08 November 2021
EMA/CHMP/625918/2021
Human Medicines Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 08-11 November 2021

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

08 November 2021, 09:00 – 19:30, virtual meeting/ room 1C

09 November 2021, 08:30 – 19:30, virtual meeting/ room 1C

10 November 2021, 08:30 – 19:30, virtual meeting/ room 1C

11 November 2021, 08:30 – 17:00, virtual meeting/ room 1C

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 08-11 November 2021. See November 2021 CHMP minutes (to be published post December 2021 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 08-11 November 2021

1.3. Adoption of the minutes

CHMP minutes for 11-14 October 2021.

Minutes from PReparatory and Organisational Matters (PROM) meeting held on 03 November 2021.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. aducanumab - EMEA/H/C/005558

Alzheimer's disease

Scope: Oral explanation

Action: Oral explanation to be held on 09 November 2021 at 16:00

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

2.1.2. tepotinib - EMEA/H/C/005524

treatment of advanced non-small cell lung cancer

Scope: Oral explanation

Action: Oral explanation to be held on 09 November 2021 at 11:00

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

2.1.3. inebilizumab - Orphan - EMEA/H/C/005818

Viela Bio; indicated for the treatment of adults with neuromyelitis optica spectrum disorders

Scope: Possible oral explanation

Action: Possible oral explanation to be held on 09 November 2021 at 14:00

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

2.1.4. casirivimab / imdevimab - EMEA/H/C/005814

prevention and treatment of COVID-19

Scope: Possible oral explanation

Action: Possible oral explanation to be held on 08 November 2021 at 14:00

2.2. Re-examination procedure oral explanations

2.2.1. Nouryant - istradefylline - EMEA/H/C/005308

Kyowa Kirin Holdings B.V.; indicated as an adjunctive treatment to levodopa-based regimens in patients with Parkinson's disease

Scope: Oral explanation/Opinion

Action: Oral explanation to be held on 09 November 2021 at 09:00

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

Opinion adopted on 22.07.2021. List of Outstanding Issues adopted on 25.02.2021. List of Questions adopted on 30.04.2020.

See 3.5

2.2.2. Nexviadyme - avalglucosidase alfa - Orphan - EMEA/H/C/005501

Genzyme Europe BV; for long-term enzyme replacement therapy for the treatment of patients with Pompe disease.

Scope: Oral explanation/Opinion

Action: Oral explanation to be held on 08 November 2021 at 16:00

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

Opinion adopted on 23.07.2021. List of Outstanding Issues adopted on 20.05.2021. List of Questions adopted on 28.01.2021.

See 3.5

2.3. Post-authorisation procedure oral explanations

2.3.1. Ferriprox - deferiprone - EMEA/H/C/000236/X/0145

Chiesi Farmaceutici S.p.A.

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant

Scope: "Extension application to introduce a new pharmaceutical form (gastro-resistant tablets). The RMP (version 14.0) is updated in accordance."

Oral explanation

Action: Oral explanation to be held on 10 November 2021 at time 15:30

List of Outstanding Issues adopted on 14.10.2021, 24.06.2021, 25.02.2021. List of Questions adopted on 17.09.2020.

See 4.1

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. bevacizumab - EMEA/H/C/005433

indicated in adults for the treatment of neovascular macular degeneration associated with aging and diabetes.

Scope: Opinion

Action: For adoption

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

3.1.2. finerenone - EMEA/H/C/005200

delay progression of kidney disease, reduce the risk of cardiovascular mortality and morbidity

Scope: Opinion

Action: For adoption

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

3.1.3. sotorasib - EMEA/H/C/005522

treatment of locally advanced or metastatic non-small cell lung cancer

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 16.09.2021. List of Questions adopted on 20.05.2021.

3.1.4. regdanvimab - EMEA/H/C/005854

Treatment of COVID-19

Scope: Opinion

Action: For adoption

3.1.5. formoterol fumarate dihydrate / glycopyrronium / budesonide - EMEA/H/C/005311

maintenance treatment of chronic obstructive pulmonary disease (COPD)

Scope: Opinion

Action: For adoption

3.1.6. avacopan - Orphan - EMEA/H/C/005523

Vifor Fresenius Medical Care Renal Pharma France; Treatment of granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 14.10.2021, 22.07.2021. List of Questions adopted on 25.02.2021.

3.1.7. tecovirimat - EMEA/H/C/005248

treatment of orthopoxvirus disease

Scope: Opinion

Action: For adoption

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

3.1.8. glucarpidase - Orphan - EMEA/H/C/005467

Serb; treatment of patients at risk of methotrexate toxicity

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 16.09.2021, 24.06.2021. List of Questions adopted on 10.12.2020.

3.1.9. eptinezumab - EMEA/H/C/005287

Indicated for the prophylaxis of migraine in adults

Scope: Opinion

Action: For adoption

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

3.1.10. semaglutide - EMEA/H/C/005422

treatment for weight loss and weight maintenance

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 14.10.2021. List of Questions adopted on 20.05.2021.

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

3.2.1. pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - EMEA/H/C/005451

prevention of invasive disease and pneumonia caused by Streptococcus pneumoniae serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.07.2021.

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

prevention of dengue disease

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 24.06.2021.

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 Questions adopted on 22.07.2021.

3.2.4. lonapegsomatropin - Orphan - EMEA/H/C/005367

Ascendis Pharma Endocrinology Division A/S; Treatment of growth hormone deficiency

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 16.09.2021, 24.06.2021. List of Questions adopted on 28.01.2021.

3.2.5. somatrogon - Orphan - EMEA/H/C/005633

Pfizer Europe MA EEIG; indicated for the long-term treatment of paediatric patients with growth disturbance due to insufficient secretion of growth hormone.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 24.06.2021.

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

prevention of dengue disease

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 24.06.2021.

3.2.7. pegfilgrastim - EMEA/H/C/004780

treatiment of neutropenia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 17.09.2020.

3.2.8. eladocagene exuparvovec - Orphan - ATMP - EMEA/H/C/005352

PTC Therapeutics International Limited; treatment of aromatic L-amino aciddecarboxylase (AADC) deficiency

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 16.04.2021. List of Questions adopted on 20.05.2020.

3.2.9. linzagolix choline - EMEA/H/C/005442

for the management of heavy menstrual bleeding (HMB) associated with uterine fibroids

Scope: List of outstanding issues

Action: For adoption

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

3.2.10. rimegepant - EMEA/H/C/005725

management of migraine

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 24.06.2021.

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

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

treatment of diabetes mellitus

Scope: List of questions

Action: For adoption

3.3.2. asciminib - Orphan - EMEA/H/C/005605

Novartis Europharm Limited; treatment of Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP)

Scope: List of questions

Action: For adoption

3.3.3. mobocertinib - EMEA/H/C/005621

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

Scope: List of questions

Action: For adoption

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

treatment of bleeding episodes and for the prevention of bleeding

Scope: List of questions

Action: For adoption

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

treatment of diabetes mellitus

Scope: List of questions

Action: For adoption

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

Accelerated assessment

Immunocore Ireland Limited; treatment of uveal melanoma

Scope: List of questions

Action: For adoption

3.3.7. voclosporin - EMEA/H/C/005256

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

Scope: List of questions

Action: For adoption

3.3.8. mitapivat - Orphan - EMEA/H/C/005540

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

Scope: List of questions

Action: For adoption

3.3.9. ranibizumab - EMEA/H/C/005019

The treatment of neovascular (wet) age-related macular degeneration (AMD), visual impairment due to diabetic macular oedema (DME), proliferative diabetic retinopathy (PDR), visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO) and visual impairment due to choroidal neovascularisation (CNV)

Scope: List of questions

Action: For adoption

3.3.10. valoctocogene roxaparvovec - Orphan - ATMP - EMEA/H/C/005830

Accelerated assessment

BioMarin International Limited; treatment of severe haemophilia A

Scope: List of questions

Action: For information

3.3.11. surufatinib - EMEA/H/C/005728

treatment of progressive neuroendocrine tumours

Scope: List of questions

Action: For adoption

3.3.12. sorafenib - EMEA/H/C/005921

treatment of hepatocellular carcinoma and renal cell carcinoma

Scope: List of questions

Action: For adoption

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

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

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

Scope: Call for expression of interest for additional experts for the SAG-Oncology.

The list of experts will be adopted via written procedure.

Action: For information

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

3.4.2. melphalan flufenamide - Orphan - EMEA/H/C/005681

Oncopeptides AB; treatment of multiple myeloma

Scope: Letter from the applicant dated 04 November 2021 requesting an extension to the clock stop to respond to the list of questions adopted in September 2021.

Action: For adoption

List of questions adopted on 16.09.2021.

3.4.3. lenadogene nolparvovec - Orphan - ATMP - EMEA/H/C/005047

GenSight Biologics S.A.; treatment of vision loss due to Leber Hereditary Optic Neuropathy (LHON)

Scope: Letter from the applicant dated 20 October 2021 requesting an extension of clock-stop to respond to the list of questions adopted in February 2021.

Action: For information

List of Questions adopted on 25.02.2021.

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

3.5.1. Nouryant - istradefylline - EMEA/H/C/005308

Kyowa Kirin Holdings B.V.; indicated as an adjunctive treatment to levodopa-based regimens in patients with Parkinson's disease

Scope: Oral explanation/Opinion

Action: For adoption

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

Opinion adopted on 22.07.2021. List of Outstanding Issues adopted on 25.02.2021. List of Questions adopted on 30.04.2020.

See 2.2

3.5.2. Nexviadyme - avalglucosidase alfa - Orphan - EMEA/H/C/005501

Genzyme Europe BV; for long-term enzyme replacement therapy for the treatment of patients with Pompe disease.

Scope: Oral explanation/Opinion

Action: For adoption

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

Opinion adopted on 23.07.2021. List of Outstanding Issues adopted on 20.05.2021. List of Questions adopted on 28.01.2021.

See 2.2

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

4.1.1. Adynovi - rurioctocog alfa pegol - EMEA/H/C/004195/X/0018

Baxalta Innovations GmbH

Rapporteur: Andrea Laslop, PRAC Rapporteur: Menno van der Elst

Scope: "Extension application to add a new strength of 3000 IU for RURIOCTOCOG ALFA PEGOL powder and solvent for solution for injection, for intravenous use.
Furthermore, the MAH took the opportunity to include editorial changes to update the naming convention from BAX855 to rurioctocog alfa pegol throughout the section and removed the reference to Baxalta as well as update table numbering throughout the documents in module 3. Furthermore, changes omitted from the dossier following approval of variations EMEA/H/C/004195/IB/0004/G and EMEA/H/C/004195/IB/0015/G were also included."

Action: For adoption

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

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

sanofi-aventis groupe

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

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

Action: For adoption

List of Questions adopted on 22.07.2021.

4.1.3. Epclusa - sofosbuvir / velpatasvir - EMEA/H/C/004210/X/0056/G

Gilead Sciences Ireland UC

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

Scope: "Extension application to introduce a new pharmaceutical form (coated granules in sachet) associated with strengths 200 mg/50 mg and 150 mg/37.5 mg. The new presentations are indicated for the treatment of chronic hepatitis C virus (HCV) infection in patients 3 years of age and older. The extension application is grouped with a type II variation (C.I.6.a) to include paediatric use in patients 3 years of age and older to the existing presentations of the film-coated tablets. 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 7.1) is updated in accordance.
In addition, the MAH took the opportunity to implement minor updates and corrections throughout the Product Information."

Action: For adoption

List of Questions adopted on 22.07.2021.

4.1.4. Ferriprox - deferiprone - EMEA/H/C/000236/X/0145

Chiesi Farmaceutici S.p.A.

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant

Scope: "Extension application to introduce a new pharmaceutical form (gastro-resistant tablets). The RMP (version 14.0) is updated in accordance."

Action: For adoption

List of Outstanding Issues adopted on 14.10.2021, 24.06.2021, 25.02.2021. List of Questions adopted on 17.09.2020.

See 2.3

4.1.5. Kaftrio - ivacaftor / tezacaftor / elexacaftor - Orphan - EMEA/H/C/005269/X/0008/G

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber

Scope: "Extension application to introduce a new strength of 37.5 mg/25 mg/50 mg film-coated tablets; grouped with a type II variation (C.I.6.a) to include paediatric use (6 to 11 years)."

Action: For adoption

List of Outstanding Issues adopted on 14.10.2021. List of Questions adopted on 22.07.2021.

4.1.6. Noxafil - posaconazole - EMEA/H/C/000610/X/0063/G

Merck Sharp & Dohme B.V.

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant

Scope: "Extension application to introduce a new pharmaceutical form (gastro-resistant powder and solvent for oral suspension), grouped with a type II variation (C.I.6.a) to extend the approved indications for Noxafil to the paediatric population.
As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC, as well as the package leaflet, are updated. The RMP (version 17.1) is updated in accordance."

Action: For adoption

List of Outstanding Issues adopted on 22.07.2021. List of Questions adopted on 25.03.2021.

4.1.7. Nuwiq - simoctocog alfa - EMEA/H/C/002813/X/0042

Octapharma AB

Rapporteur: Jan Mueller-Berghaus

Scope: "Extension application to add a new strength of 1500 IU for simoctocog alfa powder and solvent for solution for injection, for Intravenous use.
The marketing authorisation holder took the opportunity to align the PI to the latest QRD template (version 10.2)."

Action: For adoption

List of Outstanding Issues adopted on 16.09.2021. List of Questions adopted on 24.06.2021.

4.1.8. Ozempic - semaglutide - EMEA/H/C/004174/X/0021

Novo Nordisk A/S

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Annika Folin

Scope: "Extension application to add a new strength of 2 mg solution for injection."

Action: For adoption

List of Outstanding Issues adopted on 14.10.2021. List of Questions adopted on 20.05.2021.

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

Blueprint Medicines (Netherlands) B.V.

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

Scope: "Extension application to add two new strengths of film-coated tablets (25 mg and 50 mg), grouped with a type II variation (C.I.6.a) to introduce a new therapeutic indication for Ayvakyt. Extension of indication to include treatment of adult patients with advanced

systemic mastocytosis (AdvSM), including aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated haematological neoplasm (SM-AHN), and mast cell leukaemia (MCL), after at least one systemic therapy for Ayvakyt based on the results of the BLU-285-2101 and BLU-285-2202 studies. The new indication is applicable to the new and existing presentations (25 mg, 50 mg, 100 mg and 200 mg film-coated tablets). As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.4, 4.5, 4.6, 4.8, 5.1, 5.2, 5.3, 6.1 and 8 of the SmPC are updated. The Labelling and Package Leaflet are updated in accordance. Version 1.1 of the RMP has also been submitted."

Action: For adoption

List of Questions adopted on 24.06.2021.

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

4.3.1. 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

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

Almirall S.A

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

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

Action: For adoption

4.3.3. Procysbi - mercaptamine - Orphan - EMEA/H/C/002465/X/0035

Chiesi Farmaceutici S.p.A.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to introduce a new pharmaceutical form associated with two new strengths (75 and 300 mg gastro-resistant granules). The RMP (version 7.2) is updated in accordance."

Action: For adoption

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

No items

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

No items

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

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

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

Novartis Europharm Limited

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

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

Action: For adoption

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

UCB Pharma S.A.

Rapporteur: Filip Josephson, PRAC Rapporteur: Adam Przybylkowski

Scope: "- Extension of indication to include patients from 1 month to 4 years of age for the Briviact treatment; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The RMP version 8.0 has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.2 and the MAH took the opportunity to implement minor editorial updates.
- (B.II.f.1.b.2)
- (B.IV.1.a.1)
The Package Leaflet and Labelling are updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021, 24.06.2021.

5.1.3. Bydureon - exenatide - EMEA/H/C/002020/II/0073

AstraZeneca AB

Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: "Extension of indication to include the treatment of adolescents and children aged 10 years and above based on the results from study BCB114 (D5551C00002); a phase 3, double-blind, placebo-controlled, randomized, multi-center study to assess the safety and efficacy of exenatide once weekly in adolescents with type 2 diabetes, which was initially submitted and assessed by the CHMP as part of the post-authorisation measure (PAM) P46 028. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated and the Package Leaflet is updated in accordance. Version 35s1 of the RMP has also been submitted."

Action: For adoption

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

Ipsen Pharma

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

Scope: "Extension of indication to include monotherapy treatment of adults and adolescent patients aged 12 years and older, with locally advanced or metastatic differentiated thyroid carcinoma (DTC), refractory or not eligible to radioactive iodine (RAI) who have progressed during or after prior systemic therapy for Cabometyx; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 6.0 of the RMP has also been submitted."

Action: For adoption

5.1.5. Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0011

Sanofi Pasteur

Rapporteur: Christophe Focke

Scope: "To modify the approved therapeutic indication to include conditions for the eligibility to pre-vaccination serostatus screening. As a consequence, sections 4.1, 4.2 and 4.4 of the SmPC and sections 1, 2 and 3 of the Package Leaflet are updated accordingly."

Action: For adoption

Request for Supplementary Information adopted on 20.05.2021, 10.12.2020.

5.1.6. Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0012

Sanofi Pasteur

Rapporteur: Christophe Focke

Scope: "Extension of indication to include paediatric population from 6 years of age for Dengvaxia; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC and sections 1, 2

and 4 of the Package Leaflet are updated. Furthermore, the MAH takes the opportunity to add an instruction for the installation of the needle in the SmPC and the Package Leaflet of the single-dose presentation."

Action: For adoption

Request for Supplementary Information adopted on 20.05.2021, 10.12.2020.

5.1.7. Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0061

Organon N.V.

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include treatment of adolescent males (14 to less than 18 years) with hypogonadotropic hypogonadism, in combination with human Chorionic Gonadotropin (hCG) for Elonva, based on final results of the paediatric study P043. Study P043 was an open-label, non-comparative, multi-center safety and efficacy study of corifollitropin in association with hCG in male adolescents with hypogonadotropic hypogonadism, part of the paediatric investigation plan; as a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 9.2 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement some minor editorial and formatting changes throughout the PI."

Action: For adoption

5.1.8. Ilaris - canakinumab - EMEA/H/C/001109/II/0075

Novartis Europharm Limited

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include treatment of adult patients with Schnitzler syndrome for Ilaris; 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 13.0 of the RMP has also been submitted."

Action: For adoption

5.1.9. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/II/0096

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Maria del Pilar Rayon

Scope: "Extension of indication for Kalydeco tablets in combination regiment with Kaftrio to include the treatment of adults, adolescents and children aged 6 years and older with cystic fibrosis who are homozygous for the F508del mutation in the CFTR gene or heterozygous for F508del and have a minimal function (MF) mutation in the CFTR gene. This application is based on the results of study VX18-445-106, a phase 3, open-label, multicentre study in subjects 6 through 11 years of age, with F/MF and F/F genotypes. As a consequence,

sections 4.1, 4.2, 5.1 and 5.2 of the SmPC are updated. The Packaged Leaflet is updated in accordance. Version 12.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 14.10.2021, 22.07.2021.

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

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication for Keytruda in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery of adults with locally advanced, inflammatory, or early-stage triple-negative breast cancer at high-risk of recurrence; as a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 37.1 of the RMP has also been submitted."

Action: For adoption

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

Merck Sharp & Dohme B.V.

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

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

Action: For adoption

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

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication for Opdivo to include adjuvant treatment of adults with muscle invasive urothelial carcinoma (MIUC) who are at high risk of recurrence after undergoing radical resection of MIUC; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 23.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 24.06.2021.

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

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of indication to include in combination with fluoropyrimidine- and platinum-based combination chemotherapy the first-line treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC) for Opdivo based on study CA209648; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 25.0 of the RMP has also been submitted."

Action: For adoption

5.1.14. Rapiscan - regadenoson - EMEA/H/C/001176/II/0038

GE Healthcare AS

Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Jayne Crowe

Scope: "Modification of existing indication to allow use in line with new imaging technologies that have evolved since initial approval of Rapiscan; as a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 22.07.2021.

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

Shire Pharmaceuticals Ireland Limited

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

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

Action: For adoption

5.1.16. 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: "Extension of indication to add treatment of relapsed/refractory AML in paediatric patients with subsequent updates to sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC based on the new safety and efficacy data from the paediatric clinical study AAML1421. The Package leaflet is updated accordingly. The RMP version 1.1 has also been submitted. In addition, the PI is updated in line with the latest QRD template 10.2.

Submission of the final data from paediatric clinical study CPX-MA-1201 in support of the extension of indication." 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 20.05.2021.

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

Kite Pharma EU B.V.

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Claire Beuneu, PRAC Rapporteur: Anette Kirstine Stark

Scope: "Extension of indication to include the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after three or more lines of systemic therapy. Consequently, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC, Annex II (Section D) and Package Leaflet are proposed to be updated. As a consequence, the RMP (version 5.1) has been updated to align with the indication extension.
In addition, the applicant has taken the opportunity to make minor editorial corrections throughout the SmPC and package leaflet to align with the current Quality Review of Documents (QRD) template." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

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

UCB Pharma S.A.

Lead Rapporteur: Filip Josephson

Scope: "Extension of indication to include patients from 1 month to 4 years of age for treatment of partial-onset seizures with or without secondary generalisation as monotherapy and adjunctive therapy for Vimpat/Lacosamide USB. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. Version 16.0 of the RMP has also been submitted.
B.IV.1.a.1
B.II.f.1.b.2
The Package Leaflet and labelling are updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021, 24.06.2021.

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

Merck Sharp & Dohme B.V.

Lead Rapporteur: Filip Josephson

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

Action: For adoption

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

Bristol-Myers Squibb Pharma EEIG

Lead Rapporteur: Blanca Garcia-Ochoa

Scope: "Extension of indication to include first-line treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC) for Opdivo in combination with Yervoy; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 24.0 of the Opdivo RMP and version 33.0 of the Yervoy RMP have also been submitted."

Action: For adoption

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. Tookad - padeliporfin - EMEA/H/C/004182/II/0013

STEBA Biotech S.A

Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maia Uusküla

Scope: "Modification of the wording of the existing indication. The new wording will be the treatment of adult patients with previously untreated, unilateral, low-risk, adenocarcinoma of the prostate with a life expectancy ≥ 10 years and Clinical stage T1c or T2a, ISUP Grade Group ≤ 2, based on high-resolution biopsy strategies, PSA ≤ 10 ng/mL, Low core positivity for Tookad; as a consequence, section 4.1 of the SmPC is updated. Version 6.0 of the RMP has also been submitted."

Letter from the applicant dated 18 October 2021 requesting an extension to the clock stop to respond to the request for supplementary information adopted in September 2021.

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021, 20.05.2021.

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

Merck Sharp & Dohme B.V.

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

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

Letter from the applicant requesting an extension to the clock stop to respond to the request for supplementary information adopted in October 2021.

Action: For adoption

Request for Supplementary Information adopted on 14.10.2021.

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

No items

6. Ancillary medicinal substances in medical devices

6.1. Ancillary medicinal substances in medical devices; Opinions/ Day 180 list of outstanding issues / Day 120 list of questions

No items

6.2. Update of Ancillary medicinal substances in medical devices

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. etranacogene dezaparvovec - H0004827

Treatment of severe Haemophilia B

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

Action: For adoption

8.2. Priority Medicines (PRIME)

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

8.2.1. List of applications received

Action: For information

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. 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

9.1.2. Ad-hoc assessment of the therapeutic effect of monoethyl fumarate salts within Fumaderm

Implementation of the Judgment of the General Court of 5 May 2021 in Case T-611/18, *Pharmaceutical Works Polpharma v EM*A; Annulment of EMA's non-validation decision for a generic application of Tecfidera.

For the purpose of the implementation of the Judgment, the CHMP is assessing the therapeutic contribution of monoethyl fumarate (MEF) salts within the combination product Fumaderm.

Scope: Opinion

Action: For adoption

9.1.3. 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

9.1.4. Ocaliva – obeticholic acid – EMEA/H/C/004093/R/0027

Intercept Pharma International Limited

Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Renewal of conditional marketing authorisation

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021.

9.1.5. Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0110

GlaxoSmithkline Biologicals SA

Rapporteur: Christophe Focke, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jean-Michel Dogné

Scope: "Extension of indication to include the prevention of head and neck cancers causally related to certain oncogenic human papillomavirus types for Cervarix; as a consequence, sections 4.1 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 23.0 of the RMP has also been submitted to mainly reflect the updated indication. In addition, the Marketing authorisation holder (MAH) took the opportunity to

update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.1."

Withdrawal of extension of indication application

Action: For information

Request for Supplementary Information adopted on 20.05.2021, 17.09.2020.

9.1.6. Leganto – Rotigotine – EMA/H/C/002380

UCB Pharma S.A.

Rapporteur: Bruno Sepodes Co-Rapporteur : Hans Lodewijk Hillege

Scope: Withdrawal of marketing authorisation

Action: For information

9.1.7. Nulojix - belatacept - EMEA/H/C/002098/II/0065/G

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Filip Josephson

Scope: quality variation

Action: For adoption

Request for Supplementary Information adopted on 14.10.2021, 25.03.2021, 12.11.2020, 12.03.2020.

9.1.8. Kanuma - sebelipase alfa – Orphan – EMEA/H/C/004004/II/0032

Alexion Europe SAS

Rapporteur: Karin Janssen van Doorn

Scope: "Update of section 4.2 of the SmPC in order to introduce a new posology regimen (higher starting dose of 3 mg/kg once weekly) based on cumulative data from clinical studies and real-world clinical practice for patients with Rapidly Progressive LAL deficiency presenting within the first six months of life. Consequently, the dosing information for patients with Rapidly Progressive LAL deficiency and paediatric and adult patients with LAL deficiency is modified. In addition, editorial update is made in sections 4.8, 5.1, 5.2 and 6.6 following the new posology regimen. The Package Leaflet is updated accordingly."

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021.

10. Referral procedures

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

No items

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

No items

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

No items

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

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

November 2021 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

No items

13.2. Innovation Task Force briefing meetings

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Roles and responsibilities of CHMP members

Refresher course on the roles and responsibilities of Committee members

Action: For information

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 November 2021

Action: For adoption

14.2.2. Paediatric Committee (PDCO)

PIPs reaching D30 at October 2021 PDCO

Action: For information

Report from the PDCO meeting held on 12-15 October 2021

Action: For information

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

14.3.1. Safety Working Party (SWP)

Chair: Susanne Brendler-Schwaab

Response from SWP to CMDh questions on the acceptable intake for nitrosamine N-Nitrosodi-n-propylamine (NDPA)

Action: for adoption

14.3.2. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP November 2021 meeting to CHMP for adoption:

- 22 reports on products in scientific advice and protocol assistance
- 21 reports on products in pre-authorisation procedures
- 8 reports on products in plasma master file

Action: For adoption

14.3.3. Scientific Advice Working Party (SAWP)

Chair: Anja Schiel

Report from the SAWP meeting held on 25-28 October 2021. Table of conclusions

Action: For information

Scientific advice letters:

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

14.4. Cooperation within the EU regulatory network

14.4.1. Nitrosamines Multidisciplinary Expert Group (NMEG) on rifampicin

Scope: Report from NMEG and advice to CMDh

Action: For adoption

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Update on COVID-19

Action: For information

15.1.2. Sotrovimab - EMEA/H/0005676

Treatment of coronavirus disease 2019 (COVID-19)

Scope: interim opinion on 4th rolling review

Action: For adoption

15.1.3. COVID-19 vaccine - EMEA/H/C/005754

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

Scope: interim opinion on 2nd rolling review

Action: For adoption

15.1.4. COVID-19 vaccine (NVX-CoV2373) – EMEA/H/C/005808

prevention of COVID-19

Scope: Update on rolling review

Action: For information

Explanatory notes

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

Oral explanations *(section 2)*

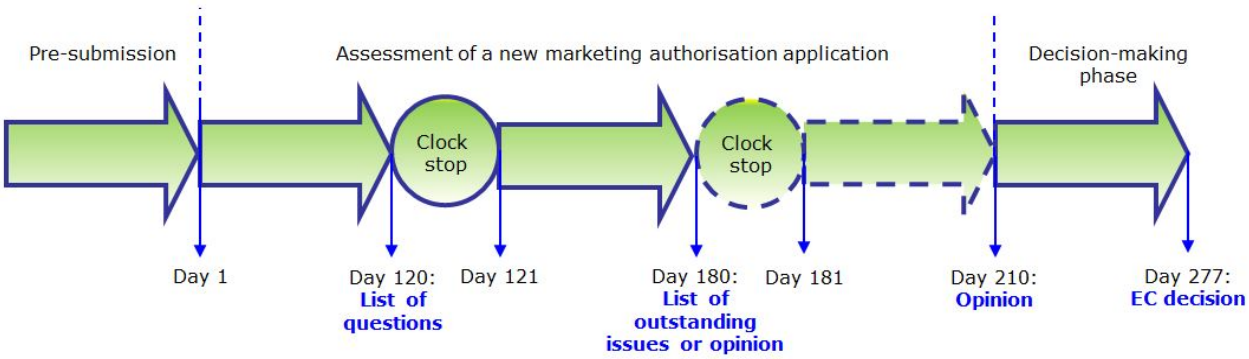
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

Initial applications *(section 3)*

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

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

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



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

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

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

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

Extensions of marketing authorisations are applications for the change or addition of new strengths,

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

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

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

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

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

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

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

Re-examination procedures *(section5.3)*

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

Withdrawal of application *(section 3.7)*

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

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

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

Pre-submission issues *(section 8)*

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

Post-authorisation issues *(section 9)*

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

Referral procedures *(section 10)*

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

particular medicine or class of medicines on behalf of the EU. Further information on such procedures can be found here.

Pharmacovigilance issues *(section 11)*

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

Inspections Issues *(section 12)*

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

Innovation task force *(section 13)*

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

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

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

Satellite groups / other committees *(section 14.2)*

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

Invented name issues *(section 14.3)*

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

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

08 November 2021
EMA/CHMP/625004/2021

Annex to 08-11 November 2021 CHMP Agenda

Pre-submission and post-authorisations issues

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A. PRE-SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for November 2021: **For adoption**

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

Final Outcome of Rapporteurship allocation for November 2021: **For adoption**

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

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

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

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

Atriance - nelarabine - EMEA/H/C/000752/S/0055
Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark

IMVANEX - smallpox vaccine (live modified vaccinia virus Ankara) - EMEA/H/C/002596/S/0069
Bavarian Nordic A/S, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski

Mepsevii - vestronidase alfa - EMEA/H/C/004438/S/0025, Orphan
Ultragenyx Germany GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia

Naglazyme - galsulfase - EMEA/H/C/000640/S/0087
BioMarin International Limited, Rapporteur: Fátima Ventura, PRAC Rapporteur: Ana Sofia Diniz Martins

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

elmiron - pentosan polysulfate sodium - EMEA/H/C/004246/R/0024
bene-Arzneimittel GmbH, Rapporteur: Jean-Michel Race, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Ana Sofia Diniz Martins

Yargesa - miglustat - EMEA/H/C/004016/R/0011
Piramal Critical Care B.V., Generic, Generic of Zavesca, Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Ulla Wändel Liminga
Request for Supplementary Information adopted on 16.09.2021.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Brineura - cerliponase alfa - EMEA/H/C/004065/R/0034, Orphan
BioMarin International Limited, Rapporteur: Martina Weise, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Ulla Wändel Liminga

Darzalex - daratumumab - EMEA/H/C/004077/R/0054, Orphan
Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Emtricitabine/tenofovir disoproxil Krka d.d. - emtricitabine / tenofovir disoproxil - EMEA/H/C/004686/R/0017
KRKA, d.d., Novo mesto, Generic, Duplicate, Duplicate of Emtricitabine/Tenofovir disoproxil Krka, Rapporteur: John Joseph Borg, PRAC Rapporteur: Ana Sofia Diniz Martins

Erelzi - etanercept - EMEA/H/C/004192/R/0037
Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Eva A. Segovia

LEDAGA - chlormethine - EMEA/H/C/002826/R/0030, Orphan
Helsinn Birex Pharmaceuticals Limited,

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Tiphaine Vaillant
Request for Supplementary Information adopted on 16.09.2021.

Qarziba - dinutuximab beta - EMEA/H/C/003918/R/0029, Orphan
EUSA Pharma (Netherlands) B.V., Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Brigitte Keller-Stanislawski

Refixia - nonacog beta pegol - EMEA/H/C/004178/R/0025
Novo Nordisk A/S, Rapporteur: Andrea Laslop, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski

Rolufta Ellipta - umeclidinium - EMEA/H/C/004654/R/0019
GlaxoSmithKline Trading Services Limited, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Ilaria Baldelli
Request for Supplementary Information adopted on 16.09.2021.

Skilarence - dimethyl fumarate - EMEA/H/C/002157/R/0030
Almirall S.A, Rapporteur: Janet Koenig, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Spinraza - nusinersen - EMEA/H/C/004312/R/0025, Orphan
Biogen Netherlands B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ulla Wändel Liminga

TAGRISSO - osimertinib - EMEA/H/C/004124/R/0044
AstraZeneca AB, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Menno van der Elst

B.2.3. Renewals of Conditional Marketing Authorisations

Caprelsa - vandetanib - EMEA/H/C/002315/R/0050
Genzyme Europe BV, Rapporteur: Alexandre Moreau, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Tiphaine Vaillant

OCALIVA - obeticholic acid - EMEA/H/C/004093/R/0027, Orphan Intercept Pharma International Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Liana Gross-Martirosyan Request for Supplementary Information adopted on 16.09.2021.	See 9.1
SIRTURO - bedaquiline - EMEA/H/C/002614/R/0045, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga	

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 25-28 October 2021
PRAC:

Signal of Toxic Encephalopathy in patients with renal impairment

Invanz – Ertapenem

Rapporteur: Fatima Ventura, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Ana Sofia Diniz Martins
PRAC recommendation on a variation
Action: For adoption

Signal of colitis

Kisplyx, Lenvima – Lenvatinib

Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Annika Folin
PRAC recommendation on a variation
Action: For adoption

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its November 2021 meeting:

EMEA/H/C/PSUSA/00000413/202103
(bimatoprost)
CAPS:
Lumigan (EMEA/H/C/000391) (bimatoprost), Allergan Pharmaceuticals Ireland, Rapporteur: Sinan B. Sarac
NAPS:
NAPs - EU
PRAC Rapporteur: Anette Kirstine Stark, "07/03/2018 To: 07/03/2021"

EMEA/H/C/PSUSA/00003127/202102
(voriconazole)
CAPS:
Vfend (EMEA/H/C/000387) (voriconazole), Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege
NAPS:
NAPs - EU
PRAC Rapporteur: Liana Gross-Martirosyan, "01/03/2018 To: 28/02/2021"

EMEA/H/C/PSUSA/00009200/202103
(ipilimumab)
CAPS:
Yervoy (EMEA/H/C/002213) (ipilimumab), Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "25/03/2020 To: 24/03/2021"

EMEA/H/C/PSUSA/00009327/202104
(vandetanib)
CAPS:
Caprelsa (EMEA/H/C/002315) (vandetanib), Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, "06/04/2020 To: 06/04/2021"

EMEA/H/C/PSUSA/00010143/202103
(dimethyl fumarate (multiple sclerosis))
CAPS:
TECFIDERA (EMEA/H/C/002601) (dimethyl fumarate), Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "26/03/2019 To: 26/03/2021"

EMEA/H/C/PSUSA/00010635/202103
(avelumab)
CAPS:
Bavencio (EMEA/H/C/004338) (avelumab), Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark, "23/09/2020 To: 22/03/2021"

EMEA/H/C/PSUSA/00010645/202103
(dupilumab)
CAPS:
Dupixent (EMEA/H/C/004390) (dupilumab), sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Kimmo Jaakkola, "28/03/2020 To: 28/03/2021"

EMEA/H/C/PSUSA/00010780/202103

(cemiplimab) CAPS: **LIBTAYO** (EMEA/H/C/004844) (cemiplimab), Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Menno van der Elst, "27/03/2020 To: 27/03/2021"	
EMEA/H/C/PSUSA/00010833/202104 (enoxaparin) CAPS: **Inhixa** (EMEA/H/C/004264) (enoxaparin sodium), Techdow Pharma Netherlands B.V., Rapporteur: Andrea Laslop NAPS: **NAPs** - EU PRAC Rapporteur: Menno van der Elst, "03/04/2020 To: 03/04/2021"	

B.4. EPARs / WPARs

ASPAVELI - pegcetacoplan - EMEA/H/C/005553, Orphan Swedish Orphan Biovitrum AB (publ), paroxysmal nocturnal haemoglobinuria (PNH), 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.
Cibinqo - abrocitinib - EMEA/H/C/005452 Pfizer Europe MA EEIG, Indicated for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy., New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
RYBREVANT - amivantamab - EMEA/H/C/005454 Janssen-Cilag International N.V., for treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating epidermal growth factor receptor (EGFR) Exon 20 insertion mutations, after failure of platinum-based chemotherapy., 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 SUN - sitagliptin fumarate - EMEA/H/C/005741 Sun Pharmaceutical Industries Europe B.V., treatment of type 2 diabetes mellitus, Generic, Generic of Januvia, Generic application (Article	For information only. Comments can be sent to the PL in case necessary.

10(1) of Directive No 2001/83/EC)	
TRODELVY - sacituzumab govitecan - EMEA/H/C/005182 Gilead Sciences Ireland UC, treatment of unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC), 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.
Vaxneuvance - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/005477 Merck Sharp & Dohme B.V., immunisation for the prevention of invasive disease and pneumonia caused by Streptococcus pneumoniae. Pneumonia caused by Streptococcus pneumoniae, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Abevmy - bevacizumab - EMEA/H/C/005327/II/0005/G Mylan IRE Healthcare Limited, Rapporteur: Jan Mueller-Berghaus	
Adakveo - crizanlizumab - EMEA/H/C/004874/II/0005, Orphan Novartis Europharm Limited, Rapporteur: Daniela Philadelphy Opinion adopted on 21.10.2021.	Positive Opinion adopted by consensus on 21.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0022/G Baxalta Innovations GmbH, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 16.09.2021.	
Aimovig - erenumab - EMEA/H/C/004447/II/0017 Novartis Europharm Limited, Rapporteur: Kristina Dunder Opinion adopted on 21.10.2021. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 21.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 02.09.2021.	
Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0156 Amgen Europe B.V., Rapporteur: Martina Weise Opinion adopted on 28.10.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Aybintio - bevacizumab - EMEA/H/C/005106/II/0009 Samsung Bioepis NL B.V., Rapporteur: Andrea Laslop Opinion adopted on 28.10.2021. Request for Supplementary Information adopted on 02.09.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Bylvay - odevixibat - EMEA/H/C/004691/II/0001, Orphan Albireo, Rapporteur: Johann Lodewijk Hillege	
Cayston - aztreonam - EMEA/H/C/000996/II/0084 Gilead Sciences Ireland UC, Rapporteur: Johann Lodewijk Hillege	
Ceprotin - human protein C - EMEA/H/C/000334/II/0124/G Takeda Manufacturing Austria AG, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 21.10.2021.	Request for supplementary information adopted with a specific timetable.
Cinryze - human c1-esterase inhibitor - EMEA/H/C/001207/II/0089 Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 28.10.2021.	Request for supplementary information adopted with a specific timetable.
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0069/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 28.10.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0075/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0078/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 29.10.2021.	Positive Opinion adopted by consensus on 29.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0017 Janssen-Cilag International N.V., Rapporteur: Christophe Focke Opinion adopted on 21.10.2021.	Positive Opinion adopted by consensus on 21.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Drovelis - drospirenone / estetrol - EMEA/H/C/005336/II/0003 Chemical Works of Gedeon Richter Plc. (Gedeon Richter Plc.), Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 23.09.2021.	
Enhertu - trastuzumab deruxtecan - EMEA/H/C/005124/II/0009 Daiichi Sankyo Europe GmbH, Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 28.10.2021.	Request for supplementary information adopted with a specific timetable.
Enhertu - trastuzumab deruxtecan - EMEA/H/C/005124/II/0010 Daiichi Sankyo Europe GmbH, Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 28.10.2021.	Request for supplementary information adopted with a specific timetable.
Entyvio - vedolizumab - EMEA/H/C/002782/II/0063/G Takeda Pharma A/S, Rapporteur: Armando Genazzani Request for Supplementary Information adopted on 28.10.2021.	Request for supplementary information adopted with a specific timetable.
Eylea - aflibercept - EMEA/H/C/002392/II/0074 Bayer AG, Rapporteur: Alexandre Moreau Opinion adopted on 28.10.2021. Request for Supplementary Information adopted on 02.09.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Herceptin - trastuzumab - EMEA/H/C/000278/II/0173 Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 28.10.2021. Request for Supplementary Information adopted on 09.09.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Herzuma - trastuzumab - EMEA/H/C/002575/II/0041/G Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 21.10.2021.	
IKERVIS - ciclosporin - EMEA/H/C/002066/II/0026/G Santen Oy, Rapporteur: Peter Kiely Request for Supplementary Information adopted on 22.07.2021.	
Jakavi - ruxolitinib - EMEA/H/C/002464/II/0057/G Novartis Europharm Limited, Rapporteur: Filip Josephson Opinion adopted on 28.10.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Levetiracetam SUN - levetiracetam - EMEA/H/C/002051/II/0026 Sun Pharmaceutical Industries Europe B.V., Generic, Generic of Keppra, Rapporteur: Konstantinos Markopoulos Request for Supplementary Information adopted on 21.10.2021.	Request for supplementary information adopted with a specific timetable.
Lonquex - lipegfilgrastim - EMEA/H/C/002556/II/0066 Teva B.V., Rapporteur: Outi Mäki-Ikola Opinion adopted on 28.10.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Lydisilka - drospirenone / estetrol - EMEA/H/C/005382/II/0003 Estetra SRL, Duplicate, Duplicate of Drovelis, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 23.09.2021.	
MabThera - rituximab - EMEA/H/C/000165/II/0186 Roche Registration GmbH, Rapporteur: Sinan B. Sarac Opinion adopted on 28.10.2021. Request for Supplementary Information adopted on 09.09.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Menveo - Meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/001095/II/0103 GSK Vaccines S.r.l, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 02.09.2021.	
Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) -	

EMEA/H/W/002300/II/0059/G GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus	
Nulojix - belatacept - EMEA/H/C/002098/II/0065/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson Request for Supplementary Information adopted on 14.10.2021, 25.03.2021, 12.11.2020, 12.03.2020.	See 9.1
Nulojix - belatacept - EMEA/H/C/002098/II/0076 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson Opinion adopted on 28.10.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ontruzant - trastuzumab - EMEA/H/C/004323/II/0032 Samsung Bioepis NL B.V., Rapporteur: Karin Janssen van Doorn Opinion adopted on 21.10.2021. Request for Supplementary Information adopted on 17.06.2021.	Positive Opinion adopted by consensus on 21.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
OPDIVO - nivolumab - EMEA/H/C/003985/II/0106/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Blanca Garcia-Ochoa Opinion adopted on 28.10.2021. Request for Supplementary Information adopted on 16.09.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Rhokiinsa - netarsudil - EMEA/H/C/004583/II/0007/G Aerie Pharmaceuticals Ireland Limited, Rapporteur: Jayne Crowe	
Rixubis - nonacog gamma - EMEA/H/C/003771/II/0041/G Baxalta Innovations GmbH, Rapporteur: Andrea Laslop Opinion adopted on 28.10.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
RoActemra - tocilizumab - EMEA/H/C/000955/II/0103/G Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus	
Skyrizi - risankizumab - EMEA/H/C/004759/II/0017/G AbbVie Deutschland GmbH & Co. KG, Rapporteur: Peter Kiely	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 28.10.2021. Request for Supplementary Information adopted on 23.09.2021.	
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0021/G AstraZeneca AB, Rapporteur: Sol Ruiz Request for Supplementary Information adopted on 16.09.2021, 22.07.2021, 24.06.2021.	
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0035/G AstraZeneca AB, Rapporteur: Sol Ruiz Opinion adopted on 03.11.2021. Request for Supplementary Information adopted on 10.09.2021, 19.08.2021.	Positive Opinion adopted by consensus on 03.11.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Verkazia - ciclosporin - EMEA/H/C/004411/II/0013/G, Orphan Santen Oy, Duplicate, Duplicate of IKERVIS, Rapporteur: Peter Kiely Opinion adopted on 28.10.2021. Request for Supplementary Information adopted on 24.06.2021, 25.03.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
VITRAKVI - larotrectinib - EMEA/H/C/004919/II/0017 Bayer AG, Rapporteur: Filip Josephson Request for Supplementary Information adopted on 30.09.2021.	
Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/II/0027/G Pfizer Ireland Pharmaceuticals, Rapporteur: Ingrid Wang Request for Supplementary Information adopted on 28.10.2021, 09.09.2021.	Request for supplementary information adopted with a specific timetable.
Zercepac - trastuzumab - EMEA/H/C/005209/II/0013/G Accord Healthcare S.L.U., Rapporteur: Sol Ruiz	
WS2135/G **Rixathon-EMEA/H/C/003903/WS2135/0052/G** **Riximyo-EMEA/H/C/004729/WS2135/0053/G** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 28.10.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2164/G	

Blitzima-EMEA/H/C/004723/WS2164/0047/G
Truxima-EMEA/H/C/004112/WS2164/0051/G
Celltrion Healthcare Hungary Kft., Duplicate, Duplicate of Truxima, Lead Rapporteur: Sol Ruiz

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

Adempas - riociguat - EMEA/H/C/002737/II/0033/G, Orphan
Bayer AG, Rapporteur: Johann Lodewijk Hillege, "Group of variations:
Type II C.I.4. update to SmPC section 4.8 and 5.1 based on the submission of the final clinical study reports of the Phase III long-term extension study PATENT-2.
Type II C.I.4. update to SmPC section 4.8 and 5.1 based on the submission of the final clinical study reports of the Phase III long-term extension study CHEST-2."

Calquence - acalabrutinib - EMEA/H/C/005299/II/0004
AstraZeneca AB, Rapporteur: Filip Josephson, "Submission of the final report of the nonclinical study 20266648 (5336BV) (Acalabrutinib: Neutral Red Uptake Phototoxicity Assay in BALB/c 3T3 Mouse Fibroblasts), in response to the CHMP recommendation to submit results from a modified 3T3 NRU phototoxicity study with adjusted wavelengths. This variation does not propose amendments to the PI."
Request for Supplementary Information adopted on 16.09.2021, 20.05.2021.

CellCept - mycophenolate mofetil - EMEA/H/C/000082/II/0165/G
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "C.I.4 (Type II) - Update of section 5.1 of the SmPC with recent findings from a clinical Pharmacology position paper on Mycophenolate mechanism of Action.
- C.I.4 (Type II) - Update of section 5.2 of the SmPC to add new information to the distribution and elimination subsections based on a Clinical Pharmacology Position Paper.
- C.I.4 (Type II) - Update of section 5.2 of the SmPC to amend the existing information on patients taking oral contraceptives based on

study Roche Report N-181041/ BP 15543. Section 4.5 of the SmPC has been updated accordingly. - C.I.Z (Type IB) - Update of section 2 and section 6 of the Package Leaflet to implement recommendations from NCA (Ireland) and EMA. The Package Leaflet is updated accordingly. In addition, the Marketing Authorisation Holder (MAH) has taken the opportunity to implement minor editorial changes to the SmPC and Package Leaflet. Furthermore, the PI is being brought in line with the latest QRD template version 10.2." Request for Supplementary Information adopted on 16.09.2021.	
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0101 UCB Pharma S.A., Rapporteur: Kristina Dunder, "C.I.4: Update of section 4.6 of the SmPC in order to update information on pregnancy based on non-interventional data from the UCB Global Safety Database on prospective Cimzia-exposed pregnancies with known outcomes; the Package Leaflet is updated accordingly."	
Copiktra - duvelisib - EMEA/H/C/005381/II/0002 Secura Bio Limited, Rapporteur: Sinan B. Sarac, "Update of section 5.1 of the SmPC based on the final overall survival results from study IPI-145-07, an interventional Phase 3 study of duvelisib (IPI-145) vs ofatumumab in patients with relapsed or refractory Chronic Lymphocytic leukaemia/Small Lymphocytic Lymphoma."	
Cresemba - isavuconazole - EMEA/H/C/002734/II/0036, Orphan Basilea Pharmaceutica Deutschland GmbH, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC in order to harmonise the EUCAST breakpoints to those published in the EUCAST breakpoint tables version 10.0, valid from 4 February 2020 for interpretation of minimum inhibitory concentrations (MICs) of antifungal agents. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet." Opinion adopted on 28.10.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Dapivirine Vaginal Ring 25 mg - dapivirine - EMEA/H/W/002168/II/0012/G	Request for supplementary information adopted with a specific timetable.

International Partnership for Microbicides Belgium AISBL, Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information with vaginal products (e.g. vaginal miconazole) that are metabolised by CYP and UGT enzymes and to update pharmacokinetic information based on the final study reports of 3 in vitro enzyme/transporter studies evaluating the interactions between dapivirine and transporters (study NPK/0025), dapivirine-miconazole interactions on CYP (study NPK/0026) and UGT enzymes (study NPK/0027). Submission of the final report from study evaluating the impact of dapivirine and miconazole on cellular tight junctions and assessing the impact of miconazole on dapivirine tissue permeability (study NPK/0028). These 4 in vitro studies were submitted to fulfil post-authorisation measures (REC) requested in the initial marketing authorisation application assessment report." Request for Supplementary Information adopted on 28.10.2021.	
Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0013 Sanofi Pasteur, Rapporteur: Christophe Focke, "Update of sections 4.2 and 5.1 of the SmPC based on final results from study CYD65, listed as a category 3 study in the RMP; this is a Phase II, observer-blind, placebo-controlled trial in order to assess Immunogenicity and Safety of Tetravalent Dengue Vaccine Given in 1-, 2-, or 3-Dose Schedules Followed by a Single Booster." Request for Supplementary Information adopted on 20.05.2021, 10.12.2020.	
Empliciti - elotuzumab - EMEA/H/C/003967/II/0028 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, "C.I.4: Update of section 5.1 of the SmPC in order to update efficacy data from the final CSR for study CA204125. This is an open label, randomized phase 2 Trial of Pomalidomide/Dexamethasone With or Without Elotuzumab in RRMM. In	Positive Opinion adopted by consensus on 21.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

addition, the MAH took the opportunity to remove the list of local representatives in the Package Leaflet and update the address of the manufacturer." Opinion adopted on 21.10.2021.	
Epidyolex - cannabidiol - EMEA/H/C/004675/II/0015, Orphan GW Pharma (International) B.V., Rapporteur: Sinan B. Sarac, "Update of sections 4.5 and 5.1 of the SmPC to add drug-drug interaction information with everolimus and P-gp substrates following the assessment the study GWCP19195, a phase I open-label pharmacokinetic drug-drug interaction trial to investigate the effect of cannabidiol on the pharmacokinetics of everolimus in healthy subject. In addition, the MAH took the opportunity to introduce editorial updates in section 5.1 and section 4.9."	
Epidyolex - cannabidiol - EMEA/H/C/004675/II/0016, Orphan GW Pharma (International) B.V., Rapporteur: Sinan B. Sarac, "Update of section 5.3 of the SmPC to reflect on the conclusions of study GWTX1504, 104 week oral (gavage) administration carcinogenicity study in mouse."	
Evrysdi - risdiplam - EMEA/H/C/005145/II/0002, Orphan Roche Registration GmbH, Rapporteur: Bruno Sepodes, "Update of sections 4.8 and 5.1 of the SmPC based on long-term results from study FIREFISH (BP39056) listed as a category 3 study in the RMP; this is an observational OLE safety and efficacy study. In addition, the MAH took the opportunity to introduce editorial changes to SmPC and to the Instruction for use (IFU)." Opinion adopted on 28.10.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Feraccru - ferric maltol - EMEA/H/C/002733/II/0033 Norgine B.V., Rapporteur: Maria Concepcion Prieto Yerro, "to remove haemoglobin threshold from section 4.4 'Special warnings and precautions for use' of summary of product characteristics for Feraccru Capsules 30 mg, deleting the reference made that states "Feraccru is not recommended for use in patients with haemoglobin (Hb) <9.5 g/dl."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 21.10.2021, 22.07.2021.	
Fetcroja - cefiderocol - EMEA/H/C/004829/II/0006/G Shionogi B.V., Rapporteur: Filip Josephson, "Submission of the final report from the in vitro RIS correlation study S-649266-PF-415-N (REC 003), to address CYP3A4 induction by cefiderocol. In addition, the MAH submitted the final report of in vitro study S-649266-CPK-008-C to investigate the DDI between cefiderocol as a CYP3A4 inducer and Midazolam using physiologically-based pharmacokinetic model."	
Giotrif - afatinib - EMEA/H/C/002280/II/0039/G Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson, "Update of sections 4.2, 5.1 and 5.2 of the SmPC in order to update the description of paediatric information based on results of paediatric study 1200.120. This is in compliance with a completed paediatric investigation plan which does not support a paediatric indication. The Package Leaflet is updated accordingly. The ATC code is also updated. In addition, the MAH took the opportunity to make some minor administrative changes to the labelling and package leaflet." Request for Supplementary Information adopted on 16.09.2021.	
Imfinzi - durvalumab - EMEA/H/C/004771/II/0034 AstraZeneca AB, Rapporteur: Sinan B. Sarac, "Update of sections 4.4 and 4.8 of the SmPC in order to reflect the outcome of the re-defined process to identify and calculate immune-mediated Adverse Event (imAE) rates from clinical study and pooled datasets within the durvalumab development programmes. In addition, the MAH implemented minor editorial corrections to sections 4.4 and 5.1 of the SmPC." Request for Supplementary Information adopted on 21.10.2021.	Request for supplementary information adopted with a specific timetable.
Kanuma - sebelipase alfa - EMEA/H/C/004004/II/0032, Orphan Alexion Europe SAS, Rapporteur: Karin Janssen van Doorn, "Update of section 4.2 of the SmPC	

in order to introduce a new posology regimen (higher starting dose of 3mg/kg once weekly) based on cumulative data from clinical studies and real-world clinical practice for patients with Rapidly Progressive LAL deficiency presenting within the first six months of life. Consequently, the dosing information for patients with Rapidly Progressive LAL deficiency and paediatric and adult patients with LAL deficiency is modified. In addition, editorial update is made in sections 4.8, 5.1, 5.2 and 6.6 following the new posology regimen. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 16.09.2021.	
Kyprolis - carfilzomib - EMEA/H/C/003790/II/0051/G, Orphan Amgen Europe B.V., Rapporteur: Blanca Garcia-Ochoa, "A.6 The ATC code of the product is updated C.I.4, Update of section 4.2 of the SmPC in order to modify administration instructions of daratumumab when Kyprolis is dosed in combination with daratumumab and dexamethasone, based on results from efficacy and safety studies MMY2040 (ongoing phase 2), MMY1001 (completed phase 1b) and CANDOR (ongoing phase 3)." Request for Supplementary Information adopted on 22.07.2021.	
Lynparza - olaparib - EMEA/H/C/003726/II/0048 AstraZeneca AB, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Amelia Cupelli, "Update of section 5.1 of the olaparib tablet SmPC based on results from study D0816C00020 (OPINION) listed as a PAES in the Annex II; this is a Phase IIIb single arm, multicentre study, investigating olaparib as a maintenance treatment in patients with platinum-sensitive relapsed ovarian, fallopian tube or primary peritoneal cancer following 2 or more lines of platinum based chemotherapy and who did not have a known deleterious or suspected deleterious gBRCA mutation; the Annex II is updated accordingly. The RMP version 22.1 has also been submitted." Request for Supplementary Information adopted on 02.09.2021.	

Mayzent - siponimod - EMEA/H/C/004712/II/0011/G

Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, "- Update of sections 4.4 and 4.5 of the SmPC to add information in case of administration of non-live attenuated vaccines, based on the vaccination study A2130.
- Update of section 4.5 of the SmPC to clarify the CYP2C9/CYP3A4 inhibitors/inducers information.
- Update of section 5.2 to add information regarding CYP2C9 genotypes less frequent alleles."
Request for Supplementary Information adopted on 23.09.2021.

NexoBrid - concentrate of proteolytic enzymes enriched in bromelain - EMEA/H/C/002246/II/0049, Orphan

MediWound Germany GmbH, Rapporteur: Janet Koenig, "Update of sections 4.2, 4.4, 4.8, 4.9, 5.1 and 5.2 of the SmPC based on interim results from study MW2010-03-02 (DETECT) listed as an obligation in the Annex II; this is a multicenter, multinational, randomized, controlled, assessor blinded, three-arm study performed in subjects with thermal burns, to evaluate the efficacy and safety of NexoBrid compared to Gel Vehicle and compared to Standard of Care. The submitted Clinical Study Report includes data of Acute Phase and 12M Follow Up Period. The MAH also took the opportunity to submit integrated pooled analyses of efficacy and safety data obtained from phase 2 and phase 3 clinical studies to provide a comprehensive assessment of the safety and efficacy of NexoBrid. The Package Leaflet is updated accordingly."
Request for Supplementary Information adopted on 25.03.2021, 15.10.2020.

Nuceiva - botulinum toxin type A - EMEA/H/C/004587/II/0017

Evolus Pharma Limited, Rapporteur: Peter Kiely, "Submission of the final reports of the non-interventional immunogenicity analysis (RMP cat 3 study)."
Request for Supplementary Information adopted on 23.09.2021.

OCALIVA - obeticholic acid - EMEA/H/C/004093/II/0029, Orphan

Intercept Pharma International Limited, Rapporteur: Blanca Garcia-Ochoa, "Update of sections 4.2, 4.5 and 5.2 of the SmPC in order to clarify information on posology recommendations in renally impaired patients and add information on pharmacokinetic properties following the results from study 474-120 (a Phase I, Open-Label Study to Investigate the Effect of Renal Impairment on the Single-Dose Pharmacokinetics of Obeticholic Acid). Editorial changes have also been made to section 4.5." Request for Supplementary Information adopted on 16.09.2021.	
Opsumit - macitentan - EMEA/H/C/002697/II/0043, Orphan Janssen-Cilag International N.V., Rapporteur: Maria Concepcion Prieto Yerro, "C.I.4 :Update of sections 4.2 and 4.4 of the SmPC to remove a sentence and a warning on the limited clinical experience in patients over the age of 75 years, following the recommendation of the EMEA/H/C/PSUSA/00010115/202010 procedure to remove 'Elderly patients' as missing information in the RMP. The Package Leaflet is being updated accordingly. In addition, the MAH took this opportunity to update the Package Leaflet to include a section on Male fertility and align it with the currently approved information in SmPC, sections 4.6 Fertility, pregnancy, and lactation and 5.3 Preclinical safety."	
Opsumit - macitentan - EMEA/H/C/002697/II/0044, Orphan Janssen-Cilag International N.V., Rapporteur: Maria Concepcion Prieto Yerro, "C.I.4: Update of SmPC sections 4.8 and 5.1, based on the long-term follow-up data from SERAPHIN open-label (OL) study. SERAPHIN OL study was a long-term single-arm open-label extension study of the SERAPHIN double-blind (DB) study, to assess the safety and tolerability of macitentan in patients with symptomatic pulmonary arterial hypertension (PAH) that have completed the DB study or that experienced a morbidity event and for who a written approval to roll over into the OL study was obtained by the sponsor."	
Phesgo - pertuzumab / trastuzumab - EMEA/H/C/005386/II/0004 Roche Registration GmbH, Rapporteur: Sinan B.	Request for supplementary information adopted with a specific timetable.

Sarac, "Update in section 4.8, Undesirable Effects, to present the pooled data from Perjeta and Phesgo studies. In addition to this, the MAH has taken the opportunity to introduce minor updates in the SmPC and the package leaflet: • Update in section 9 of the SmPC to reflect the date of first authorisation • Editorial update in section 4 of the package leaflet to add a space • Update in section 6 of the package leaflet to adapt to the revised QRD Template v10.2" Request for Supplementary Information adopted on 21.10.2021, 22.07.2021.	
Plenadren - hydrocortisone - EMEA/H/C/002185/II/0034, Orphan Shire Services BVBA, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC to add bradycardias a new ADR with frequency unknown." Request for Supplementary Information adopted on 28.10.2021.	Request for supplementary information adopted with a specific timetable.
Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0128 Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, "C.I.4, Update of section 4.2 of the SmPC in order to update the dosing information for Pradaxa coated granules and to introduce a new format of the dosing tables for all dosage forms of Pradaxa to avoid incorrect interpretation and possible mistakes. In addition, a guidance related to the Schwartz formula is proposed to be included in section 4.2 of the SmPC. The Package Leaflet was updated accordingly. Furthermore, the MAH took the opportunity to request introduction of the link to a training video by scanning the QR code in Annex IIIA and IIIB and to include additional updates to Annex IIIA and mock-ups." Request for Supplementary Information adopted on 22.07.2021.	
REKAMBYS - rilpivirine - EMEA/H/C/005060/II/0006 Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC in order to amend an existing warning on section post-injections reactions,	Request for supplementary information adopted with a specific timetable.

based on the availability of new information from ongoing phase 3/3b clinical trials. Section 2 of the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement some minor editorial changes." Request for Supplementary Information adopted on 21.10.2021.	
Revestive - teduglutide - EMEA/H/C/002345/II/0053, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Sinan B. Sarac, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update the Product information with results from two studies included in the paediatric investigation plan (PIP). Study SHP633-1 was performed to evaluate the safety, efficacy/pharmacodynamics (PD), and pharmacokinetics (PK) of teduglutide in infants 4 to 12 months gestational age with SBS and who are dependent on parenteral support. The second study is a paediatric population PK model including data from study SHP633-301. The Package Leaflet was updated accordingly. In addition, the MAH took the opportunity to make editorial changes to section 4.5 of the SmPC." Request for Supplementary Information adopted on 14.10.2021, 24.06.2021.	
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0034 Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, "To update sections 2, 4.2, 4.4, 4.8, 5.1, 6.5 and 6.6 of the SmPC to include a booster dose for Spikevax, based on new clinical data from studies mRNA-1273-P201, a Phase 2a, Randomized, Observer-Blind, Placebo-Controlled, Dose-Confirmation Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older (NCT04405076), mRNA-1273-P301, an ongoing Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older (NCT04470427) and DMID 21-0012, a Phase 1/2 Study of Delayed Heterologous SARS-CoV-2 Vaccine Dosing	Positive Opinion adopted by consensus on 25.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

(Boost) After Receipt of EUA Vaccines (NCT04889209). The labelling and the package leaflet are updated accordingly."
Opinion adopted on 25.10.2021.

Spinraza - nusinersen - EMEA/H/C/004312/II/0023, Orphan
Biogen Netherlands B.V., Rapporteur: Bruno Sepodes, "Update of section 5.1 of the SmPC to include information on real-world use of nusinersen in adults."
Request for Supplementary Information adopted on 16.09.2021.

TAGRISSO - osimertinib - EMEA/H/C/004124/II/0045
AstraZeneca AB, Rapporteur: Blanca Garcia-Ochoa, "Update of section 5.3 of the SmPC in order to reflect the outcome of the 104 Week Oral (Gavage) Carcinogenicity Study (507363) in the Rat submitted as recommended by the CHMP."

Talzenna - talazoparib - EMEA/H/C/004674/II/0010/G
Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, "Update of section 4.4 of the SmPC in order to update the frequency of myelodysplastic syndrome/acute myeloid syndrome (MDS/AML) based on a cumulative safety review; Update of section 5.1 of the SmPC with the revised ATC code. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and make minor corrections in the SmPC and PL."
Request for Supplementary Information adopted on 30.09.2021.

Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0088
MCM Vaccine B.V., Rapporteur: Christophe Focke, "Update of section 5.1 of the SmPC in order to include information about long-term durability of the immune protection against HBV infection based on study V419-013 A Hepatitis B Vaccine Challenge Study to Demonstrate the Durability of Protection Against Hepatitis B Virus Infection in Healthy Children Vaccinated

Approximately 9 Years Previously With a 2- or 3-Dose Infant Series and Toddler Dose of Vaxelis (study report P013V419). In addition, the MAH is updating sections 4.7 and 4.8 of the SmPC to implement EMA proposed wording and a typo error. The MAH took the opportunity to update the list of local representatives in the PL and implement minor editorial changes in sections 4.8 and 6.6 of the SmPC and section 2 of the PL. Furthermore, the PI is brought in line with the latest QRD template version 10.2 rev. 1."	
Vectibix - panitumumab - EMEA/H/C/000741/II/0097 Amgen Europe B.V., Rapporteur: Ingrid Wang, "Update of sections 4.4 and 4.8 of the SmPC in order to add the risk of corneal perforation to the risks of keratitis and ulcerative keratitis and to add corneal perforation (including keratorhexis, which also includes lowest level term corneal rupture) to the list of the adverse reactions, respectively following a safety evaluation. The package leaflet has been updated accordingly. In addition, the applicant took the opportunity to remove frequency information due to variations in case frequency in section 4.8 of the SmPC and section 4 of the PL. Furthermore, the PI is being brought in line with the latest QRD template (version 10.2) and minor editorial changes were made in the PL." Opinion adopted on 21.10.2021. Request for Supplementary Information adopted on 22.07.2021.	Positive Opinion adopted by consensus on 21.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Veltassa - patiromer - EMEA/H/C/004180/II/0024 Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Jayne Crowe, "Update of section 4.2 of the SmPC in order to update the posology with information to add the option to use various liquids and soft foods instead of the currently approved options (water, apple, cranberry juice) for preparation of Veltassa oral suspension. This is based on results from a new compatibility study report of Veltassa with juices/liquids and soft foods (REP074062TC). The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 16.09.2021.	

Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0204 Gilead Sciences Ireland UC, Rapporteur: Jean-Michel Race, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Nathalie Gault, "Submission of final study report for study GS-US-174-0144, listed as category 3 study in the RMP for Viread. This is a randomized, double-blind evaluation of the antiviral efficacy, safety and tolerability of Tenofovir disporoxil fumarate. This application fulfils the Article 46 commitment to provide the final week 192 study results for clinical measure 'Study 5' (study GS_US_174-0144) listed in the PIP. Section 5.1 of the SmPC is being amended accordingly. Additionally, the risk minimisation measures for paediatrics are being removed from the RMP and Annex II of the PI. The Package Leaflet has been updated accordingly. The MAH took the opportunity to implement minor linguistic amendments throughout the PI. In addition, the expression of lactose content in Annex I for the tablets was changed, to refer to lactose base (not as monohydrate), in line with current practice. The RMP version 25.1 has been submitted." Request for Supplementary Information adopted on 08.07.2021.	
Xolair - omalizumab - EMEA/H/C/000606/II/0109 Novartis Europharm Limited, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to update information on efficacy and safety based on final results from study WA40169; this is a single-arm, open-label extension study to evaluate the safety, efficacy and durability of response of Xolair in an open-label setting in adult patients with chronic rhinosinusitis with nasal polyps (CRSwNP)." Opinion adopted on 21.10.2021.	Positive Opinion adopted by consensus on 21.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Zejula - niraparib - EMEA/H/C/004249/II/0032/G, Orphan GlaxoSmithKline (Ireland) Limited, Rapporteur: Ingrid Wang, "Submission of the final reports from two non-clinical studies (TSRO/REP/07-08-09 and KB-0139-DV-HB) investigating the carboxylesterase (CE) and UDP-glucuronosyltransferase (UGT) enzymes involved in the metabolism of niraparib."	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 28.10.2021.	
WS2114 **Mekinist-EMEA/H/C/002643/WS2114/0050** **Tafinlar-EMEA/H/C/002604/WS2114/0054** Novartis Europharm Limited, Lead Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC with the final efficacy data from study BRF113928 (CDRB436E2201), conducted in patients with stage IV BRAF V600 mutant NSCLC, in fulfilment of a post-authorisation measure (REC) from the initial MA."	
WS2130/G **Elebrato Ellipta-EMEA/H/C/004781/WS2130/0023/G** **Temybric Ellipta-EMEA/H/C/005254/WS2130/0011/G** **Trelegy Ellipta-EMEA/H/C/004363/WS2130/0020/G** GlaxoSmithKline Trading Services Limited, Lead Rapporteur: Peter Kiely, "Update of section 4.8 of the SmPC to add the ADR (dysgeusia') and change frequencies for already reported ADRs ('nasopharyngitis', 'viral respiratory tract infection', and 'dysphonia') based on an updated safety analysis. The PL is updated accordingly." Request for Supplementary Information adopted on 16.09.2021.	
WS2156 **Nuwiq-EMEA/H/C/002813/WS2156/0047** **Vihuma-EMEA/H/C/004459/WS2156/0029** Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus, "Submission of the final report from study GENA-99 including the integrated analysis report of studies GENA-99, GENA-13, GENA-15, GENA-21, GENA-21b and GENA-100. GENA-99 is a Prospective, multinational, non-interventional post-authorisation study to document the long-term immunogenicity, safety, and efficacy of Human-cl rhFVIII (simoctocog alfa) in patients with haemophilia A treated in routine clinical practice." Request for Supplementary Information adopted on 28.10.2021.	Request for supplementary information adopted with a specific timetable.

B.5.3. CHMP-PRAC assessed procedures

ADCETRIS - brentuximab vedotin - EMEA/H/C/002455/II/0093, Orphan Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.8, 5.1, 5.2, and 6.6 of the SmPC based on results from study C25004, an open-label study in order to assess the safety and tolerability, of brentuximab vedotin when combined with multiagent chemotherapy regimen for first-line treatment of advanced-stage Hodgkin lymphoma in paediatric patients. The RMP version 16 has also been submitted." Request for Supplementary Information adopted on 30.09.2021.	
Adenuric - febuxostat - EMEA/H/C/000777/II/0062 Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop, PRAC Rapporteur: Jan Neuhauser, "C.I.4 - Update of sections 4.4 and 4.5 of the SmPC in order to amend an existing warning on the drug-drug interaction information with mercaptopurine/azathioprine based on final results from study FAI-01 listed as a category 3 study in the RMP; this is a phase I, drug-drug interaction study investigating the PK profile of 6-mercaptopurine following co-administration of two doses febuxostat and azathioprine in healthy subjects. The RMP version 9.0 has also been submitted." Request for Supplementary Information adopted on 16.09.2021.	
Defitelio - defibrotide - EMEA/H/C/002393/II/0056, Orphan 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. The MAH has also taken the opportunity to align the PI to the latest QRD template 10.2 which	Request for supplementary information adopted with a specific timetable.

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." Request for Supplementary Information adopted on 28.10.2021, 08.07.2021.	
GIVLAARI - givosiran - EMEA/H/C/004775/II/0006, Orphan Alnylam Netherlands B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Martin Huber, "Type II C.I.4 : Update of SmPC section 4.8 to add 'blood homocysteine increase' as a new ADR and update to SmPC section 4,4 to add a related warning. The package leaflet is being updated accordingly. RMPv1.1 is also being submitted: consequences of blood homocysteine increase is being added as a new important potential risk, the clinical and post-marketing exposure is being updated and the due dates for ALN-AS1-002 and ALN-AS1-003 final study reports are being postponed. In addition, the MAH took the opportunity to make editorial changes to the Product Information in other EU languages and to update the contact number of the local representatives for Malta and Cyprus." Request for Supplementary Information adopted on 28.10.2021, 02.09.2021.	Request for supplementary information adopted with a specific timetable.
Increlex - mecasermin - EMEA/H/C/000704/II/0067 Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "Update of the conditions of the non-interventional PASS which is listed as a specific obligation in Annex II, by using different criteria of patient exposure and long-term follow up to assess the relevant safety data, with consequential amendment of the study completion date. The RMP version 13 has also been submitted, also including an amended Global registry protocol (amendment 8). The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, in line with the latest QRD	

template version 10.2 rev.1." Request for Supplementary Information adopted on 22.07.2021.	
Natpar - parathyroid hormone - EMEA/H/C/003861/II/0029, Orphan Takeda Pharmaceuticals International AG, Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Rhea Fitzgerald, "Submission of the final results of study SHP634-101: An Open-Label, Randomized, Crossover Study to Assess the Pharmacokinetic and Pharmacodynamic Profiles of Once-Daily and Twice-Daily Dose Regimens of recombinant human Parathyroid Hormone (rhPTH[1-84]) Administered Subcutaneously to Subjects with Hypoparathyroidism. Further clinical evaluation of an alternative dosing regimen is no longer warranted, as outlined in the current specific obligation (study SHP634-403). The conditional marketing authorisation can therefore be converted into a standard marketing authorisation (no longer subject to a specific obligation) valid for 5 years." Request for Supplementary Information adopted on 24.06.2021.	
NINLARO - ixazomib - EMEA/H/C/003844/II/0033, Orphan Takeda Pharma A/S, Rapporteur: Armando Genazzani, PRAC Rapporteur: Annika Folin, "C.I.11 Submission of the final report for the final analysis of OS for study C16010 listed as an obligation in the Annex II of the Product Information. This is a phase 3, randomized, double-blind study to evaluate ixazomib in combination with LenDex in adult patients with relapsed and/or refractory multiple myeloma. The Annex II and the RMP (submitted version 7.0) are updated accordingly." Request for Supplementary Information adopted on 28.10.2021, 02.09.2021.	Request for supplementary information adopted with a specific timetable.
Piqray - alpelisib - EMEA/H/C/004804/II/0008/G 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	Request for supplementary information adopted with a specific timetable. See 9.1

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." Request for Supplementary Information adopted on 28.10.2021.	
Reagila - cariprazine - EMEA/H/C/002770/II/0023 Gedeon Richter Plc., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of sections 4.4, 4.5, 4.6 and 5.2 of the SmPC in order to update pharmacokinetic information based on final results from RGH-188-302 (CAROLA) study listed as a category 3 study in the RMP; this is an open-label, single-arm, fixed-sequence, phase 1 trial in female schizophrenia patients to investigate the effect of multiple-dose administration of cariprazine on the pharmacokinetics of a combined oral contraceptive containing ethinylestradiol and levonorgestrel; the Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to implement minor editorial changes in sections 4.8 and 5.3 of the SmPC and in the PL." Request for Supplementary Information adopted on 28.10.2021.	Request for supplementary information adopted with a specific timetable.
Rubraca - rucaparib - EMEA/H/C/004272/II/0029 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	See 9.1

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."

Rydapt - midostaurin - EMEA/H/C/004095/II/0018/G, Orphan

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

results from study CPKC412A2116 listed as a category 3 study in the RMP. This is an open label, multiple dose study to evaluate the PK of midostaurin in subjects with mild, moderate and severe hepatic impairment compared to matched healthy subjects; (MEA010) The RMP version 6.0 has also been submitted. In addition, MAH takes this opportunity to introduce minor changes to edit the wording related to the ethanol excipient in the Package Leaflet, according the Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (SANTE-2017-11668), by rounding the volume of alcohol to the next integer number, i.e. from 16.9 to 17 ml. The requested group of variations proposed amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP)." Request for Supplementary Information adopted on 24.06.2021.	
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0069/G Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "C.I.4 type II variation: Update of section 4.8 of the SmPC in order to add rhinorrhoea to the list of adverse drug reactions (ADRs) with frequency unknown based on a systematic review of information from clinical and non-clinical studies, post-marketing data and scientific literature. The Package Leaflet has been updated accordingly. C.I.4 type II variation: Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study 109MS303 (ENDORSE) listed as a category 3 study in the RMP. This is a dose-blind, multicenter, extension study to determine the long-term safety and efficacy of two doses of BG00012 monotherapy in subjects with Relapsing-Remitting Multiple Sclerosis. The RMP version 11.1 has also been submitted." Request for Supplementary Information adopted on 28.10.2021, 02.09.2021, 08.07.2021, 06.05.2021, 14.01.2021.	Request for supplementary information adopted with a specific timetable.
Tremfya - guselkumab - EMEA/H/C/004271/II/0031	Request for supplementary information adopted with a specific timetable.

Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, "C.I.4 Update of the sections 4.8 and 5.1 of the SmPC based on the 2-year data from the psoriatic arthritis Phase 3 clinical study CNTO1959PSA3002 and to remove this study as an additional PV activity from the EU RMP. The RMP version 8.2 has also been submitted." Request for Supplementary Information adopted on 28.10.2021.	
Trogarzo - ibalizumab - EMEA/H/C/004961/II/0015 Theratechnologies Europe Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: David Olsen, "Submission of an updated RMP version 2.0 in order to reflect the new timelines of the PROMISE study and to align the information included in the RMP with the latest PSUR. As the PROMISE study is a condition of the Trogarzo marketing authorisation, the delayed start date results in a change to Annex II of the marketing authorisation. The date for providing the final study report is changing ." Opinion adopted on 28.10.2021. Request for Supplementary Information adopted on 30.09.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2134 **OPDIVO-EMEA/H/C/003985/WS2134/0109** **Yervoy-EMEA/H/C/002213/WS2134/0091** Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Paula Boudewina van Hennik, Lead PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.2, 4.8 and 5.1 of the SmPC based on final results from study CA209908; this is a Phase Ib/II clinical trial of nivolumab monotherapy and nivolumab in combination with ipilimumab in paediatric subjects with high grade primary CNS malignancies; The RMP version 22.4 for Opdivo has also been submitted." Opinion adopted on 28.10.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2153 **OPDIVO-EMEA/H/C/003985/WS2153/0111** **Yervoy-EMEA/H/C/002213/WS2153/0093** Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Paula Boudewina van Hennik, Lead	

PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.2 and 6.6 of the SmPC to change the infusion time for ipilimumab when used as monotherapy or in combination with nivolumab in the melanoma indications; the Package Leaflet for Yervoy is updated accordingly. The RMP versions 34.0 for Yervoy and 26.0 for Opdivo have also been submitted. In addition, an administrative update in Annex II of Yervoy is introduced."	

B.5.4. PRAC assessed procedures

PRAC Led **Afinitor - everolimus - EMEA/H/C/001038/II/0076** Novartis Europharm Limited, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Update of the SmPC section 4.8 to include Lymphoedema as an adverse drug reaction with the frequency common based on the post-marketing data as requested by the PRAC. The PL is updated accordingly." Opinion adopted on 28.10.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Azarga - brinzolamide / timolol - EMEA/H/C/000960/II/0045** Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "Update to the current risk management plan (Version 3.0) to remove important identified risks (Respiratory disorders, Cardiovascular disorders, Corneal decompensation and Metabolic acidosis), Important potential risk (Long term use of preserved eye drops) and Missing information (Use in paediatric patients)" Opinion adopted on 28.10.2021. Request for Supplementary Information adopted on 08.07.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Eylea - aflibercept - EMEA/H/C/002392/II/0075** Bayer AG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Nathalie Gault, PRAC-CHMP liaison: Alexandre Moreau, "Submission of this type II variation as response to commitment undertaken in procedure II/68 covering the	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

following elements: 1) validation of a follow-up questionnaire on Intraocular pressure (IOP) increase, 2) simplification of the educational material (prescriber guide and injection video) based on the data being collected and after the consultation with the panel of ophthalmologists, 3) RMP submission to include follow-up questionnaire on IOP increase and timing of IOP increase report submission" Opinion adopted on 28.10.2021. Request for Supplementary Information adopted on 02.09.2021.	
PRAC Led **Fampyra - fampridine - EMEA/H/C/002097/II/0049** Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Following a PSUR 10 assessment, update to section 4.8 of the SmPC to include new symptoms of trigeminal neuralgia. The package leaflet to be updated accordingly. The Marketing authorisation holder (MAH) introduced further editorial updates including bringing SmPC template to version 10.2 and updating contact details of the local representatives." Opinion adopted on 28.10.2021. Request for Supplementary Information adopted on 08.07.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Hemlibra - emicizumab - EMEA/H/C/004406/II/0026** Roche Registration GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Armando Genazzani, "Update of section 4.8 of the SmPC to include new data related to hypersensitivity, in compliance with the PRAC recommendation following the assessment of PSUSA/00010668/202011. The PIL is updated in accordance with the changes to the SmPC." Opinion adopted on 28.10.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Lojuxta - lomitapide - EMEA/H/C/002578/II/0047** Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur:	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Introduction of an enhanced pharmacovigilance system to evaluate the occurrence and outcomes of pregnancy in females of reproductive potential treated with lomitapide who decide to continue the pregnancy following advice from a teratologist/clinician, replacing the currently agreed Pregnancy Exposure Register (PER), which is listed as part of the specific obligations in the Annex II. The RMP version 6.5 has also been submitted. In addition, the MAH took the opportunity to introduce minor administrative changes." Opinion adopted on 28.10.2021. Request for Supplementary Information adopted on 10.06.2021.	
PRAC Led **Moventig - naloxegol - EMEA/H/C/002810/II/0034** Kyowa Kirin Holdings B.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "C.I.13: Submission of the final report from the observational Post Authorisation Safety Study (PASS)- Drug Utilisation in Selected European Populations (D3820R00006), listed as a category 3 study in the RMP. The RMP version 7.0 has also been submitted." Request for Supplementary Information adopted on 28.10.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Opsumit - macitentan - EMEA/H/C/002697/II/0042, Orphan** Janssen-Cilag International N.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Type II C.I.11 variation to update the risk management plan to v12.1 and update to the Product Information based on the outcome of the PRAC assessment of EMEA/H/C/PSUSA/00010115/202010: - The controlled distribution system and Prescriber Kit (SmPC, prescribing check list and HCP brochure) is being removed as additional risk minimisation measures (aRMM) in the RMP and in the product information Annex II.D. Only the patient alert card is remaining as an aRMM.	Request for supplementary information adopted with a specific timetable.

- Off-label use is being removed from the list of safety concerns. - "Elderly patients aged over 75 years", "patients with moderate to severe hepatic impairment" and "Patients with severe renal impairment and/ or undergoing dialysis" are being removed as missing information. - The MAH has also taken the opportunity to include in the RMP Annex 4, the updated Specific Follow-up Questionnaires Forms (pregnancies, menstrual disorders, and ovarian cysts) due to revision of internal company template. In addition, the MAH has taken this opportunity to update the formatting of the headings of the product information (annex I II and III) in line with the latest QRD template." Request for Supplementary Information adopted on 28.10.2021.	
PRAC Led **PecFent - fentanyl - EMEA/H/C/001164/II/0054** Kyowa Kirin Holdings B.V., Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of an updated RMP (version 7.1) in line with the outcome of the last PSUR single assessment (PSUSA) procedure (PSUSA 00001369/202004) finalised in January 2021 in order to update the key messages of the educational materials in line with Instanyl (fentanyl). As a result, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated accordingly. Finally, the MAH took the opportunity to bring the RMP in line with revision 2 of GVP module V on 'Risk management systems' and the product information in line with the latest quality review of documents (QRD) template (version 10.2). The requested variation proposed amendments to the Annex II and to the Risk Management Plan (RMP)." Request for Supplementary Information adopted on 28.10.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0015/G** Moderna Biotech Spain, S.L., Rapporteur: Jan	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Mueller-Berghaus, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, "Grouped variation to address PRAC requests raised in the 3rd Spikevax Monthly Safety Summary Report (MSSR) procedure (EMEA/H/C/005791/MEA/011.2): - Update of section 4.8 of the SmPC to include details regarding time to onset and duration of the delayed injection site reactions. The Package Leaflet is updated accordingly. - Update of section 4.8 of the SmPC to include "diarrhoea" as an adverse reaction, with the frequency 'Common'. The Package Leaflet is updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to make minor editorial changes." Opinion adopted on 28.10.2021. Request for Supplementary Information adopted on 02.09.2021, 08.07.2021.	
PRAC Led **Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0022** Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 2.0 to include clinical safety data from study mRNA-1273 P203 (NCT04649151), a Phase 2/3, randomised, observer-blind, placebo-controlled study evaluating the safety, reactogenicity, and effectiveness of the mRNA-1273 vaccine in healthy adolescents aged ≥ 12 to < 18 years." Request for Supplementary Information adopted on 28.10.2021, 02.09.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0028** Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 2.1 to include myocarditis and pericarditis as an important identified risk, as requested by PRAC as an outcome of the myocarditis and pericarditis signal assessment procedure." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 28.10.2021, 02.09.2021.	
PRAC Led **Toviaz - fesoterodine - EMEA/H/C/000723/II/0062** Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "Submission of an updated RMP version 10.0 in order to align the important identified risks, important potential risks, and missing information with the new Guideline on good pharmacovigilance practice (GVP) Module V - Risk management systems (Revision 2.0), and to address the PSUR PRAC recommendation (EMEA/H/C/PSUSA/00001387/202004). RMP Version 10.0 is accepted." Opinion adopted on 28.10.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0038** AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Christophe Focke, "Submission of the final report from study MS1222-0003 ''Assessment of anti-PF4 antibodies prior to, and following, vaccination with AZD1222" listed as a category 3 study in the RMP. This is a study where sera of vaccinated individuals in study D8110C00001 are tested to elucidate whether vaccination with Vaxzevria leads to increased levels of circulating anti-PF4 antibodies, a key component of the hypothesized mechanism underlying thrombosis with thrombocytopenia syndrome (TTS)." Request for Supplementary Information adopted on 28.10.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0040** AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Christophe Focke, "Submission of an updated RMP version 4.1 in order to: - Add 'Thrombosis in combination with thrombocytopenia' as an important potential risk, as per PRAC outcome of Signal Assessment	Request for supplementary information adopted with a specific timetable.

procedure on Immune Thrombocytopenia dated 08 July 2021 (EPITT no: 19678); - Add Acute Macular neuroretinopathy / Acute Macular outer retinopathy, Paracentral acute middle maculopathy and Parasthesia and dysaesthesia in the list of AESIs, as per PRAC outcome of Signal Assessment procedure on Acute Macular Outer Retinopathy dated 08 July 2021 (EPITT no: 19703); - Remove the Enhanced active surveillance (EAS) studies D8111R00003 [EU], D8110R00001 [US], D8111C00004 [UK]); - Update the important potential risk of `Nervous system disorders, including immune-mediated neurological conditions' to reflect recent label updates regarding Guillain-Barré syndrome (IB/0034), as per PRAC outcome of Vaxzevria 4th Monthly Summary Safety Update (MEA 027.3), dated 26 June 2021; - Add the UK effectiveness study (D8111R00007), as per CHMP conclusion from MEA 010.1 dated 22 July 2021; - Addition of a study D8111R00010 to assess the relationship between the exposure to COVID-19 vaccines and risk of thrombotic thrombocytopenia syndrome." Request for Supplementary Information adopted on 28.10.2021.	
PRAC Led **XGEVA - denosumab - EMEA/H/C/002173/II/0078** Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from study 20101102 "Osteonecrosis of the Jaw (ONJ) Case Registry", listed as a category 3 study in the RMP. This is an observational PASS with the primary objective to estimate the rate and describe the time course of resolution of ONJ, in subjects 18 years of age with cancer who had newly diagnosed, positively adjudicated ONJ." Opinion adopted on 28.10.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Zostavax - varicella vaccine (live) - EMEA/H/C/000674/II/0138** MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Berghaus, "Submission of an updated RMP version 9.1 to reflect the completion of this long-term effectiveness study (Protocol 024) and to align the RMP template with EMA GVP Module V (rev 2) guidance." Opinion adopted on 28.10.2021.	
PRAC Led **WS1919** **Lyrica-EMEA/H/C/000546/WS1919/0109** **Pregabalin Pfizer-EMEA/H/C/003880/WS1919/0038** Upjohn EESV, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP (version 13.2) to include results from recently completed PASS studies, namely: 1) study A0081359: a population-based cohort study of pregabalin to characterize pregnancy outcomes; 2) study A0081106: a 12-month open-label study to evaluate the safety and tolerability of pregabalin as adjunctive therapy in paediatric subjects 1 month to 16 years of age with partial onset seizures and paediatric and adult subjects 5 to 65 years of age with primary generalized tonic-clonic seizures; 3) study A0081042: a double-blind, placebo-controlled, parallel-group, multicentre study of the efficacy and safety of pregabalin as adjunctive therapy in children 1 month through <4 years of age with partial onset seizures; 4) study A0081105: a randomized, double-blind, placebo-controlled, parallel group, multicentre trial of pregabalin as adjunctive therapy in paediatric and adult subjects with primary generalized tonic-clonic seizures. In addition, information on A0081096: a prospective randomized 12-week controlled study of visual field change in subjects with partial seizures receiving pregabalin or placebo has been updated as well as A0081365: a phase 4, randomised, double-blind, double-dummy, placebo- and active-controlled, single-dose, six-way crossover study to evaluate the potential for abuse with pregabalin. However, further issues noted with the RMP should be updated at the next regulatory opportunity. In the light of the results from the pregnancy outcomes study, section 4.6 of the SmPC is being updated concerning the risks of	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

pregabalin treatment during pregnancy, indicating that women of childbearing potential have to use effective contraception, pregabalin may cross the human placenta and the description of major congenital malformations (MCM). In addition, section 4.4 is updated to highlight that pregabalin should not be used during pregnancy unless clearly necessary and women of childbearing potential have to use effective contraception based on the new data on MCM." Opinion adopted on 28.10.2021. Request for Supplementary Information adopted on 10.06.2021, 01.10.2020.	
PRAC Led **WS2151** **Aflunov-EMEA/H/C/002094/WS2151/0071** **Foclivia-EMEA/H/C/001208/WS2151/0068** Seqirus S.r.l, Lead Rapporteur: Armando Genazzani, Lead PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Armando Genazzani, "Submission of an updated RMP version 3.9 in order to align safety concerns for both products AFLUNOV and FOCLIVIA. Module on 'Epidemiology of the indication and target population' and section on 'use in pregnancy and lactation' are updated. Some potential risks have been reclassified following the definition as per GVP Module V rev.2. Reference to adverse drug reaction follow-up forms for routine pharmacovigilance activity are removed." Request for Supplementary Information adopted on 28.10.2021.	Request for supplementary information adopted with a specific timetable.

B.5.5. CHMP-CAT assessed procedures

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0001/G, Orphan, ATMP Celgene Europe B.V., Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang
Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0002, Orphan, ATMP Celgene Europe B.V., Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0047/G, ATMP Amgen Europe B.V., Rapporteur: Heli Suila, CHMP Coordinator: Johanna Lähteenvuo	
Zolgensma - onasemnogene abeparvovec - EMEA/H/C/004750/II/0019/G, Orphan, ATMP Novartis Gene Therapies EU Limited, Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege	

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

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

WS2060 **HyQvia-EMEA/H/C/002491/WS2060/0071** **Kiovig-EMEA/H/C/000628/WS2060/0109** Takeda Manufacturing Austria AG, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 21.10.2021. Request for Supplementary Information adopted on 10.06.2021.	Positive Opinion adopted by consensus on 21.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2096 **Comtess-EMEA/H/C/000170/WS2096/0061** **Entacapone Orion-EMEA/H/C/002440/WS2096/0020** Orion Corporation, Lead Rapporteur: Outi Mäki-Ikola, "To update sections 2 and 4.4. of the SmPC, section 3 of the Labelling and section 2 of the PL to add a statement warning for the excipient sodium. The proposed update is not in accordance with the Annex of the "Excipients in the labelling and package leaflet of medicinal products". The marketing authorisation holder took the opportunity to align the PI to the latest QRD template (version 10.2). The details of the local representatives are updated for Comtess in United Kingdom (Northern Ireland) and for Entacapone Orion in Germany, Greece, Ireland, Poland and United Kingdom (Northern Ireland)." Opinion adopted on 21.10.2021.	Positive Opinion adopted by consensus on 21.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2112 **Hexacima-EMEA/H/C/002702/WS2112/**	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP

0119 **Hexyon-EMEA/H/C/002796/WS2112/0123** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 28.10.2021. Request for Supplementary Information adopted on 02.09.2021.	Members were in agreement with the CHMP recommendation.
WS2116/G **Kivexa-EMEA/H/C/000581/WS2116/0092/G** **Triumeq-EMEA/H/C/002754/WS2116/0096/G** **Trizivir-EMEA/H/C/000338/WS2116/0126/G** **Ziagen-EMEA/H/C/000252/WS2116/0121/G** ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson Request for Supplementary Information adopted on 09.09.2021.	
WS2128/G **Eucreas-EMEA/H/C/000807/WS2128/0090/G** **Icandra-EMEA/H/C/001050/WS2128/0093/G** **Zomarist-EMEA/H/C/001049/WS2128/0092/G** Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder	
WS2137 **Relvar Ellipta-EMEA/H/C/002673/WS2137/0050** **Revinty Ellipta-EMEA/H/C/002745/WS2137/0048** GlaxoSmithKline (Ireland) Limited, Lead Rapporteur: Maria Concepcion Prieto Yerro, "The marketing authorisation holder took the opportunity to align the PI to the latest QRD template (version 10.2). To amend the exposure multiple for the no-effect level seen in the carcinogenicity study in rats with VI following an error. In addition the MAH is updating the list of local representatives in BG, CY, EE, EL, FI, HU, HR, LT, LV, MT, RO, SI, SK, UK(NI). The MAH has also amended the Revinty EN annexes with regards to the local representative details in ES, IT, FR, DE and PT as an error had	Positive Opinion adopted by consensus on 21.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

been identified." Opinion adopted on 21.10.2021.	
WS2143 **HBVAXPRO-EMEA/H/C/000373/ WS2143/0072** **Vaxelis-EMEA/H/C/003982/WS2143/0089** MCM Vaccine B.V., Lead Rapporteur: Christophe Focke	
WS2167 **Aflunov-EMEA/H/C/002094/WS2167/ 0073** **Foclivia-EMEA/H/C/001208/WS2167/ 0070** Seqirus S.r.l, Lead Rapporteur: Armando Genazzani, "To change the order of addition of the monovalent antigens during the formulation of the finished product."	
WS2176 **Enurev Breezhaler-EMEA/H/C/002691/WS2176/0039** **Seebri Breezhaler-EMEA/H/C/002430/WS2176/0039** **Tovanor Breezhaler-EMEA/H/C/002690/WS2176/0043** Novartis Europharm Limited, Lead Rapporteur: Sinan B. Sarac, "To update the PI for Seebri Breezhaler (glycopyrronium bromide) and its two duplicates, Enurev Breezhaler and Tovanor Breezhaler in line with current QRD template v10.2, Rev. 1 and QRD template v10.1 as follows: - Package leaflet is updated to include Northern Ireland in the list of the local representatives of the Marketing Authorisation Holder (QRD v10.2) - ANNEX II (C and D sections) and Labelling are updated in line with the QRD template v10.1. The MAH also updated section 4.4 (subsection 'Excipients') of the SmPC (Annex I) to change the word from "the Lapp" to "total" to align with the latest European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use' (SANTE-2017-11668), dated 22-Nov-2019. In addition, the MAH has taken the opportunity to update the Instructions for use (IFU) in section 6.6 of the SmPC (Annex I) and also at the end of the Package leaflet." Opinion adopted on 28.10.2021.	Positive Opinion adopted by consensus on 28.10.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

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

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

sutimlimab - EMEA/H/C/005776, Orphan Genzyme Europe BV, treatment of haemolysis in adult patients with cold agglutinin disease (CAD)	
gozetotide - EMEA/H/C/005488 indicated for the identification of prostate-specific membrane antigen (PSMA)-positive lesions after radiolabelling with gallium-68	
bardoxolone methyl / bardoxolone methyl - EMEA/H/C/005869, Orphan Reata Ireland Limited, treatment of chronic kidney disease	
lutetium (177lu) vipivotide tetraxetan - EMEA/H/C/005483 treatment of prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC)	
pegfilgrastim - EMEA/H/C/005587 treatment of neutropenia	
mosunetuzumab - EMEA/H/C/005680 refractory follicular lymphoma (FL)	**Accelerated review**
tirzepatide - EMEA/H/C/005620 treatment of adults with type 2 diabetes mellitus	
plerixafor - EMEA/H/C/005943 treatment of lymphoma and multiple myeloma	
ruxolitinib - EMEA/H/C/005843 treatment of non-segmental vitiligo	
spesolimab - EMEA/H/C/005874 treatment of flares in adult patients with generalised pustular psoriasis	
teriflunomide - EMEA/H/C/005960 treatment of multiple sclerosis (MS)	
deucravacitinib - EMEA/H/C/005755 treatment of moderate to severe plaque psoriasis in adults who are candidates for	

systemic therapy	
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.	
ganaxolone - EMEA/H/C/005825, Orphan Marinus Pharmaceuticals Emerald Limited, treatment of epileptic seizures associated with cyclindependent kinase-like 5 deficiency disorder (CDD)	**Accelerated review**
loncastuximab tesirine - EMEA/H/C/005685, Orphan FGK Representative Service GmbH, treatment of adult patients with relapsed or refractory large B-cell lymphoma	

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

Calquence - acalabrutinib - EMEA/H/C/005299/X/0009/G AstraZeneca AB, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "Extension application to introduce a new pharmaceutical form, film-coated tablet. The active substance in the new formulation, acalabrutinib maleate, is a free base equivalent of acalabrutinib, the active substance used in the hard capsules formulation. A.6 - To change the ATC Code of acalabrutinib from L01XE51 to L01EL02."	
COMIRNATY - tozinameran - EMEA/H/C/005735/X/0077 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Menno van der Elst, "Extension application to add a new strength (0.1 mg/ml). The new presentations are indicated for children from 5 to 11 years of	

age."

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

betaine anhydrous - EMEA/H/C/005637
treatment of homocystinuria
List of Questions adopted on 22.04.2021.

difelikefalin - EMEA/H/C/005612
treatment of pruritus
List of Questions adopted on 22.07.2021.

teriparatide - EMEA/H/C/004932
Treatment of osteoporosis in postmenopausal women and in men at increased risk of fracture
List of Questions adopted on 28.01.2021.

Mayzent - siponimod - EMEA/H/C/004712/X/0007
Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Maria del Pilar Rayon, "Extension application to add a new strength of 1 mg film-coated tablet. The RMP (version 3.0) is updated in accordance."
List of Questions adopted on 16.09.2021.

Nucala - mepolizumab - EMEA/H/C/003860/X/0042
GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension application to introduce a new strength of 40 mg for Nucala solution for injection in a pre-filled syringe for subcutaneous use to be used in children aged 6 to 11 years."
List of Questions adopted on 16.09.2021.

opicapone - EMEA/H/C/005782
treatment of Parkinson's disease and motor fluctuations
List of Questions adopted on 22.07.2021.

relugolix - EMEA/H/C/005353
treatment of adult patients with advanced prostate cancer.
List of Questions adopted on 22.07.2021.

daridorexant - EMEA/H/C/005634
treatment of insomnia
List of Questions adopted on 22.07.2021.

teriparatide - EMEA/H/C/005827
treatment of osteoporosis
List of Questions adopted on 22.07.2021.

Yuflyma - adalimumab - EMEA/H/C/005188/X/0005
Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Ulla Wändel Liminga, "Extension application to introduce a new strengths of 80 mg solution for injection. Version 1.1 of the RMP has also been submitted."
List of Questions adopted on 16.09.2021.

Zejula - niraparib - EMEA/H/C/004249/X/0029, Orphan
GlaxoSmithKline (Ireland) Limited, Rapporteur: Ingrid Wang, PRAC Rapporteur: Jan Neuhauser, "Extension application to introduce a new pharmaceutical form (100 mg film-coated tablet). The RMP (version 5.1) is updated in accordance."
List of Questions adopted on 14.10.2021.

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

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

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

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

Bosulif - bosutinib - EMEA/H/C/002373/R/0051
Pfizer Europe MA EEIG, Rapporteur: Janet Koenig, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Martin Huber

COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/R/0023
Janssen-Cilag International N.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Ulla

Wändel Liminga

Deltyba - delamanid - EMEA/H/C/002552/R/0052, Orphan
Otsuka Novel Products GmbH, Rapporteur: Christophe Focke, PRAC Rapporteur: Laurence de Fays

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

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

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

JEMPERLI - dostarlimab - EMEA/H/C/005204/R/0004
GlaxoSmithKline (Ireland) Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

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

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

Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/R/0048
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Jean-Michel Race, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins

Natpar - parathyroid hormone - EMEA/H/C/003861/R/0034, Orphan

Takeda Pharmaceuticals International AG, Rapporteur: Karin Janssen van Doorn, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Rhea Fitzgerald

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

Pemazyre - pemigatinib - EMEA/H/C/005266/R/0003, Orphan
Incyte Biosciences Distribution B.V., Rapporteur: Alexandre Moreau, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Menno van der Elst

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

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

WAYLIVRA - volanesorsen - EMEA/H/C/004538/R/0016, Orphan
Akcea Therapeutics Ireland Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Martin Huber

B.6.6. VARIATIONS – START OF THE PROCEDURE

Timetables for adoption provided that the validation has been completed.

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

Enhertu - trastuzumab deruxtecan - EMEA/H/C/005124/II/0012
Daiichi Sankyo Europe GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "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)	
Hemlibra - emicizumab - EMEA/H/C/004406/II/0027 Roche Registration GmbH, Rapporteur: Alexandre Moreau, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Amelia Cupelli, "Extension of indication to include treatment of adult and paediatric patients with haemophilia A without factor VIII (FVIII) inhibitors who have mild or moderate disease for whom prophylaxis is clinically indicated. Consequently, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC and section 1 of the package leaflet are updated. In addition, section 4.2 is updated to make it clear that the maintenance dose for Hemlibra applies from week 5 of dosing. The PIL is updated accordingly. Version 4.0 of the RMP has also been submitted."	
IMCIVREE - setmelanotide - EMEA/H/C/005089/II/0002/G, Orphan Rhythm Pharmaceuticals Netherlands B.V., Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Michal Radik, "Group of variations consisting of: C.I.6.a - To add the new therapeutic indication for the treatment of obesity and the control of hunger associated with genetically confirmed Bardet-Biedl syndrome (BBS). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC and sections 1, 3 and 4 of the PL are updated accordingly. The updated RMP version 1.0 has also been submitted. C.I.6.a - To add the new therapeutic indication for the treatment of obesity and the control of hunger associated with genetically confirmed	

Alström syndrome (AS). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC and sections 1, 3 and 4 of the PL are updated accordingly. The updated RMP version 1.0 has also been submitted."

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, "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."

Lynparza - olaparib - EMEA/H/C/003726/II/0051/G
AstraZeneca AB, Rapporteur: Alexandre Moreau, Co-Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Amelia Cupelli, "Extension of indication to include adjuvant treatment of breast cancer for Lynparza (for tablets); as a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. In addition, sections 4.8 of the SmPC for Lynparza hard capsules are revised based on the updated safety data analysis. The Package Leaflet is updated in accordance. Version 23 of the RMP has also been submitted."

NovoSeven - eptacog alfa (activated) - EMEA/H/C/000074/II/0116
Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst, "Extension of indication to include treatment of severe postpartum haemorrhage for NovoSeven. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is also updated in accordance. Version 8.0 of the RMP has also been submitted."

Reblozyl - luspatercept - EMEA/H/C/004444/II/0009, Orphan
Bristol-Myers Squibb Pharma EEIG, Rapporteur:

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

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0024 Baxalta Innovations GmbH, Rapporteur: Andrea Laslop	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0078/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	See B.6.8
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0083/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0026/G Janssen-Cilag International N.V., Rapporteur: Christophe Focke	
Cyramza - ramucirumab - EMEA/H/C/002829/II/0044 Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik	
Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0062 Organon N.V., Rapporteur: Paula Boudewina van Hennik	
Emtricitabine/Tenofovir disoproxil Mylan - emtricitabine / tenofovir disoproxil -	

EMEA/H/C/004050/II/0019
Mylan S.A.S, Generic, Generic of Truvada, Rapporteur: Romaldas Mačiulaitis

Fasenra - benralizumab - EMEA/H/C/004433/II/0038/G
AstraZeneca AB, Rapporteur: Fátima Ventura

Fasenra - benralizumab - EMEA/H/C/004433/II/0040
AstraZeneca AB, Rapporteur: Fátima Ventura

ProQuad - measles, mumps, rubella and varicella vaccine (live) - EMEA/H/C/000622/II/0154
MSD Vaccins, Rapporteur: Jan Mueller-Berghaus

Revestive - teduglutide - EMEA/H/C/002345/II/0055, Orphan
Shire Pharmaceuticals Ireland Limited, Rapporteur: Sinan B. Sarac

RoActemra - tocilizumab - EMEA/H/C/000955/II/0104/G
Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus

Supemtek - quadrivalent influenza vaccine (recombinant, prepared in cell culture) - EMEA/H/C/005159/II/0005/G
Sanofi Pasteur, Rapporteur: Jan Mueller-Berghaus

Synagis - palivizumab - EMEA/H/C/000257/II/0127/G
AstraZeneca AB, Rapporteur: Sinan B. Sarac

Thyrogen - thyrotropin alfa - EMEA/H/C/000220/II/0109/G
Genzyme Europe BV, Rapporteur: Peter Kiely

Vaxchora - cholera vaccine, oral, live - EMEA/H/C/003876/II/0009
Emergent Netherlands B.V., Rapporteur: Ingrid Wang

Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0050
AstraZeneca AB, Rapporteur: Sol Ruiz

Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0051/G
AstraZeneca AB, Rapporteur: Sol Ruiz

VEYVONDI - vonicog alfa - EMEA/H/C/004454/II/0020
Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus

Yuflyma - adalimumab - EMEA/H/C/005188/II/0009/G
Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola

ZABDENO - ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005337/II/0006/G
Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege

WS2182/G
Fluenz Tetra-EMEA/H/C/002617/WS2182/0110/G
Pandemic influenza vaccine H5N1 AstraZeneca-EMEA/H/C/003963/WS2182/0045/G
AstraZeneca AB, Lead Rapporteur: Christophe Focke

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

Adtralza - tralokinumab - EMEA/H/C/005255/II/0001
LEO Pharma A/S, Rapporteur: Jayne Crowe, "C.I.4
Update of sections 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information with cytochrome P450 and CYP substrates based on final results from study ECZTRA 4 (LP0162-1342). This is an open-label drug–drug interaction trial to investigate the effects of tralokinumab on the pharmacokinetics of selected CYP substrates in adult subjects with moderate-to-severe atopic dermatitis. In addition, the MAH took the opportunity make editorial changes to sections 4.8, 6.5 and 9 of SmPC."

Bimzelx - bimekizumab - EMEA/H/C/005316/II/0002
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 multicenter, 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."

Cyramza - ramucirumab - EMEA/H/C/002829/II/0043

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."

Methylthioninium chloride Proveblue - methylthioninium chloride - EMEA/H/C/002108/II/0052/G

Provepharm SAS, Rapporteur: Kristina Dunder, "-Update of sections 4.2 and 5.2 of the SmPC in order to change the posology recommendations in patients with renal and hepatic impairment and update the pharmacokinetic information respectively, based on results from: an open-label, parallel group, population-matched, single-dose study to investigate the influence of renal impairment on the pharmacokinetics of ProvayBlue (Study Report PVP-2016006). The package leaflet and labelling are updated accordingly. The applicant takes this opportunity to update the Product Information according to the QRD template v10.1 and v10.2.
-Update of sections 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information with other medicinal products and update the pharmacokinetic information respectively, based on results from: an open-label, randomized, two-period, crossover study to assess the effect of a single dose of methylene blue 5 mg/ml on the pharmacokinetics of the probe drugs midazolam, caffeine, warfarin, omeprazole and dextromethorphan in healthy subjects (Study Report PVP-2016004). The package leaflet and labelling are updated accordingly."

Obizur - susoctocog alfa - EMEA/H/C/002792/II/0042

Baxalta Innovations GmbH, Rapporteur: Andrea

Laslop, "Submission of the final report from OBIZUR study 241502. This is a Phase 3, multicenter, single-arm, open-label study of the efficacy and safety of B-Domain deleted recombinant porcine factor VIII (BAX 802) in subjects with congenital hemophilia A with factor VIII inhibitors undergoing surgical or other invasive procedures. No changes to the PI are proposed."

REKAMBYS - rilpivirine - EMEA/H/C/005060/II/0008

Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on week 96 results from the clinical study 207966 (ATLAS-2M). This is an open-label, randomized, Phase IIIb trial to demonstrate non-inferior antiviral activity and safety of CAB + RPV Q8W compared with CAB + RPV Q4W. Supporting Cabotegravir (CAB) Long-acting Injectable (LA) + Rilpivirine (RPV) LA every 2 months (Q8W) dosing regimen for the treatment of HIV-1 infection."

RETSEVMO - selpercatinib - EMEA/H/C/005375/II/0010

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."

Revatio - sildenafil - EMEA/H/C/000638/II/0098

Upjohn EESV, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8 and 5.1 to include long-term safety data in adults for the approved dose, and evidence of safe and effective use in adults in higher than recommended doses, based on study A1481324; a multinational, multicentre randomized, double-blind, parallel-group study in 385 adults with Pulmonary Arterial Hypertension (PAH) undertaken to assess the effects of different dose levels of oral sildenafil on mortality. In addition, the MAH took the opportunity to implement editorial changes in

the SmPC.”
Rydapt - midostaurin - EMEA/H/C/004095/II/0022, Orphan Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, “Update of section 5.1 of the SmPC in order to update efficacy information in elderly patients, based on final results from study ADE02T listed as PAES in the Annex II; this is a phase II study to investigate the efficacy of midostaurin in combination with intensive induction, consolidation including allogenic SCT and single agent maintenance in patients aged 18-70 with FLT3 ITD mutated AML .”
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0047 AstraZeneca AB, Rapporteur: Sol Ruiz, “Submission of the final report from MS1222-0004 study "Binding of PF4 to AZD1222 and Purified ChAdOx1" and the Greinacher et al (Greinacher et al 2021) paper, titled "A prothrombotic thrombocytopenic disorder resembling heparin-induced thrombocytopenia following Coronavirus-19 vaccination" listed as a category 3 study in the RMP.”
Veklury - remdesivir - EMEA/H/C/005622/II/0028/G Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, “ C.I.4. Grouping variation to update of section 5.1 of the SmPC in order to add information related to in vitro testing reports of B.1.1.28 and B.1.617 variants with additional provision of the cell culture resistance report to further understand the antiviral activity of Remdesivir. They are listed as part of the specific obligation (SOB 012) in the Annex II of the renewal procedure EMEA/H/C/005622/R/0015 for Veklury. C.I.13.Grouping variation for the submission of the virology reports for GS-US-540-5773 and GS-US-540-5774 studies and the submission of the ACTT-1 final viral load analysis included as part of the specific obligation (SOB 012) in the Annex II of the renewal procedure EMEA/H/C/005622/R/0015 for Veklury.”
Vocabria - cabotegravir -

EMEA/H/C/004976/II/0008
ViiV Healthcare B.V., Rapporteur: Jean-Michel Race, "Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on week 96 results from the clinical study 207966 (ATLAS-2M). This is an open-label, randomized, Phase IIIb trial to demonstrate non-inferior antiviral activity and safety of CAB + RPV Q8W compared with CAB + RPV Q4W. Supporting Cabotegravir (CAB) Long-acting Injectable (LA) + Rilpivirine (RPV) LA every 2 months (Q8W) dosing regimen for the treatment of HIV-1 infection."

WS2163
Combivir-EMEA/H/C/000190/WS2163/0103
Kivexa-EMEA/H/C/000581/WS2163/0093
Trizivir-EMEA/H/C/000338/WS2163/0127
ViiV Healthcare B.V., Lead Rapporteur: Jean-Michel Race, "Update of section 5.2 of the SmPC in order to add new information on the elimination half-life of lamivudine, based on final results from studies 204993 and 204994. Study 204993 was a phase I, relative oral bioavailability study of different fixed dose combinations of dolutegravir and lamivudine in healthy subjects. Study 204994 was an open-label, randomized, single dose, crossover, bioequivalence study of fixed-dose combination tablet(s) of dolutegravir and lamivudine versus dolutegravir and lamivudine single entities and food effect assessment in healthy volunteers. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2 and to introduce minor editorial changes."

B.6.10. CHMP-PRAC assessed procedures

LUTATHERA - lutetium (177lu) oxodotreotide - EMEA/H/C/004123/II/0030, Orphan
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."	
Mekinist - trametinib - EMEA/H/C/002643/II/0051 Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: David Olsen, "Update of section 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."	
Onpattro - patisiran - EMEA/H/C/004699/II/0022, Orphan Alnylam Netherlands B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Rhea Fitzgerald, "Type II variation C.I.4 in the Summary of Product Characteristics (SmPC), Labelling or Package Leaflet (PL) due to new quality, preclinical, clinical or pharmacovigilance data: update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC to confirm that the safety profile of pasitiran in liver transplant recipients is comparable to data in patients without liver transplant, based on final results from study ALN-TTR02-008, a global phase 3b, open-label, extension study to evaluate safety, efficacy and pharmacokinetics of patisiran in patients with hereditary transthyretin-mediated amyloidosis (HATTR amyloidosis) with disease progression post-orthotopic liver transplant (OLT). The RMP version 1.1 has also been submitted. In addition, the MAH took the opportunity to make some minor changes to the English PI in SmPC sections 5.1, 6.3 (In line with EMA recommendation from procedure EMEA/H/C/004699/IB/0014), PL sections 2 (minor typographical error changes), 6 (update to contact numbers of local MAH representatives in Cyprus and Malta, and MAH local representative from 'United Kingdom' to 'United Kingdom [Northern Ireland] in line with the QRD template version 10.2) and implement minor linguistic changes and typographical error	

corrections in the Italian PI translation."

B.6.11. PRAC assessed procedures

PRAC Led

COMIRNATY - tozinameran - EMEA/H/C/005735/II/0080

BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC in order to amend an existing warning on anxiety-related reactions to add "numbness" based on the outcome of the Post-Authorisation Measure PAM MEA-002.8 (EMEA/H/C/005735/MEA/002.8, dated 30. September 2021).
In addition, the MAH took the opportunity to make minor editorial changes throughout the product information."

B.6.12. CHMP-CAT assessed procedures

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0005/G, Orphan, ATMP

Celgene Europe B.V., Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang

Zolgensma - onasemnogene abeparvovec - EMEA/H/C/004750/II/0020/G, Orphan, ATMP

Novartis Gene Therapies EU Limited, Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege

WS2181
Tecartus-EMEA/H/C/005102/WS2181/0014
Yescarta-EMEA/H/C/004480/WS2181/0044

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

B.6.13. CHMP-PRAC-CAT assessed procedures

Skysona - elivaldogene autotemcel - EMEA/H/C/003690/II/0002, Orphan, ATMP

bluebird bio (Netherlands) B.V, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina

Dunder, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Submission of the final CSR for study ALD-102. Risk Management Plan version 2.0 is updated accordingly."

B.6.14. PRAC assessed ATMP procedures

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

WS2169 **Mirapexin-** **EMEA/H/C/000134/WS2169/0101** **Sifrol-EMEA/H/C/000133/WS2169/0092** Boehringer Ingelheim International GmbH, Lead Rapporteur: Sinan B. Sarac, "To update the annexes to bring them in line with QRD version 10.1. In addition, a thorough review of the annexes has been performed and inconsistencies have been corrected."

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.1.1. List of procedures concluding at 08-11 November 2021 CHMP plenary:

G.1.2. List of procedures starting in November 2021 for December 2021 CHMP adoption of outcomes

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