanced or metastatic oesophageal squamous cell carcinoma after prior chemotherapy | |
| **raltegravir potassium - EMEA/H/C/005813**<br>treatment of human immunodeficiency virus (HIV-1) | |
| **tislelizumab - EMEA/H/C/005542**<br>treatment of locally advanced or metastatic non-squamous non-small cell lung cancer in adults, treatment of locally advanced or metastatic squamous non-small cell lung cancer in adults, locally advanced or metastatic non-small cell lung cancer after prior chemotherapy in adults | |
| **ivosidenib - EMEA/H/C/005936, Orphan**<br>Les Laboratoires Servier, treatment of acute myeloid leukaemia and treatment of metastatic cholangiocarcinoma | |
| **tremelimumab - EMEA/H/C/006016, Orphan**<br>AstraZeneca AB, For use in combination with durvalumab for the treatment of adults with unresectable hepatocellular carcinoma. | |

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

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| **Refixia - nonacog beta pegol - EMEA/H/C/004178/X/0027/G**<br>Novo Nordisk A/S, Rapporteur: Andrea Laslop"Extension application to introduce a new strength (3000 IU Powder and solvent for solution for injection). The extension application is grouped with a type II variation (B.II.d.1.e) . Sections 1, 2, 5.3, 6.3, 6.6 and 8 of the SmPC, | |

the Labelling and Package Leaflet are updated."

**Tenkasi - oritavancin - EMEA/H/C/003785/X/0036**
Menarini International Operations Luxembourg S.A., Rapporteur: Janet Koenig, PRAC Rapporteur: Adam Przybylkowski, "Extension application to add a new strength of 1200 mg for powder for concentrate for solution for infusion. The RMP (version 4) is updated in accordance."

**Ultomiris - ravulizumab - EMEA/H/C/004954/X/0027/G**
Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Kimmo Jaakkola, "Extension application to introduce a new pharmaceutical form (solution for injection) associated with new strength (245 mg) and route of administration (subcutaneous use), grouped with a type II variation (C.I.4) to align the Summary of product characteristics and Labelling of Ultomiris intravenous formulation (IV) with the proposed Ultomiris subcutaneous formulation (SC).
The RMP (version 5.0) is updated in accordance."

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

**vutrisiran - EMEA/H/C/005852, Orphan**
Alnylam Netherlands B.V., treatment of hereditary transthyretin-mediated amyloidosis
List of Questions adopted on 27.01.2022.

**Calquence - acalabrutinib - EMEA/H/C/005299/X/0009/G**
AstraZeneca AB, Rapporteur: Filip Josephson, PRAC Rapporteur: Željana Margan Koletić, "Extension application to introduce a new pharmaceutical form, film-coated tablet.
A.6 - To change the ATC Code of acalabrutinib from L01XE51 to L01EL02."
List of Questions adopted on 24.02.2022.

**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).
List of Questions adopted on 11.11.2021.

**lutetium (177lu) chloride - EMEA/H/C/005859**
is a radiopharmaceutical precursor, and it is not intended for direct use in patients. It is to be used only for the radiolabelling of carrier molecules that have been specifically developed and authorised for radiolabelling with Lutetium (177Lu) chloride.
List of Questions adopted on 16.12.2021.

**voclosporin - EMEA/H/C/005256**
is indicated in combination with background immunosuppressive therapies for the treatment of adult patients with class III, IV or V (including mixed class III/V and IV/V) lupus nephritis (LN).
List of Questions adopted on 11.11.2021.

**octreotide - EMEA/H/C/005826, Orphan**
FGK Representative Service GmbH, treatment of acromegaly
List of Questions adopted on 16.12.2021.

**fosdenopterin - EMEA/H/C/005378, Orphan**
Comharsa Life Sciences Ltd, treatment of molybdenum cofactor deficiency type A
List of Questions adopted on 22.02.2022.

**relatlimab / nivolumab - EMEA/H/C/005481**
indicated for the first-line treatment of advanced (unresectable or metastatic) melanoma in adults and adolescents (12 years and older and weighing at least 40 kg).
List of Questions adopted on 27.01.2022.

**pemetrexed - EMEA/H/C/005848**
treatment of malignant pleural mesothelioma and non-small cell lung cancer
List of Questions adopted on 16.12.2021.

**thalidomide - EMEA/H/C/005715**
treatment of multiple myeloma
List of Questions adopted on 16.09.2021.

**faricimab - EMEA/H/C/005642**
treatment of neovascular (wet) age-related macular degeneration (nAMD) and visual impairment due to diabetic macular oedema (DME)
List of Questions adopted on 14.10.2021.

**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.
List of Questions adopted on 24.02.2022.

**olipudase alfa - EMEA/H/C/004850, Orphan**
Genzyme Europe BV, treatment of non-Central Nervous System (CNS) manifestations of Acid Sphingomyelinase Deficiency (ASMD) in paediatric and adult patients.
Disease-modifying enzyme replacement therapy for long-term treatment of non-Central Nervous System
List of Questions adopted on 22.02.2022.

### 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

**AYVAKYT - avapritinib - EMEA/H/C/005208/R/0017, Orphan**
Blueprint Medicines (Netherlands) B.V.,
Rapporteur: Blanca Garcia-Ochoa, PRAC
Rapporteur: Menno van der Elst

**MINJUVI - tafasitamab - EMEA/H/C/005436/R/0003, Orphan**
Incyte Biosciences Distribution B.V.,
Rapporteur: Thalia Marie Estrup Blicher, Co-Rapporteur: Alexandre Moreau, PRAC
Rapporteur: Annika Folin

**VITRAKVI - larotrectinib - EMEA/H/C/004919/R/0024**
Bayer AG, Rapporteur: Filip Josephson, PRAC
Rapporteur: Rugile Pilviniene

### 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

**Veklury - remdesivir -**
**EMEA/H/C/005622/II/0035/G**
Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, PRAC Rapporteur: Eva Jirsová,
"Grouped application of two extensions of indication to include:
- treatment of paediatric patients (at least 4 weeks of age and weighing at least 3 kg) with pneumonia requiring supplemental oxygen (low- or high-flow oxygen) or other non-invasive ventilation at start of treatment, based on interim results from study GS-US-540-5823; a phase 2/3 single-arm, open-label study to evaluate the safety, tolerability, pharmacokinetics, and efficacy of Remdesivir in participants from birth to <18 years of age with COVID-19;
- treatment of paediatric patients (weighing at least 40 kg) who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19, based on data from 8 adolescent patients who were included in study GS-US-540-9012, which was initially assessed by the CHMP as part of procedure II/16 (extension of indication to include treatment of adults).
As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet as well as the instructions for healthcare professionals have been updated accordingly. Version 3.2 of the RMP has also been submitted."

### B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

**Benepali - etanercept -**
**EMEA/H/C/004007/II/0063/G**
Samsung Bioepis NL B.V., Rapporteur: Andrea Laslop

**Benlysta - belimumab -**
**EMEA/H/C/002015/II/0104**
GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder

**COMIRNATY - tozinameran -**
**EMEA/H/C/005735/II/0116/G**
BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson

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| **COMIRNATY - tozinameran - EMEA/H/C/005735/II/0120/G**<br>BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson | |
| **COMIRNATY - tozinameran - EMEA/H/C/005735/II/0121/G**<br>BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson | See also B.5.1 |
| **Darzalex - daratumumab - EMEA/H/C/004077/II/0059/G, Orphan**<br>Janssen-Cilag International N.V., Rapporteur: Thalia Marie Estrup Blicher | |
| **Elaprase - idursulfase - EMEA/H/C/000700/II/0098/G**<br>Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege | |
| **Fasturtec - rasburicase - EMEA/H/C/000331/II/0063/G**<br>sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege | |
| **IMCIVREE - setmelanotide - EMEA/H/C/005089/II/0005/G, Orphan**<br>Rhythm Pharmaceuticals Netherlands B.V., Rapporteur: Karin Janssen van Doorn | |
| **Increlex - mecasermin - EMEA/H/C/000704/II/0076**<br>Ipsen Pharma, Rapporteur: Outi Mäki-Ikola | |
| **Lynparza - olaparib - EMEA/H/C/003726/II/0055/G**<br>AstraZeneca AB, Rapporteur: Alexandre Moreau | |
| **Ngenla - somatrogon - EMEA/H/C/005633/II/0001/G, Orphan**<br>Pfizer Europe MA EEIG, Rapporteur: Peter Kiely | |
| **NUVAXOVID - sars-cov-2, spike protein, recombinant, expressed in sf9 cells derived from spodoptera frugiperda - EMEA/H/C/005808/II/0004**<br>Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege | See also B.5.1 |
| **NUVAXOVID - sars-cov-2, spike protein, recombinant, expressed in sf9 cells derived from spodoptera frugiperda - EMEA/H/C/005808/II/0007**<br>Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege | |

**Oncaspar - pegaspargase -**
**EMEA/H/C/003789/II/0045/G**
Les Laboratoires Servier, Rapporteur: Alexandre Moreau

**Privigen - human normal immunoglobulin -**
**EMEA/H/C/000831/II/0185**
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

**ReFacto AF - moroctocog alfa -**
**EMEA/H/C/000232/II/0163/G**
Pfizer Europe MA EEIG, Rapporteur: Thalia Marie Estrup Blicher

**Rixubis - nonacog gamma -**
**EMEA/H/C/003771/II/0044**
Baxalta Innovations GmbH, Rapporteur: Andrea Laslop

**Shingrix - herpes zoster vaccine (recombinant, adjuvanted) -**
**EMEA/H/C/004336/II/0053**
GlaxoSmithkline Biologicals SA, Rapporteur: Christophe Focke

**Sivextro - tedizolid phosphate -**
**EMEA/H/C/002846/II/0046**
Merck Sharp & Dohme B.V., Rapporteur: Bruno Sepodes

**Voraxaze - glucarpidase -**
**EMEA/H/C/005467/II/0002, Orphan**
SERB S.A.S., Rapporteur: Ondřej Slanař

**WS2231**
**Ambirix-**
**EMEA/H/C/000426/WS2231/0121**
**Twinrix Adult-**
**EMEA/H/C/000112/WS2231/0156**
**Twinrix Paediatric-**
**EMEA/H/C/000129/WS2231/0157**
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke

**WS2232/G**
**Infanrix hexa-**
**EMEA/H/C/000296/WS2232/0314/G**
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke

**WS2252**
**Prolia-EMEA/H/C/001120/WS2252/0096**
**XGEVA-EMEA/H/C/002173/WS2252/0080**
Amgen Europe B.V., Lead Rapporteur: Kristina

Dunder

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

**Adakveo - crizanlizumab - EMEA/H/C/004874/II/0007, Orphan**
Novartis Europharm Limited, Rapporteur: Daniela Philadelphy, "Update of section 5.2 of the SmPC in order to update pharmacokinetic information based on the results from PK re-analysis. In addition, the MAH took the opportunity to introduce minor editorial changes to the SmPC."

**Avonex - interferon beta-1a - EMEA/H/C/000102/II/0192**
Biogen Netherlands B.V., Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 4.4 of the SmPC in order to add a new warning regarding the risk of injection site necrosis based on post-marketing experience. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet."

**Biktarvy - bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449/II/0047**
Gilead Sciences Ireland UC, Rapporteur: Jean-Michel Race, "Update of sections 4.8 and 5.1 of the SmPC in order to include efficacy and safety data for antiretroviral therapy (ART)-naive adults based on final results from interventional studies GS-US-380-1489 (A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of GS-9883/Emtricitabine/Tenofovir Alafenamide Versus Abacavir /Dolutegravir /Lamivudine in HIV-1 Infected, Antiretroviral Treatment-Naive Adults) and GS-US-380-1490 (A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of GS-9883/Emtricitabine/Tenofovir Alafenamide Versus Dolutegravir + Emtricitabine/Tenofovir Alafenamide in HIV-1 Infected, Antiretroviral Treatment-Naïve Adults).
In addition, the MAH took this opportunity to introduce some minor administrative updates."

**IMCIVREE - setmelanotide - EMEA/H/C/005089/II/0006, Orphan**

Rhythm Pharmaceuticals Netherlands B.V., Rapporteur: Karin Janssen van Doorn, "Submission of the final report from study RM-493-011 "Setmelanotide (RM-493) Treatment Trial in Patients with Rare Genetic Disorders of Obesity". This is a Phase 2, open-label, uncontrolled, non-randomized study with an additional long-term safety extension. The primary objective was to assess changes in body weight within each patient population with rare genetic disorders of obesity (POMC, LEPR, BBS and AS) following 3-months of setmelanotide treatment."

**INREBIC - fedratinib - EMEA/H/C/005026/II/0010/G, Orphan**

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.4 of the SmPC in order to add new warnings on major adverse cardiac events (MACE), thrombosis and secondary malignancies. The updates pertain to three signals, assessed by the FDA, which were identified with another JAK inhibitor (tofacitinib) indicated in rheumatoid arthritis; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

**JEMPERLI - dostarlimab - EMEA/H/C/005204/II/0009**

GlaxoSmithKline (Ireland) Limited, Rapporteur: Blanca Garcia-Ochoa, "Type II (C.I.4) - To update section 6.6 of the SmPC to include the requirement to use an in-line filter during finished product administration, to amend the administration equipment compatibilities and to provide additional administration dilution instructions. The Package Leaflet is updated accordingly.
In addition, the Applicant took the opportunity to correct a typographical error from SmPC section 5.1 Pharmacodynamic properties."

**Luminity - perflutren - EMEA/H/C/000654/II/0039**

Lantheus EU Limited, Rapporteur: Peter Kiely, "Update of section 4.4 of the SmPC in order to add a new warning on sickle cell anaemia, and update of section 4.8 of the SmPC to include the new ADRs Kounis Syndrome, sickle cell anaemia and vaso-occlusive crisis based on reports in the

post-marketing setting. The Package Leaflet is updated accordingly."

**Orladeyo - berotralstat - EMEA/H/C/005138/II/0006**

BioCryst Ireland Limited, Rapporteur: Peter Kiely, "Update of sections 4.4 and 4.5 of the SmPC in order to remove the warning for women of childbearing potential and amend drug-drug interaction information with desogestrel based on final results from study BCX7353-111; this is a phase 1 drug interaction study to evaluate the effects of berotralstat on the pharmacokinetics of a combination oral contraceptive, desogestrel with ethinyl estradiol; the Package Leaflet is updated accordingly."

**Samsca - tolvaptan - EMEA/H/C/000980/II/0046/G**

Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Armando Genazzani, "Update of section 4.5 of the SmPC in order to include information on the transporter substrates P-glycoprotein, BCRP and OCT1 upon request by PRAC following the assessment of PSUSA/00002994/202105 based on final results from the drug-drug interaction studies 156-201-00233 and 156-201-00234 (to align with the Jinarc PI); the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

**Spikevax - elasomeran - EMEA/H/C/005791/II/0057**

Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, "Update of section 4.2 of the Spikevax SmPC to include a 50 µg booster dose for adolescents 12 to 18 years of age, based on the extrapolation of safety and efficacy data from young adults (18 to 24 years of age). The package leaflet is updated accordingly."

**Spikevax - elasomeran - EMEA/H/C/005791/II/0059**

Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, "To update Annex IIE of the Spikevax Product Information to delete SOB 001 & SOB 002. The latest data to complete the characterisation of the active substance and finished product manufacturing processes (SOB

001) and to confirm the consistency of the active substance and finished product manufacturing process (initial and final scales) (SOB 002) have already been submitted and assessed in the context of previous procedures and are now considered fulfilled."

**Tasigna - nilotinib - EMEA/H/C/000798/II/0115/G**

Novartis Europharm Limited, Rapporteur: Thalia Marie Estrup Blicher, "C.I.4: Update of section 4.8 of the SmPC in order to update the ADRs frequency category based on pooled safety data from 13 interventional clinical studies, 5 of which have not been previously assessed (CAMN107A2303 - 120 months data; CAMN107A2404; CAMN107E2401; CAMN107ECN02 and CAMN107EIC01).
In addition, the MAH took the opportunity to merge the current 2 SmPCs (one for 150 mg and one for 50 mg/200 mg) into one single SmPC, by including all information from the 150 mg SmPC into the 50 mg/200 mg SmPC; and to implement editorial changes. The Package Leaflet is proposed to be updated accordingly.
A.6: Update of nilotinib ATC code based on the last update of the WHO ATC index."

**Tygacil - tigecycline - EMEA/H/C/000644/II/0121**

Pfizer Europe MA EEIG, Rapporteur: Blanca Garcia-Ochoa, "Update of section 5.1 of the SmPC in order to reflect updated breakpoint tables regarding antimicrobial susceptibility testing (EUCAST).
In addition, the MAH is taking the opportunity to update section 4.6 of the SmPC to remove reference to "pharmacodynamic/toxicological" data and update the contact details of the local representatives in the Package Leaflet."

**Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0052**

AstraZeneca AB, Rapporteur: Sol Ruiz, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to introduce a booster dose of Vaxzevria (homologous or heterologous) based on interim immunogenicity and safety data from the pivotal study D7220C00001, a partially double-blinded, randomised, multinational, active-controlled phase II/III clinical study and

supportive literature evidence from studies COV001, RHH-001, COV-BOOST and Com-COV studies. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes/corrections throughout the product information."

**Veltassa - patiromer - EMEA/H/C/004180/II/0029**

Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Jayne Crowe, "Update of sections 4.2 and 4.5 of the SmPC in order to introduce new drug-drug interaction information based on results from four in vitro studies: RLY-TR-0174, titled "In Vitro Evaluation of Potential RLY5016S and Immunosuppressant Drug-Drug Interactions"; RLY-TR-0184 (titled "In Vitro Evaluation of Potential Drug-Drug Interactions Between Patiromer and Sevelamer Hydrochloride"); "In Vitro Evaluation of Drug-Drug Interactions of commonly prescribed renal and cardiovascular Drugs with Patiromer DS" and "Drug-drug interactions of commonly prescribed renal and cardiovascular Drugs with Patiromer DS in a simulated GI tract passage study". The Package Leaflet is updated accordingly."

**Vidaza - azacitidine - EMEA/H/C/000978/II/0057**

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.2 of the SmPC in order to include a statement advising health care professionals not to interchange azacitidine formulations (injectable versus oral), and update section 4.6 of the SmPC to revise the recommended duration of contraception use for women and men. The Package Leaflet is updated accordingly."

**VPRIV - velaglucerase alfa - EMEA/H/C/001249/II/0054, Orphan**

Takeda Pharmaceuticals International AG, Rapporteur: Martina Weise, "Submission of the final report from study SHP-GCB-402: a multicentre, open-label, single-arm, phase 4 study designed to prospectively evaluate the effects of VPRIV on bone-related pathology in treatment-naïve subjects with type 1 Gaucher disease."

**Vyxeos liposomal - daunorubicin / cytarabine - EMEA/H/C/004282/II/0030, Orphan**

Jazz Pharmaceuticals Ireland Limited, Rapporteur: Johanna Lähteenvuo, "Update of sections 4.2, 4.4 and 5.2 of the SmPC to amend information and delete the existing warning for patients with renal impairment based on the final results from study CPX351-102 (PMR2): a phase 1, open-label, PK and safety study to evaluate the potential impact of renal impairment on the pharmacokinetics and safety of CPX-351 (Daunorubicin and Cytarabine) liposome for injection treatment in adult patients with hematologic malignancies."

**Xevudy - sotrovimab - EMEA/H/C/005676/II/0001/G**

Glaxosmithkline Trading Services Limited, Rapporteur: Thalia Marie Estrup Blicher, "Type II (C.I.4) - Update of section 5.1 of the SmPC to include new virology data based on the results from pharmacology studies, describing the conservation of the epitope as well as assessing any susceptibility changes due to either individual amino acid substitutions or emerging variants, including data against Omicron BA.1, BA.2 and BA.3. In addition, the MAH took the opportunity to implement editorial changes in sections 5.1, 6.6 and 9 of the SmPC. The package leaflet is updated accordingly. Type IA (A.6) - To include the ATC Code J06BD05 in section 5.1 of the Summary of Product Characteristics (SmPC)."

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

Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.8 and 5.1 of the SmPC in order to add safety and efficacy data based on the final CSR from the category 3 study GENA-21b; a prospective, open-label, multicentre phase 3b study to assess the efficacy and safety of personalized prophylaxis with Human-cl rhFVIII in previously treated adult patients with severe haemophilia A. Further, upon request by the CHMP following the assessment of study GENA-05 (P46 013 and P46 014), the MAH is updating the numbers of

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| evaluated subjects in SmPC section 4.8 and is removing of the sentence "A prospective open-label clinical study in PUPs with severe haemophilia A (<1% FVIII:C) is ongoing" in section 5.1 of the SmPC. The Package Leaflet is updated accordingly." | |
| **WS2250**<br>**Prezista-**<br>**EMEA/H/C/000707/WS2250/0116**<br>**Rezolsta-**<br>**EMEA/H/C/002819/WS2250/0046**<br>**Symtuza-**<br>**EMEA/H/C/004391/WS2250/0043**<br>Janssen-Cilag International N.V., Lead Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.3 and 4.5 of the SmPC in order to update the safety information based on final results from study TMC114FD1HTX1002; this is an interventional phase 1, 2-Panel, Fixed-Sequence, Open-Label Single-Center Study to Assess the Effect of Single and Multiple Doses of Darunavir in Combination with Cobicistat or Ritonavir on the Pharmacokinetics of Single Dose Dabigatran Etexilate in Healthy Participants. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce editorial changes in order to update the contact details of the local representatives in the Package Leaflet." | |
| **WS2253**<br>**Eucreas-**<br>**EMEA/H/C/000807/WS2253/0096**<br>**Galvus-EMEA/H/C/000771/WS2253/0076**<br>**Icandra-**<br>**EMEA/H/C/001050/WS2253/0100**<br>**Jalra-EMEA/H/C/001048/WS2253/0078**<br>**Xiliarx-EMEA/H/C/001051/WS2253/0077**<br>**Zomarist-**<br>**EMEA/H/C/001049/WS2253/0098**<br>Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Annika Folin, "Update of section 4.8 of the SmPC in order to add the new ADRs 'cutaneous vasculitis'." | |

**B.6.10. CHMP-PRAC assessed procedures**

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| **Apexxnar - pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) -** | |

**EMEA/H/C/005451/II/0002**
Pfizer Europe MA EEIG, Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Jean-Michel Dogné, "Update of sections 4.5, 4.8 and 5.1 of the SmPC to add information regarding the co-administration of Apexxnar with seasonal quadrivalent influenza vaccine (QIV) based on final study results from study B7471004, "A Phase 3, Randomized, Double-Blind Trial to Evaluate the Safety and Immunogenicity of a 20 valent Pneumococcal Conjugate Vaccine (20vPnC) When Coadministered with Seasonal Inactivated Influenza Vaccine (SIIV) in Adults ≥65 Years of Age." listed as a category 3 study in the RMP.
The Package Leaflet is updated accordingly.
The updated RMP version 1.1 has also been submitted."

**Jorveza - budesonide - EMEA/H/C/004655/II/0015, Orphan**
Dr. Falk Pharma GmbH, Rapporteur: Martina Weise, PRAC Rapporteur: Zane Neikena, "Update of section 4.8 of the SmPC in order to update the list of adverse reactions based on final results from the long-term maintenance study BUL-2/EER; this is a double-blind, randomized, placebo-controlled, phase III study on the efficacy and tolerability of a 48-week treatment with two different doses of budesonide effervescent tablets vs. placebo for maintenance of clinico-pathological remission in adult patients with eosinophilic esophagitis. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 3.0 has also been submitted. The MAH also submitted the final report of study BUL-6/BIO, which was previously assessed within the scope of extension EMEA/H/C/004655/X/0007/G as applicant's response to CHMP Day 120 List of Questions."

**Neofordex - dexamethasone - EMEA/H/C/004071/II/0017/G**
Laboratoires CTRS, Rapporteur: Ondřej Slanař, PRAC Rapporteur: Tiphaine Vaillant"1. C.I.11.z (Type IB): To update the RMP for Neofordex to version 4.3 with a completion of category 3 activity 'Removal of the score line for sub-

division of the 40 mg tablet, and consequent deletion of the 20 mg posology' and to include the Direct Healthcare Professional Communication (DHPC);"

### B.6.11. PRAC assessed procedures

PRAC Led

**HEPLISAV B - hepatitis B surface antigen - EMEA/H/C/005063/II/0014**

Dynavax GmbH, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from study (HBV25) listed as a category 3 PASS study in the RMP. This is a post-marketing observational surveillance study comparing the occurrence of Acute Myocardial Infarction (AMI) in recipients of HEPLISAV-B with recipients of another hepatitis B vaccine. As a consequence, the RMP version 1.2 has also been submitted, in which the MAH proposes the removal of AMI as an important potential risk from the list of safety concerns."

PRAC Led

**Lemtrada - alemtuzumab - EMEA/H/C/003718/II/0041**

Sanofi Belgium, Duplicate, Duplicate of Lemtrada (WD), PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Thalia Marie Estrup Blicher, "Submission of an updated RMP version 10.0 in order to include the new important identified risk "Autoimmune Encephalitis" and to introduce changes in accordance to the rapporteurs' requests received as part of procedure EMEA/H/C/003718/II/0038."

PRAC Led

**Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0090**

Genzyme Europe BV, PRAC Rapporteur: Nathalie Gault, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final report from non-interventional PASS Pompe Safety Sub-Registry - AGLU06909/LTS13930. This final study report is submitted to address the assessment report conclusion of the Pompe registry report 2020 (MEA024.15 and MEA025.15 Annual Pompe Registry Report 2020)."

PRAC Led

**Uptravi - selexipag -**
**EMEA/H/C/003774/II/0035**
Janssen-Cilag International N.V., PRAC Rapporteur: Nathalie Gault, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 9.3 in order to include the amendment of the ongoing EXPOSURE study protocol, to add the EXTRACT study (67896049PAH0002) as an additional pharmacovigilance activity (PASS) and to include the update of the PRAC-approved EDUCATE PASS protocol (assessed in EMEA/H/C/003774/MEA/003.4)."

### B.6.12. CHMP-CAT assessed procedures

**Imlygic - talimogene laherparepvec -**
**EMEA/H/C/002771/II/0050, ATMP**
Amgen Europe B.V., Rapporteur: Maija Tarkkanen, CHMP Coordinator: Johanna Lähteenvuo

**Imlygic - talimogene laherparepvec -**
**EMEA/H/C/002771/II/0052/G, ATMP**
Amgen Europe B.V., Rapporteur: Maija Tarkkanen, CHMP Coordinator: Johanna Lähteenvuo

**Kymriah - tisagenlecleucel -**
**EMEA/H/C/004090/II/0053, Orphan, ATMP**
Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang, "Submission of the final report from study CCTL019H2301 (BELINDA) listed as an obligation in the Annex II of the Product Information. This is a randomized open-label parallel-group multicentre Phase III trial to evaluate the efficacy and safety of tisagenlecleucel in adult patients with relapsed or refractory B-cell aggressive NHL after failure of rituximab and anthracycline containing first-line immune-chemotherapy. The Annex II is updated accordingly."

**WS2247**
**Tecartus-**
**EMEA/H/C/005102/WS2247/0020**
**Yescarta-**
**EMEA/H/C/004480/WS2247/0050**
Kite Pharma EU B.V., Lead Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan

Mueller-Berghaus

### B.6.13. CHMP-PRAC-CAT assessed procedures

### B.6.14. PRAC assessed ATMP procedures

PRAC Led
**Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0051, ATMP**
Amgen Europe B.V., PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from study 20180062; "Observational Research Study Report (ORSR)" listed as a category 3 study in the RMP. This is a multinational, non-interventional, cross-sectional survey study for the Patients aged ≥ 18 years who have received IMLYGIC at least once in the 3 months prior to completing the survey to evaluate the effectiveness of the patient-directed aRMMS. The primary objective of this study is to evaluate patients' knowledge levels of the key messages included in the IMLYGIC Patient Safety Brochure among patients who receive IMLYGIC."

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

**WS2227**
**Esperoct- EMEA/H/C/004883/WS2227/0011**
**NovoEight- EMEA/H/C/002719/WS2227/0040**
Novo Nordisk A/S, Lead Rapporteur: Jan Mueller-Berghaus

**WS2229/G**
**Efficib- EMEA/H/C/000896/WS2229/0105/G**
**Janumet- EMEA/H/C/000861/WS2229/0104/G**
**Ristfor- EMEA/H/C/001235/WS2229/0092/G**
**Velmetia- EMEA/H/C/000862/WS2229/0108/G**
Merck Sharp & Dohme B.V., Lead Rapporteur: Johann Lodewijk Hillege

**WS2237**
**Copalia HCT-**
**EMEA/H/C/001159/WS2237/0098**
**Dafiro HCT-**
**EMEA/H/C/001160/WS2237/0100**
**Exforge HCT-**
**EMEA/H/C/001068/WS2237/0097**
Novartis Europharm Limited, Lead Rapporteur: Thalia Marie Estrup Blicher, "To update sections 4.4 and 4.8 of the SmPC in line with assessment of a PSUSA/00001662/202101 procedure on hydrochlorothiazide/spironolactone regarding the risk of acute respiratory distress syndrome (ARDS) linked to hydrochlorothiazide. The Package Leaflet has been updated in accordance."

**WS2239/G**
**Hexacima-**
**EMEA/H/C/002702/WS2239/0128/G**
**Hexyon-**
**EMEA/H/C/002796/WS2239/0132/G**
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

**WS2240**
**HyQvia-EMEA/H/C/002491/WS2240/0077**
**Kiovig-EMEA/H/C/000628/WS2240/0116**
Baxalta Innovations GmbH, Lead Rapporteur: Jan Mueller-Berghaus

## 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. Timetables – 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 March 2022 CHMP plenary:

| | |
|---|---|
| ***Oncology*** | |
| Treatment of glioblastoma at first recurrence in combination with lomustine (SME) | The CHMP denied eligibility to PRIME and adopted the critical summary report. |
| ***Neurology*** | |
| Treatment of Amyotrophic Lateral Sclerosis (ALS) (SME) | The CHMP denied eligibility to PRIME and adopted the critical summary report. |

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

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