21 June 2021
EMA/CHMP/347670/2021
Human Medicines Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 21-24 June 2021

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

21 June 2021, 09:00 – 19:30, virtual meeting/ room 1C

22 June 2021, 08:30 – 19:30, virtual meeting/ room 1C

23 June 2021, 08:30 – 19:30, virtual meeting/ room 1C

24 June 2021, 08:30 – 15:00, virtual meeting/ room 1C

Disclaimers

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

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

Note on access to documents

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

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Table of contents

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 21-24 June 2021. See June 2021 CHMP minutes (to be published post July 2021 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 21-24 June 2021

1.3. Adoption of the minutes

CHMP minutes for 17-20 May 2021

Minutes from PRocedural and Organisational Matters (PROM) meeting held on 14 June 2021

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. zanubrutinib - Orphan - EMEA/H/C/004978

BeiGene Ireland Ltd; treatment of Waldenström's macroglobulinaemia (WM)

Scope: Possible oral explanation

Action: Possible oral explanation to be held on 22 June 2021 at 14:00

List of Outstanding Issues adopted on 22.04.2021. List of Questions adopted on 15.10.2020.

2.1.2. istradefylline - EMEA/H/C/005308

indicated as an adjunctive treatment to levodopa-based regimens in patients with Parkinson's disease

Scope: Possible oral explanation

Action: Possible oral explanation to be held on 23 June 2021 at 11:00

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

2.1.3. vosoritide - Orphan - EMEA/H/C/005475

BioMarin International Limited; indicated for the treatment of achondroplasia.

Scope: Possible oral explanation, opinion

Action: Possible oral explanation to be held on 22 June 2021 at 16:00

List of Outstanding Issues adopted on 22.04.2021. List of Questions adopted on 10.12.2020.

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

2.3.1. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0052

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of indication to include Tecentriq in combination with nab-paclitaxel and anthracycline-based chemotherapy for the neoadjuvant treatment of adult patients with locally advanced or early Triple Negative Breast Cancer (TNBC) based on the results of the pivotal study WO39392 (IMpassion031); as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the Tecentriq 840 mg concentrate for solution for infusion SmPC and section 4.8 of the Tecentriq 1,200 mg concentrate for solution for infusion SmPC are updated. The Package Leaflet is updated in accordance. Version 18 of the RMP has also been submitted."

Oral explanation

Action: Oral explanation to be held on 23 June 2021 at 15:30

Request for Supplementary Information adopted on 25.02.2021.

See 5.1

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. idecabtagene vicleucel - Orphan - ATMP - EMEA/H/C/004662

Celgene Europe BV; treatment of multiple myeloma

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 19.02.2021, 04.12.2020. List of Questions adopted on 11.09.2020.

3.1.2. abiraterone acetate - EMEA/H/C/005368

treatment of metastatic castration resistant prostate cancer

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 22.04.2021, 25.02.2021. List of Questions adopted on 23.07.2020.

3.1.3. bimekizumab - EMEA/H/C/005316

treatment of plaque psoriasis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 22.04.2021. List of Questions adopted on 10.12.2020.

3.1.4. ranibizumab - EMEA/H/C/005545

treatment of neovascular age-related macular degeneration (AMD)

Scope: Opinion

Action: For adoption

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

3.1.5. roxadustat - EMEA/H/C/004871

treatment of anaemia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 25.02.2021. List of Questions adopted on 17.09.2020.

3.1.6. eflornithine / sulindac - Orphan - EMEA/H/C/005043

Cancer Prevention Pharma (Ireland) Limited; treatment of adult patients with familial adenomatous polyposis (FAP)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 25.03.2021. List of Questions adopted on 15.10.2020.

3.1.7. tafasitamab - Orphan - EMEA/H/C/005436

Incyte Biosciences Distribution B.V.; is indicated in combination with lenalidomide followed by tafasitamab monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), including DLBCL arising from low grade lymphoma, who are not eligible for, or refuse, autologous stem cell transplant (ASCT).

Scope: Opinion

Action: For adoption

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

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

3.2.1. abrocitinib - EMEA/H/C/005452

indicated for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy.

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.01.2021.

3.2.2. artesunate - Orphan - EMEA/H/C/005550

Amivas Ireland Ltd; treatment of malaria

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.01.2021.

3.2.3. fingolimod - EMEA/H/C/005661

treatment of multiple sclerosis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 25.03.2021.

3.2.4. pralsetinib - EMEA/H/C/005413

treatment of non-small cell lung cancer (NSCLC)

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 22.04.2021, 28.01.2021. List of Questions adopted on 17.09.2020.

3.2.5. 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 Questions adopted on 28.01.2021.

3.2.6. imatinib - EMEA/H/C/005595

treatment of Philadelphia chromosome (bcr-abl) positive (Ph+) chronic myeloid leukaemia (CML), Philadelphia chromosome positive acute lymphoblastic leukaemia (Ph+ ALL), myelodysplastic/myeloproliferative diseases (MDS/MPD), hypereosinophilic syndrome (HES), eosinophilic leukaemia (CEL), Kit (CD 117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumours (GIST), and unresectable dermatofibrosarcoma protuberans (DFSP)

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 22.04.2021. List of Questions adopted on 12.11.2020.

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

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 25.06.2020.

3.2.8. pegcetacoplan - Orphan - EMEA/H/C/005553

Apellis Ireland Limited; paroxysmal nocturnal haemoglobinuria (PNH)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.01.2021.

3.2.9. ripretinib - Orphan - EMEA/H/C/005614

Deciphera Pharmaceuticals (Netherlands) B.V.; Treatment of patients with advanced gastrointestinal stromal tumour (GIST)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.01.2021.

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

Protherics Medicines Development Europe B.V.; treatment of patients at risk of methotrexate toxicity

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 10.12.2020.

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

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

Accelerated assessment

prevention of dengue disease

Scope: List of questions

Action: For adoption

3.3.2. ertapenem - EMEA/H/C/005815

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

Scope: List of questions

Action: For adoption

3.3.3. gefapixant - EMEA/H/C/005476

treatment of refractory or unexplained chronic cough

Scope: List of questions

Action: For adoption

3.3.4. gefapixant - EMEA/H/C/005884

treatment of refractory or unexplained chronic cough

Scope: List of questions

Action: For adoption

3.3.5. 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 questions

Action: For adoption

3.3.6. enfortumab vedotin - EMEA/H/C/005392

Accelerated assessment

treatment of locally advanced (LA) or metastatic urothelial cancer (mUC)

Scope: List of questions

Action: For adoption

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

Accelerated assessment

prevention of dengue disease

Scope: List of questions

Action: For adoption

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

treatment and for the prevention of bleeding

Scope: List of questions

Action: For adoption

3.3.9. sacituzumab govitecan - EMEA/H/C/005182

Accelerated assessment

treatment of unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC)

Scope: List of questions

Action: For adoption

3.3.10. rimegepant - EMEA/H/C/005725

management of migraine

Scope: List of questions

Action: For adoption

3.3.11. retifanlimab - Orphan - EMEA/H/C/005632

Incyte Biosciences Distribution B.V.; Treatment of locally advanced or metastatic squamous carcinoma of the anal canal (SCAC) who have progressed on or who are intolerant of platinum-based chemotherapy

Scope: List of questions

Action: For adoption

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

3.4.1. lisocabtagene maraleucel / lisocabtagene maraleucel - Orphan - ATMP - EMEA/H/C/004731

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

Scope: Letter from the applicant dated 28 May 2021 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in April 2021.

Action: For information

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

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

prevention of venous thromboembolic events

Scope: Letter from the applicant dated 06 May 2021 requesting an extension of clock-stop to respond to the list of questions adopted in November 2020.

Action: For adoption

List of Questions adopted on 12.11.2020.

3.4.3. adrenaline - EMEA/H/C/005584

For the emergency treatment of allergic reactions, including anaphylaxis

Scope: Request by the applicant for an extension to the clock stop to respond to the list of questions adopted in March 2021.

Action: For adoption

List of Questions adopted on 25.03.2021.

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

No items

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

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. Rinvoq - upadacitinib - EMEA/H/C/004760/X/0006/G

AbbVie Deutschland GmbH & Co. KG

Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension application to introduce a new strength (30 mg prolonged-release tablet), grouped with a type II variation (C.I.6.a) to add a new indication (treatment of moderate to severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy for Rinvoq). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC as well as the Package Leaflet are updated.
The RMP (version 4.0) is updated in accordance.
In addition, the marketing authorisation holder (MAH) took the opportunity to include a minor update in the Annex II."

Action: For adoption

List of Outstanding Issues adopted on 20.05.2021. List of Questions adopted on 25.02.2021.

4.1.2. Xeljanz - tofacitinib - EMEA/H/C/004214/X/0024/G

Pfizer Europe MA EEIG

Rapporteur: Armando Genazzani, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Extension application to introduce a new pharmaceutical form (oral solution, 1 mg/ml) grouped with a type II variation (C.I.6.a) to add a new indication (treatment of active polyarticular course juvenile idiopathic arthritis (pJIA) in patients 2 years of age and older). The RMP (version 12.1) is updated in accordance. Additionally, the marketing authorisation holder took the opportunity to align the PI with the latest QRD template."

Action: For adoption

List of Outstanding Issues adopted on 25.03.2021. List of Questions adopted on 15.10.2020.

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. Akynzeo - fosnetupitant / netupitant / palonosetron - EMEA/H/C/003728/X/0031

Helsinn Birex Pharmaceuticals Limited

Rapporteur: Peter Kiely, PRAC Rapporteur: Ilaria Baldelli

Scope: "Extension application to introduce a new pharmaceutical form (concentrate for solution for infusion)."

Action: For adoption

List of Questions adopted on 28.01.2021.

4.2.2. 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 25.02.2021. List of Questions adopted on 17.09.2020.

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

Blueprint Medicines (Netherlands) B.V.

Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Bjorg Bolstad, 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

4.3.2. 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

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. Brilique - ticagrelor - EMEA/H/C/001241/II/0049

AstraZeneca AB

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include, in co-administration with acetylsalicylic acid (ASA), the prevention of stroke in adult patients with acute ischaemic stroke or transient ischaemic attack (TIA), based on the final results of study D5134C00003 (THALES), a phase III, international, multicentre, randomised, double-blind, placebo-controlled study to investigate the efficacy and safety of ticagrelor and ASA compared with ASA in the

prevention of stroke and death in patients with acute ischaemic stroke or transient ischaemic attack; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 13 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 28.01.2021, 17.09.2020.

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)
- Addition of a 1 ml oral syringe and its adaptor for the paediatric population. (B.IV.1.a.1)
The Package Leaflet and Labelling are updated in accordance."

Action: For adoption

5.1.3. Comirnaty - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0030

BioNTech Manufacturing GmbH

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

Scope: "Extension of the existing indication from "individuals 16 years of age and older" to "individuals 12 years of age and older" for Comirnaty; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.0 of the RMP has also been submitted."

Opinion was adopted at an extraordinary meeting held remotely on 28 May 2021.

Action: For information

5.1.4. Galafold - migalastat - Orphan - EMEA/H/C/004059/II/0029

Amicus Therapeutics Europe Limited

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication for Galafold (migalastat) to include long-term treatment of adolescents 12 to < 16 years with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency) and who have an amenable mutation. As a consequence, sections 4.1, 4.2, 4.8 and 5.2 of the SmPC and sections 1 and 2 of the Package Leaflet are updated accordingly. A revised RMP version 4.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 25.03.2021.

5.1.5. Jakavi - ruxolitinib - EMEA/H/C/002464/II/0053

Novartis Europharm Limited

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

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

Action: For adoption

5.1.6. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0099

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 to include in combination with chemotherapy, treatment of locally recurrent unresectable or metastatic triple negative breast cancer in adults whose tumours express PD L1 with a CPS ≥ 10 and who have not received prior chemotherapy for metastatic disease; as a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 31.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 25.03.2021.

5.1.7. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0104

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication for Keytruda to include in combination with lenvatinib first line treatment of adults with advanced renal cell carcinoma (RCC); as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 32.1 of the RMP has also been submitted."

Action: For adoption

5.1.8. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0105

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication to include pembrolizumab in combination with lenvatinib for the treatment of advanced endometrial carcinoma in adults who have disease progression following prior systemic therapy in any setting and who are not candidates for curative surgery or radiation; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 33.1 of the RMP has also been submitted."

Action: For adoption

5.1.9. Kisplyx - lenvatinib - EMEA/H/C/004224/II/0045

Eisai GmbH

Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: David Olsen

Scope: "Extension of indication for Kisplyx to include in combination with pembrolizumab first-line treatment of adults with advanced renal cell carcinoma (RCC); 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 of the RMP has also been submitted. In addition, the marketing authorisation holder took the opportunity to update the list of local representatives in the Package Leaflet."

Action: For adoption

5.1.10. Lenvima - lenvatinib - EMEA/H/C/003727/II/0042

Eisai GmbH

Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Annika Folin

Scope: "Extension of indication to include lenvatinib in combination with pembrolizumab for the treatment of adult patients with advanced endometrial carcinoma (EC) who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 14.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to make minor editorial changes to the SmPC and update the list of local representatives in the Package Leaflet in line with the latest QRD template version 10.2.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

5.1.11. Nucala - mepolizumab - EMEA/H/C/003860/II/0035

GlaxoSmithKline Trading Services Limited

Rapporteur: Peter Kiely, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) for Nucala (mepolizumab). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 7 of the

RMP has also been submitted. In addition, the marketing authorisation holder took the opportunity to update the local (IT) representative in the PL."

Action: For adoption

Request for Supplementary Information adopted on 28.01.2021.

5.1.12. Nucala - mepolizumab - EMEA/H/C/003860/II/0036/G

GlaxoSmithKline Trading Services Limited

Rapporteur: Peter Kiely, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include Eosinophilic Granulomatosis with Polyangiitis (EGPA) for Nucala (mepolizumab); as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 7 of the RMP has also been submitted. In addition, the marketing authorisation holder took the opportunity to update the local representative (IT) in the PL.
2 Variations : Type I B.11.e.5.a.2 - To add a new pack size for pre-filled pens for Nucala, 100 mg/ml, solution for injection and another pack size for pre-filled syringes for Nucala, 100 mg/ml, solution for injection.
As a consequence, sections 6.5 and 8 of the SmPCs and section 6 of the PLs are updated accordingly. Annex IIIA is also being updated to include information relating to the new pack sizes.", 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 28.01.2021.

5.1.13. Nucala - mepolizumab - EMEA/H/C/003860/II/0037

GlaxoSmithKline Trading Services Limited

Rapporteur: Peter Kiely, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include hypereosinophilic syndrome (HES) for Nucala (mepolizumab); as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 (in addition 6.6 for the powder for solution for injection ONLY) of the SmPC are updated. The Package Leaflet is updated in accordance. Version 7 of the RMP has also been submitted.
In addition, the Marketing Authorisation Holder took the opportunity to update the local representative (IT) in the PL."

Action: For adoption

Request for Supplementary Information adopted on 28.01.2021.

5.1.14. Opdivo - nivolumab - EMEA/H/C/003985/II/0095

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of indication to include adjuvant treatment of adult patients with resected oesophageal, or gastro-oesophageal junction cancer who have residual pathologic disease following prior neoadjuvant chemoradiotherapy for Opdivo (study CA209577); 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 22.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 25.03.2021.

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

Bristol-Myers Squibb Pharma EEIG

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

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

Action: For adoption

5.1.16. Repatha - evolocumab - EMEA/H/C/003766/II/0049/G

Amgen Europe B.V.

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Kimmo Jaakkola

Scope: "C.I.6 (EoI) Extension of indication to include one new paediatric indication in paediatric patients aged 10 years and over with heterozygous familial hypercholesterolaemia as an adjunct to diet, alone or in combination with other lipid-lowering therapy, to reduce LDL-C based on results of study 20120123 (HAUSER-RCT). It is a randomized, multicenter, placebo-controlled, double blind, parallel group, 24-week trial in 158 paediatric patients aged 10 to > 18 years with heterozygous familial hypercholesterolaemia. As a consequence, sections 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet are updated in accordance. Version 7.0 of the RMP has also been submitted.
C.I.6 (EoI) Extension of indications to modify the existing indication for treatment of adults and paediatric patients aged 10 years and over with homozygous familial hypercholesterolaemia in combination with other lipid-lowering therapies based on interim results from study 20120124 (HAUSER-OLE). It was an open label, single arm, multicenter, 80-week trial to evaluate the safety, tolerability and efficacy of Repatha for LDL-C reduction in paediatric patients from aged ≥ 10 to < 18 years of age with homozygous familial hypercholesterolaemia. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated accordingly."

Action: For adoption

5.1.17. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0052

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of indication to include Tecentriq in combination with nab-paclitaxel and anthracycline-based chemotherapy for the neoadjuvant treatment of adult patients with locally advanced or early Triple Negative Breast Cancer (TNBC) based on the results of the pivotal study WO39392 (IMpassion031); as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the Tecentriq 840 mg concentrate for solution for infusion SmPC and section 4.8 of the Tecentriq 1,200 mg concentrate for solution for infusion SmPC are updated. The Package Leaflet is updated in accordance. Version 18 of the RMP has also been submitted."

Oral explanation to be held on 23 June 2021 at 15:30

Action: For adoption

Request for Supplementary Information adopted on 25.02.2021.

See 2.3

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

Eli Lilly Nederland B.V.

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

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

Action: For adoption

Request for Supplementary Information adopted on 25.02.2021.

5.1.19. Zepatier - elbasvir / grazoprevir - EMEA/H/C/004126/II/0029

Merck Sharp & Dohme B.V.

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "Extension of indication to include treatment of chronic hepatitis C (CHC) in paediatric patients 12 years of age and older who weigh at least 30 kg for Zepatier; 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 4.1 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."

Action: For adoption

5.1.20. WS1941
Edistride - dapagliflozin - EMEA/H/C/004161/WS1941/0043
Forxiga - dapagliflozin - EMEA/H/C/002322/WS1941/0062

AstraZeneca AB

Lead Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: "Update of sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC for Forxiga and Edistride based on the results from the renal outcomes study D169AC00001 (DAPA-CKD). The Annex II.B and Package Leaflet of these products are updated accordingly. The DAPA-CKD study is a category 3, Post-Authorisation Safety Study (PASS) listed in the dapagliflozin RMP to evaluate the potential risk of lower limb amputation; it is a multicentre, event-driven, randomized, double-blind, parallel group, placebo-controlled study, evaluating the effect of dapagliflozin versus placebo, given once daily in addition to standard of care, to prevent the progression of chronic kidney disease (CKD) or cardiovascular (CV)/renal death. In addition, the Risk Management Plan for dapagliflozin (version 22) has been updated."

Action: For adoption

Request for Supplementary Information adopted on 25.02.2021.

5.1.21. WS1953
Segluromet - ertugliflozin / metformin hydrochloride - EMEA/H/C/004314/WS1953/0012
Steglatro - ertugliflozin - EMEA/H/C/004315/WS1953/0013

Merck Sharp & Dohme B.V.

Lead Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst

Scope: "Update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC of Steglatro and Segluromet in order to modify the indication, update posology recommendations and include efficacy and safety information based on final results from the VERTIS CV study (protocol 8835-004/B1521021) listed as a category 3 study in the RMP. This is a multi-centre, multi-national, randomised, double-blind, placebo-controlled study to evaluate the effect of ertugliflozin on cardiovascular risk in adult patients with type 2 diabetes and established atherosclerotic cardiovascular disease. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 25.02.2021.

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

UCB Pharma S.A.

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

Scope: "Extension of indication to include patients from 1 month to 4 years of age for treatment of partial-onset seizures with or without secondary generalisation as monotherapy and adjunctive therapy for Vimpat/Lacosamide USB. As a consequence,

sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. Version 16.0 of the RMP has also been submitted.
B.IV.1.a.1 - type IB
B.II.f.1.b.2 - type IB
The Package Leaflet and labelling are updated in accordance."

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

No items

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

No items

6. 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. dexmedetomidine hydrochloride – H0005811

Acute treatment of agitation associated with schizophrenia or bipolar disorder in adults.

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

Action: For adoption

8.1.2. efgartigimod alfa – Orphan - H0005849

argenx BV; Treatment of adult patients with generalised myasthenia gravis.

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

Action: For adoption

8.1.3. lenacapavir - H0005638

in combination with other antiretroviral(s), is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults with multidrug resistant HIV 1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations.

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

Action: For adoption

8.1.4. lutetium – H0005483

treatment of metastatic castration-resistant prostate cancer in adult male patients

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

Action: For adoption

8.1.5. tebentafusp – H0004929

treatment of advanced uveal melanoma

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. Caprelsa - vandetanib - EMEA/H/C/002315/II/0043

Genzyme Europe BV

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant

Scope: "C.I.4 Update of section 5.1 of the SmPC in order to update pharmacodynamic information based on interim results from study D4200C00104, listed as a specific obligation in the Annex II. This is an observational study (including a retrospective arm to evaluate the Benefit/Risk of vandetanib (Caprelsa) 300 mg in RET mutation negative and RET mutation positive patients with symptomatic, aggressive, sporadic, unresectable, locally advanced/metastatic thyroid cancer (MTC)), to confirm the efficacy and safety of Caprelsa in RET-negative patients with the aim to fulfil SOB001 and convert Caprelsa from conditional to normal Marketing Authorization. In addition the MAH takes to opportunity to rectify the Dutch translation of the Caprelsa Product Information."

Action: For adoption

Request for Supplementary Information adopted on 28.05.2020.

9.1.2. Cometriq - cabozantinib - EMEA/H/C/002640/II/0044, Orphan

Ipsen Pharma

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

Scope: "Update of the annex IIE and SmPC section 5.1 to remove the specific obligation (SOB 001) and the reference to the conditional approval based on the final results from the study XL184-401 (EXAMINER), a randomised, double-blind study to evaluate the efficacy and safety of cabozantinib (XL184) at 60 mg/day compared to a 140 mg/day in progressive, metastatic medullary thyroid cancer patients. The package leaflet is updated accordingly. The updated RMP version 5.4 has also been submitted. With this submission, the MAH is proposing to revert from conditional marketing authorisation to full marketing

authorisation.
Additionally, the MAH took the opportunity to bring the Product Information in line with the latest QRD template version 10.2 Rev 1, to add the sodium content in the Summary of Product Characteristics and Package Information Leaflet in line with the guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' and update details of local representatives."
Action: For adoption

9.1.3. Cosentyx - secukinumab - EMEA/H/C/003729/II/0076

Novartis Europharm Limited

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

Scope: C.I.4 - Update of sections 4.2 and 5.1 of the SmPC in order to introduce a new posology regimen for adult plaque psoriasis patients and psoriatic arthritis patients with concomitant moderate to severe plaque psoriasis based on the final results study CAIN457A2324 and exposure-response modelling; this is a randomized, double-blind, multicenter study assessing short (16 weeks) and long-term efficacy (up to 1 year), safety, and tolerability of sub-cutaneous secukinumab in subjects of body weight 90 kg or higher with moderate to severe chronic plaque-type psoriasis; the Package Leaflet is updated accordingly. The RMP version 9.0 has also been submitted.

Action: For adoption

9.1.4. Esbriet - pirfenidone - EMEA/H/C/002154/II/0069

Roche Registration GmbH

Rapporteur: Peter Kiely, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Extension of indication to include the treatment of unclassifiable interstitial lung disease (UILD) for Esbriet; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 11.0 of the RMP has also been submitted."

Withdrawal of extension of indication application

Action: For information

Request for Supplementary Information adopted on 22.04.2021

9.1.5. Hepcludex - bulevirtide - EMEA/H/C/004854/R/0003

MYR GmbH

Rapporteur: Filip Josephson, PRAC Rapporteur: Adam Przybylkowski

Scope: "Annual renewal"

Action: For adoption

Request for Supplementary Information adopted on 22.04.2021.

9.1.6. Jardiance - empagliflozin - EMEA/H/C/002677/II/0057

Boehringer Ingelheim International GmbH

Rapporteur: Johann Lodewijk Hillege

Scope: "Update of sections 4.2 and 4.4 of the SmPC to lower the renal threshold for initiation and use of empagliflozin depending on eGFR, and of the section 5.1 wording about endpoints with reference to EMPA-REG OUTCOME study. The PL is updated accordingly."

Action: For adoption
Request for Supplementary Information adopted on 25.03.2021.

9.1.7. Lextemy - bevacizumab - EMEA/H/C/005611

Mylan IRE Healthcare Limited; 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.

Similar biological application (Article 10(4) of Directive No 2001/83/EC), Duplicate of Abevmy

Withdrawal of marketing authorisation

Action: For information

9.1.8. Natpar **-** parathyroid hormone - EMEA/H/C/003861/II/0029

Shire Pharmaceuticals Ireland Limited

Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Rhea Fitzgerald

Scope: "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."

Action: For adoption

9.1.9. Nodetrip – duloxetine – EMEA/H/C/000573

Esteve Pharmaceuticals S.A.; treatment of major depressive episodes and diabetic peripheral neuropathic pain

Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Filip Josephson

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

Withdrawal of marketing authorisation

Action: For information

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

Rapporteur: TBC, Co-Rapporteur: TBC

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 will assess the therapeutic effect of monoethyl fumarate (MEF) salts within the combination product Fumaderm.

Scope: Appointment of Rapporteurs, LoQ, timetable

Action: For adoption

9.1.11. Xeljanz - tofacitinib - EMEA/H/C/004214/II/0027

Pfizer Europe MA EEIG

Rapporteur: Armando Genazzani, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Update of sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of Xeljanz 11 mg prolonged-release tablets SmPC in order to include the treatment of active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have been intolerant to a prior disease modifying antirheumatic drug therapy; as an alternative to the immediate release film-coated tablets; section 4.2 of Xeljanz film-coated tablets is also updated to include switching with the prolonged-release tablet in the treatment of PsA. The Package Leaflet is updated accordingly. The RMP version 13.1 has also been submitted."

Request for Supplementary Information adopted on 25.03.2021, 10.12.2020.

Action: For adoption

9.1.12. Vaxzevria – COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0021/G

AstraZeneca AB

Rapporteur: Sol Ruiz, Co-Rapporteur: Hans Hillege, PRAC Rapporteur: Jean-Michel Dogné

Scope: Quality variation

Action: For discussion

9.1.13. Vaxzevria – COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0020/G

AstraZeneca AB

Rapporteur: Sol Ruiz, Co-Rapporteur: Hans Hillege, PRAC Rapporteur: Jean-Michel Dogné

Scope: Quality variation

Action: For adoption

Request for Supplementary Information adopted on 08.06.2021.

10. Referral procedures

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

No items

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

No items

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

No items

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

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

International Drug Development France

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

Scope: List of outstanding issues/ opinion

Action: For adoption

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

List of questions adopted on 25.03.2021.

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

No items

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

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

ANSM France

Referral Rapporteur: TBC, Co-Rapporteur: TBC

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

Action: For adoption

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

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

June 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

No items

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 June 2021

Action: For adoption

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

14.3.1. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP June 2021 meeting to CHMP for adoption:

- 20 reports on products in scientific advice and protocol assistance
- 14 reports on products in pre-authorisation procedures
- 5 reports on products in plasma master file

Action: For adoption

14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 26-27 May 2021.

Action: For adoption

14.3.3. Scientific Advice Working Party (SAWP)

Chair: Anja Schiel

Report from the SAWP meeting held on 07-10 June 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

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Update on COVID-19

Action: For information

15.1.2. Procedural guidance for variation for variant update to covid-19 vaccines

Final procedural guidance for variation for variant update to covid-19 vaccines.

Action: For adoption

15.1.3. etesivimab – EMEA/H/C/005837/0000

Scope: Rolling review 3rd interim opinion

Rolling review 3rd interim opinion was adopted at an extraordinary meeting held remotely on 28 May 2021.

Action: For information

15.1.4. bamlanivimab – EMEA/H/C/005836/0000

Scope: Rolling review 3rd interim opinion

Rolling review 3rd interim opinion was adopted at an extraordinary meeting held remotely on 28 May 2021.

Action: For information

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

prevention of COVID-19

Scope: Interim opinion and overview for the rolling review 2 adopted via written procedure on 14 June 2021

Action: For information

15.1.6. regdanvimab – EMEA/H/C/005854

treatment of COVID-19

Scope: Interim opinion adopted via written procedure on 11 June 2021

Action: For information

15.1.7. COVID-19 Vaccine Moderna – COVID-19 mRNA VAccine (nucleoside-modified) – EMEA/H/C/005791/II/0021

Moderna Biotech Spain, S.L.; extension of indication to include use in adolescents 12 to 17 years of age for COVID-19 vaccine

Scope: Timetable adopted via written procedure on 9 June 2021.

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)*

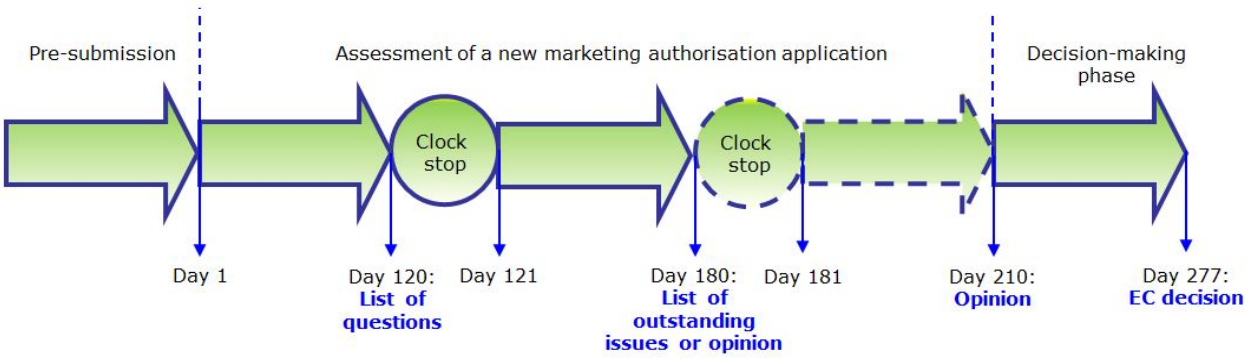
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

28 July 2021
EMA/CHMP/349493/2021 Corr.1[1]

Annex to 21-24 June 2021 CHMP Agenda

Pre-submission and post-authorisations issues

[1] Correction in section B.6.1

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A. PRE-SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

Final Outcome of Rapporteurship allocation for June 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

Evoltra - clofarabine - EMEA/H/C/000613/S/0072
Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant

Lamzede - velmanase alfa - EMEA/H/C/003922/S/0019, Orphan
Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jan Neuhauser

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Afstyla - lonoctocog alfa - EMEA/H/C/004075/R/0037
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Johanna Lähteenvuo,

PRAC Rapporteur: Sonja Hrabcik

Darunavir Mylan - darunavir - EMEA/H/C/004068/R/0014
Mylan S.A.S, Generic, Generic of Prezista, Rapporteur: John Joseph Borg, PRAC Rapporteur: Liana Gross-Martirosyan

Emtricitabine/Tenofovir disoproxil Krka - emtricitabine / tenofovir disoproxil - EMEA/H/C/004215/R/0018
KRKA, d.d., Novo mesto, Generic, Generic of Truvada, Rapporteur: John Joseph Borg, PRAC Rapporteur: Ana Sofia Diniz Martins

Emtricitabine/Tenofovir disoproxil Mylan - emtricitabine / tenofovir disoproxil - EMEA/H/C/004050/R/0016
Mylan S.A.S, Generic, Generic of Truvada, Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Ana Sofia Diniz Martins

Fiasp - insulin aspart - EMEA/H/C/004046/R/0028
Novo Nordisk A/S, Rapporteur: Kristina Dunder, Co-Rapporteur: Ingrid Wang, PRAC Rapporteur: Annika Folin

Granpidam - sildenafil - EMEA/H/C/004289/R/0009
Accord Healthcare S.L.U., Generic, Generic of Revatio, Rapporteur: Kolbeinn Gudmundsson, PRAC Rapporteur: Menno van der Elst

Inhixa - enoxaparin sodium - EMEA/H/C/004264/R/0076
Techdow Pharma Netherlands B.V., Duplicate, Duplicate of Thorinane (EXP), Rapporteur: Andrea Laslop, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 22.04.2021.

Movymia - teriparatide - EMEA/H/C/004368/R/0024
STADA Arzneimittel AG, Duplicate, Duplicate of Terrosa, Rapporteur: Daniela Philadelphy, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ronan Grimes

Olumiant - baricitinib - EMEA/H/C/004085/R/0025
Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Christophe

Focke, PRAC Rapporteur: Adam Przybylkowski

Parsabiv - etelcalcetide - EMEA/H/C/003995/R/0017
Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Andrea Laslop (AT) (MNAT with AT for Clinical Safety, AT for Non-Clinical, AT for Coordination, AT for Clinical Efficacy, AT for Clinical Pharmacology, DE-BfArM for Quality), PRAC Rapporteur: Ilaria Baldelli

SomaKit TOC - edotreotide - EMEA/H/C/004140/R/0019, Orphan
Advanced Accelerator Applications, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Ronan Grimes

Tenofovir disoproxil Mylan - tenofovir disoproxil - EMEA/H/C/004049/R/0022
Mylan S.A.S, Generic, Generic of Viread, Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Adrien Inoubli

Terrosa - teriparatide - EMEA/H/C/003916/R/0020
Gedeon Richter Plc., Rapporteur: Daniela Philadelphy, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ronan Grimes

B.2.3. Renewals of Conditional Marketing Authorisations

Adakveo - crizanlizumab - EMEA/H/C/004874/R/0003, Orphan
Novartis Europharm Limited, Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Laurence de Fays

Hepcludex - bulevirtide - EMEA/H/C/004854/R/0003, Orphan
MYR GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Adam Przybylkowski
Request for Supplementary Information adopted on 22.04.2021.

VITRAKVI - larotrectinib - EMEA/H/C/004919/R/0014
Bayer AG, Rapporteur: Filip Josephson, PRAC Rapporteur: Rugile Pilviniene
Request for Supplementary Information adopted on 20.05.2021.

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 07-10 June 2021
PRAC:

Signal of capillary leak syndrome

Vaxzevria - COVID-19 Vaccine (ChAdOx1-S [recombinant])
Rapporteur: Sol Ruiz, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jean-Michel Dogné

PRAC recommendation on a variation, DHPC, Communication plan; adopted via written procedure on Monday 14 June 2021
Action: For information

Signal of major adverse cardiovascular events (MACE) and malignancies excluding non-melanoma skin cancer (NMSC) from a clinical trial

Xeljanz - tofacitinib
Rapporteur: Armando Genazzani, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan
PRAC recommendation on a variation / DHPC
Action: For adoption

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

EMEA/H/C/PSUSA/00002480/202010
(posaconazole)
CAPS:
Noxafil (EMEA/H/C/000610) (posaconazole), Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau
NAPS: **NAPs** - EU
PRAC Rapporteur: Adrien Inoubli, "10/07/2019 To: 25/10/2020"

EMEA/H/C/PSUSA/00002652/202011
(rituximab)
CAPS:
Blitzima (EMEA/H/C/004723) (rituximab), Celltrion Healthcare Hungary Kft., Rapporteur:

Sol Ruiz
MabThera (EMEA/H/C/000165) (rituximab), Roche Registration GmbH, Rapporteur: Sinan B. Sarac
Ritemvia (EMEA/H/C/004725) (rituximab), Celltrion Healthcare Hungary Kft., Rapporteur: Sol Ruiz
Rixathon (EMEA/H/C/003903) (rituximab), Sandoz GmbH, Rapporteur: Jan Mueller-Berghaus
Riximyo (EMEA/H/C/004729) (rituximab), Sandoz GmbH, Rapporteur: Jan Mueller-Berghaus
Ruxience (EMEA/H/C/004696) (rituximab), Pfizer Europe MA EEIG, Rapporteur: Paula Boudewina van Hennik
Truxima (EMEA/H/C/004112) (rituximab), Celltrion Healthcare Hungary Kft., Rapporteur: Sol Ruiz, PRAC Rapporteur: Anette Kirstine Stark, "17/11/2019 To: 17/11/2020"

EMEA/H/C/PSUSA/00002822/202009
(sulfur hexafluoride)
CAPS:
SonoVue (EMEA/H/C/000303) (sulphur hexafluoride), Bracco International B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, "30/09/2017 To: 30/09/2020"

EMEA/H/C/PSUSA/00010133/202009
(regorafenib)
CAPS:
Stivarga (EMEA/H/C/002573) (regorafenib), Bayer AG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "27/09/2017To: 26/09/2020"

EMEA/H/C/PSUSA/00010301/202011
(ibrutinib)
CAPS:
Imbruvica (EMEA/H/C/003791) (ibrutinib), Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "13/11/2019 To: 12/11/2020"

EMEA/H/C/PSUSA/00010319/202010
(nintedanib (respiratory indication))
CAPS:
OFEV (EMEA/H/C/003821) (nintedanib), Boehringer Ingelheim International GmbH, Rapporteur: Peter Kiely, PRAC Rapporteur:

Nikica Mirošević Skvrce, "15/04/2020 To: 15/10/2020"

EMEA/H/C/PSUSA/00010458/202011
(susoctocog alpha)
CAPS:
Obizur (EMEA/H/C/002792) (susoctocog alfa), Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski, "12/05/2020 To: 11/11/2020"

EMEA/H/C/PSUSA/00010638/202010
(midostaurin)
CAPS:
Rydapt (EMEA/H/C/004095) (midostaurin), Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "28/10/2019To: 27/10/2020"

EMEA/H/C/PSUSA/00010761/202011
(pegvaliase)
CAPS:
Palynziq (EMEA/H/C/004744) (pegvaliase), BioMarin International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, "22/05/2020 To: 22/11/2020"

EMEA/H/C/PSUSA/00010819/202010
(fostamatinib)
CAPS:
Tavlesse (EMEA/H/C/005012) (fostamatinib), Instituto Grifols, S.A., Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Menno van der Elst, "16/04/2020 To: 16/10/2020"

EMEA/H/C/PSUSA/00010839/202011
(givosiran)
CAPS:
GIVLAARI (EMEA/H/C/004775) (givosiran), Alnylam Netherlands B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Martin Huber, "18/05/2020 To: 18/11/2020"

EMEA/H/C/PSUSA/00010840/202011
(remdesivir)
CAPS:
Veklury (EMEA/H/C/005622) (remdesivir), Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, PRAC Rapporteur: Eva Jirsová, "07/05/2020 To: 06/11/2020"

EMEA/H/C/PSUSA/00010888/202011
(crizanlizumab)

CAPS: **Adakveo** (EMEA/H/C/004874) (crizanlizumab), Novartis Europharm Limited, Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Laurence de Fays, "15/11/2019 To: 14/11/2020"	

B.4. EPARs / WPARs

Bylvay - odevixibat - EMEA/H/C/004691, Orphan Albireo, treatment of progressive familial intrahepatic cholestasis (PFIC), 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.
Icatibant Accord - icatibant - EMEA/H/C/005083 Accord Healthcare S.L.U., treatment of hereditary angioedema, Generic, Generic of Firazyr, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
IMCIVREE - setmelanotide - EMEA/H/C/005089, Orphan Rhythm Pharmaceuticals Limited, Treatment of obesity and the control of hunger associated with deficiencies in the leptin-melanocortin pathway, 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.
Klisyri - tirbanibulin - EMEA/H/C/005183 Almirall, S.A., topical field treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis, 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.
OZAWADE - pitolisant - EMEA/H/C/005117 BIOPROJET PHARMA, Treatment of Excessive Daytime Sleepiness (EDS) in patients with Obstructive Sleep Apnoea (OSA), 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.
Ryeqo - relugolix / estradiol / norethisterone acetate - EMEA/H/C/005267 Gedeon Richter Plc., treatment of uterine fibroids, 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.
Skysona - elivaldogene autotemcel - EMEA/H/C/003690, Orphan, ATMP bluebird bio (Netherlands) B.V, treatment of	For information only. Comments can be sent to the PL in case necessary.

early cerebral adrenoleukodystrophy, New active substance (Article 8(3) of Directive No 2001/83/EC)	
Verquvo - vericiguat - EMEA/H/C/005319 Bayer AG, treatment of symptomatic chronic heart failure, 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

Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0088/G, Orphan Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 20.05.2021.	
ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0021/G Baxalta Innovations GmbH, Rapporteur: Andrea Laslop	
Bemfola - follitropin alfa - EMEA/H/C/002615/II/0029 Gedeon Richter Plc., Rapporteur: Paula Boudewina van Hennik Opinion adopted on 28.05.2021.	Positive Opinion adopted by consensus on 28.05.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Benlysta - belimumab - EMEA/H/C/002015/II/0094 GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder Opinion adopted on 03.06.2021.	Positive Opinion adopted by consensus on 03.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Bridion - sugammadex - EMEA/H/C/000885/II/0041/G Merck Sharp & Dohme B.V., Rapporteur: Outi Mäki-Ikola Opinion adopted on 28.05.2021.	Positive Opinion adopted by consensus on 28.05.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Briviact - brivaracetam - EMEA/H/C/003898/II/0034/G UCB Pharma S.A., Rapporteur: Filip Josephson	
COMIRNATY - covid-19 mRNA vaccine (nucleoside-modified) -	Positive Opinion adopted by consensus on 25.05.2021. The Icelandic and Norwegian CHMP

EMEA/H/C/005735/II/0033/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 25.05.2021.	Members were in agreement with the CHMP recommendation.
COMIRNATY - covid-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0034 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 28.05.2021.	Positive Opinion adopted by consensus on 28.05.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
COMIRNATY - covid-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0035/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 01.06.2021.	Positive Opinion adopted by consensus on 01.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
COMIRNATY - covid-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0039/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 08.06.2021.	Positive Opinion adopted by consensus on 08.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
COMIRNATY - covid-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0043 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/0005 Janssen-Cilag International N.V., Rapporteur: Christophe Focke	
COVID-19 Vaccine Moderna - covid-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0013/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 25.05.2021.	Positive Opinion adopted by consensus on 25.05.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
COVID-19 Vaccine Moderna - covid-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0016/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 04.06.2021.	Positive Opinion adopted by consensus on 04.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
COVID-19 Vaccine Moderna - covid-19 mRNA vaccine (nucleoside-modified) -	Positive Opinion adopted by consensus on 11.06.2021. The Icelandic and Norwegian CHMP

EMEA/H/C/005791/II/0018/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 11.06.2021.	Members were in agreement with the CHMP recommendation.
Cyramza - ramucirumab - EMEA/H/C/002829/II/0041 Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik	
Darzalex - daratumumab - EMEA/H/C/004077/II/0048/G, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 20.05.2021.	
Empliciti - elotuzumab - EMEA/H/C/003967/II/0026 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 03.06.2021. Request for Supplementary Information adopted on 15.04.2021.	Positive Opinion adopted by consensus on 03.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0128 CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus	
Increlex - mecasermin - EMEA/H/C/000704/II/0068/G Ipsen Pharma, Rapporteur: Outi Mäki-Ikola	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0106/G Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani Opinion adopted on 28.05.2021.	Positive Opinion adopted by consensus on 28.05.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0107 Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani Opinion adopted on 03.06.2021.	Positive Opinion adopted by consensus on 03.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kineret - anakinra - EMEA/H/C/000363/II/0084 Swedish Orphan Biovitrum AB (publ), Rapporteur: Kirstine Moll Harboe	
Nepexto - etanercept - EMEA/H/C/004711/II/0002 Mylan IRE Healthcare Limited, Rapporteur: Martina Weise	

Request for Supplementary Information adopted on 10.09.2020.	
Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0108/G Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad	
Nyvepria - pegfilgrastim - EMEA/H/C/005085/II/0002/G Pfizer Europe MA EEIG, Rapporteur: Ondřej Slanař	
Ontruzant - trastuzumab - EMEA/H/C/004323/II/0032 Samsung Bioepis NL B.V., Rapporteur: Karin Janssen van Doorn	
Orfadin - nitisinone - EMEA/H/C/000555/II/0075 Swedish Orphan Biovitrum International AB, Rapporteur: Armando Genazzani Opinion adopted on 28.05.2021. Request for Supplementary Information adopted on 28.01.2021.	Positive Opinion adopted by consensus on 28.05.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Palynziq - pegvaliase - EMEA/H/C/004744/II/0019, Orphan BioMarin International Limited, Rapporteur: Johann Lodewijk Hillege	
Pemetrexed Sandoz - pemetrexed - EMEA/H/C/004011/II/0011/G Sandoz GmbH, Generic, Generic of Alimta, Rapporteur: Bjorg Bolstad	
ReFacto AF - moroctocog alfa - EMEA/H/C/000232/II/0158/G Pfizer Europe MA EEIG, Rapporteur: Kirstine Moll Harboe Request for Supplementary Information adopted on 10.06.2021, 11.03.2021.	Request for supplementary information adopted with a specific timetable.
Remsima - infliximab - EMEA/H/C/002576/II/0101/G Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 03.06.2021.	Request for supplementary information adopted with a specific timetable.
Replagal - agalsidase alfa - EMEA/H/C/000369/II/0112/G Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 10.06.2021.	
Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0053/G CSL Behring GmbH, Rapporteur: Kristina Dunder	
SCENESSE - afamelanotide - EMEA/H/C/002548/II/0037, Orphan Clinuvel Europe Limited, Rapporteur: Janet Koenig Request for Supplementary Information adopted on 28.05.2021.	Request for supplementary information adopted with a specific timetable.
TAKHZYRO - lanadelumab - EMEA/H/C/004806/II/0021/G, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Kristina Dunder	
Tremfya - guselkumab - EMEA/H/C/004271/II/0029/G Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics	
Ultomiris - ravulizumab - EMEA/H/C/004954/II/0015/G Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa	
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and Haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0077 MCM Vaccine B.V., Rapporteur: Christophe Focke Opinion adopted on 28.05.2021.	Positive Opinion adopted by consensus on 28.05.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and Haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0079 MCM Vaccine B.V., Rapporteur: Christophe Focke	
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0016 AstraZeneca AB, Rapporteur: Sol Ruiz Opinion adopted on 27.05.2021. Request for Supplementary Information adopted on 12.05.2021.	Positive Opinion adopted by consensus on 27.05.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0020/G AstraZeneca AB, Rapporteur: Sol Ruiz Request for Supplementary Information adopted on 08.06.2021.	Request for supplementary information adopted with a specific timetable. See 9.1
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0021/G AstraZeneca AB, Rapporteur: Sol Ruiz	See 9.1
Verkazia - ciclosporin - EMEA/H/C/004411/II/0013/G, Orphan Santen Oy, Duplicate, Duplicate of IKERVIS, Rapporteur: Peter Kiely Request for Supplementary Information adopted on 25.03.2021.	
Xofigo - radium-223 - EMEA/H/C/002653/II/0041 Bayer AG, Rapporteur: Janet Koenig Request for Supplementary Information adopted on 10.06.2021.	Request for supplementary information adopted with a specific timetable.
Xofigo - radium-223 - EMEA/H/C/002653/II/0042/G Bayer AG, Rapporteur: Janet Koenig Request for Supplementary Information adopted on 10.06.2021.	Request for supplementary information adopted with a specific timetable.
Zirabev - bevacizumab - EMEA/H/C/004697/II/0019 Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad	
WS1908/G **Hefiya-EMEA/H/C/004865/WS1908/0030/G** **Hyrimoz-EMEA/H/C/004320/WS1908/0030/G** Sandoz GmbH, Lead Rapporteur: Daniela Philadelphy	
WS2037 **Gardasil-EMEA/H/C/000703/WS2037/0092** **Gardasil 9-EMEA/H/C/003852/WS2037/0045** MSD Vaccins, Lead Rapporteur: Kristina Dunder	
WS2044 **Herceptin-EMEA/H/C/000278/WS2044/0171**	

MabThera-EMEA/H/C/000165/WS2044/0184 Roche Registration GmbH, Lead Rapporteur: Jan Mueller-Berghaus	
WS2062 **M-M-RVAXPRO-EMEA/H/C/000604/WS2062/0106** **ProQuad-EMEA/H/C/000622/WS2062/0146** MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 10.06.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2068/G **Blitzima-EMEA/H/C/004723/WS2068/0042/G** **Ritemvia-EMEA/H/C/004725/WS2068/0042/G** **Truxima-EMEA/H/C/004112/WS2068/0045/G** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz Opinion adopted on 10.06.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2074 **Riarify-EMEA/H/C/004836/WS2074/0012** **Trimbow-EMEA/H/C/004257/WS2074/0017** **Trydonis-EMEA/H/C/004702/WS2074/0012** Chiesi Farmaceutici S.p.A., Lead Rapporteur: Janet Koenig	

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

Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0089, Orphan Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, "Submission of long-term follow-up data for clinical trial Echelon-2 (SGN035-014): A randomized, double-blind, placebo-controlled, phase 3 study of brentuximab vedotin and CHP (A+CHP) versus CHOP in the frontline treatment of patients with CD30-positive mature T-cell lymphoma. The study is submitted to fulfil the post-approval-measure MEA 015.1."	
Bridion - sugammadex - EMEA/H/C/000885/II/0039	Positive Opinion adopted by consensus on 03.06.2021. The Icelandic and Norwegian CHMP

Merck Sharp & Dohme B.V., Rapporteur: Outi Mäki-Ikola, "Update of sections 4.8 and 5.1 of the SmPC in order to update information on the safety profile in American Society of Anesthesiologists (ASA) Class 3 or 4 patients (patients with severe systemic disease or patients with severe systemic disease that is a constant threat to life) based on final results from study 8616-P145, an interventional safety study of sugammadex for the reversal of neuromuscular blockage induced by rocuronium or vecuronium in adult ASA 3-4 participants." Opinion adopted on 03.06.2021. Request for Supplementary Information adopted on 09.04.2021.	Members were in agreement with the CHMP recommendation.
Calquence - acalabrutinib - EMEA/H/C/005299/II/0005 AstraZeneca AB, Rapporteur: Filip Josephson, "Submission of the final report from study XS-1468 to further characterise the plasma protein binding of acalabrutinib and its metabolite ACP-5862 in different species."	
Cholib - fenofibrate / simvastatin - EMEA/H/C/002559/II/0029/G Mylan IRE Healthcare Limited, Rapporteur: Alar Irs, "Update of section 4.4 of the SmPC in order to amend the existing warning on immune-mediated necrotizing myopathy (IMNM) and section 4.5 of the SmPC to add drug-drug interaction information with cobicistat, following the update of the company's core data sheet (CCDS) due to new data. Section 4.3 of the SmPC was consequently amended, also to include the necessary cross-references. Section 4.8 of the SmPC was also amended to add immune-mediated necrotizing myopathy with a rare frequency. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list the UK (Northern Ireland) local representative in the Package Leaflet." Opinion adopted on 03.06.2021. Request for Supplementary Information adopted on 09.04.2021.	Positive Opinion adopted by consensus on 03.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0098 UCB Pharma S.A., Rapporteur: Kristina Dunder, "Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and efficacy	Request for supplementary information adopted with a specific timetable.

information on reduction of anterior uveitis flares in patients diagnosed with active axial spondyloarthritis based on the final results from study AS0007 (C-VIEW); this is a multicenter, open-label study to assess the effects of certolizumab pegol on the reduction of anterior uveitis flares in axial spondyloarthritis subjects with a history of anterior uveitis." Request for Supplementary Information adopted on 28.05.2021.	
Dapivirine Vaginal Ring 25 mg - dapivirine - EMEA/H/W/002168/II/0007 International Partnership for Microbicides Belgium AISBL, Rapporteur: Paula Boudewina van Hennik, "Submission of the final report for study report no. 15760.01, conducted to evaluate the antiviral activity of dapivirine on hepatitis E virus (HEV) in vitro. In addition, the SOH took the opportunity to submit data on: antiviral activity of Dapivirine against influenza A and B viruses; the effects of a vaginal film formulation of dapivirine on various species of Lactobacilli present in the vagina; the antitumor activity of dapivirine in glioblastoma cells. With this submission, the post-authorisation measure REC 001 is addressed." Request for Supplementary Information adopted on 28.05.2021.	Request for supplementary information adopted with a specific timetable.
Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0018 Sanofi Pasteur, Rapporteur: Christophe Focke, "Submission of the final report from study DNG10042, listed as a category 3 study in the RMP. This report summarises the findings on the dengue vaccine (Dengvaxia) effectiveness against virologically confirmed symptomatic infection, carried out after the mass vaccination program conducted by the Brazilian state of Paraná from 2016 to 2018." Opinion adopted on 10.06.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Dovprela - pretomanid - EMEA/H/C/005167/II/0004/G, Orphan Mylan IRE Healthcare Limited, Rapporteur: Filip Josephson, "Grouped application including three type II variations under category C.I.4. Update of sections 4.5 and 5.3 of the SmPC based on data from three non-clinical studies: - Assessment of pretomanid as an inhibitor of	Request for supplementary information adopted with a specific timetable.

human OCT2-, OATP1B3-, BCRP-, and P-gp mediated transport; - In vitro evaluation of induction/inhibition of CYP 2C8, 2C9, and 2C19 in human hepatocytes; - A 24-Month Oral (Gavage) Carcinogenicity Study in Rats." Request for Supplementary Information adopted on 10.06.2021, 09.04.2021.	
Dupixent - dupilumab - EMEA/H/C/004390/II/0044 sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus, "C.I.4 – Update section 4.8 of the SmPC to include the long-term safety data of dupilumab in adult patients with moderate to severe AD, following interim results from the OLE study (R668-AD-1225) listed as category 3 study in the RMP." Request for Supplementary Information adopted on 20.05.2021.	
Entyvio - vedolizumab - EMEA/H/C/002782/II/0059/G Takeda Pharma A/S, Rapporteur: Armando Genazzani, "C.I.4 Update of section 4.6 of the SmPC in order to implement information on lactation based on study Vedolizumab-4001 (An Open-Label, Multicenter and Open Enrollment Model, Postmarketing, Milk-Only Lactation Study to Assess Concentration of Vedolizumab in Breast Milk of Lactating Women With Active Ulcerative Colitis or Crohn's Disease Who Are Receiving Vedolizumab Therapeutically). The study aimed to determine the PK parameters of vedolizumab in breast milk and to estimate mean daily infant dosage over the dosing interval through breast milk, and percentage of maternal dose consumed in breast milk by the infants. C.I.4 Update of section 5.2 of the SmPC in order to adjust the values for clearance and serum half-life of vedolizumab IV and SC in subjects with ulcerative colitis and Crohn's disease. The updated pop PK dataset consists of pooled data across 4 phase 3 studies (C13006, C13007, MLN0002SC-3027, MLN0002SC-3031) and 1 open-label extension study (MLN0002SC-3030). In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, to correct minor typographical	Request for supplementary information adopted with a specific timetable.

errors and to bring the PI in line with the latest QRD template version 10.2 rev. 1." Request for Supplementary Information adopted on 10.06.2021.	
Epidyolex - cannabidiol - EMEA/H/C/004675/II/0007, Orphan GW Pharma (International) B.V., Rapporteur: Kirstine Moll Harboe, "Update of section 4.2 of the SmPC in order to add information regarding enteral administration using nasogastric and gastrostomy tubes." Request for Supplementary Information adopted on 25.02.2021, 23.07.2020.	
Erleada - apalutamide - EMEA/H/C/004452/II/0013 Janssen-Cilag International N.V., Rapporteur: Blanca Garcia-Ochoa, "Update of sections 4.6 and 5.3 of the SmPC in order to update information on pregnancy and update non-clinical information following results of a developmental toxicity study in rats." Opinion adopted on 10.06.2021. Request for Supplementary Information adopted on 06.05.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Esbriet - pirfenidone - EMEA/H/C/002154/II/0070 Roche Registration GmbH, Rapporteur: Peter Kiely, "Update of section 4.8 of the SmPC to revise the MeDRA frequency categories for some adverse drug reactions (ADR) and to combine the ADR 'anorexia' with the preferred term 'decreased appetite' based on a safety update report previously submitted in variation EMEA/H/C/2154/II/0021. The package leaflet is updated accordingly. Minor formatting changes were introduced in Annex II, IIIA and IIIB in the list of local representatives." Opinion adopted on 10.06.2021. Request for Supplementary Information adopted on 09.04.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Eylea - aflibercept - EMEA/H/C/002392/II/0067 Bayer AG, Rapporteur: Alexandre Moreau, "C.I.4 - change in the expression of Qualitative and quantitative composition." Request for Supplementary Information adopted on 25.03.2021, 14.01.2021.	

Imfinzi - durvalumab - EMEA/H/C/004771/II/0030/G AstraZeneca AB, Rapporteur: Sinan B. Sarac, "Update of sections 4.2 and 4.4 the SmPC in order to change posology recommendations for management of immune-mediated adverse reactions and amend an existing warning on Immune-mediated type 1 diabetes mellitus to include diabetic ketoacidosis; these changes are based on case studies reports, updated guidelines. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make some minor corrections to section 4.8 of the SmPC."	
Jardiance - empagliflozin - EMEA/H/C/002677/II/0057 Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 4.4 of the SmPC to lower the renal threshold for initiation and use of empagliflozin depending on eGFR, and of the section 5.1 wording about endpoints with reference to EMPA-REG OUTCOME study. The PL is updated accordingly." Request for Supplementary Information adopted on 25.03.2021.	See 9.1
Jinarc - tolvaptan - EMEA/H/C/002788/II/0033/G Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Armando Genazzani, "Update of section 4.5 of the SmPC in order to update the safety information based on final results from study 156-201-00233 and 156-201-00234; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 10.06.2021.	Request for supplementary information adopted with a specific timetable.
Kisqali - ribociclib - EMEA/H/C/004213/II/0028 Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 5.3 of the SmPC in order to update non-clinical information based on results from a 2-year carcinogenicity study in rats." Opinion adopted on 28.05.2021.	Positive Opinion adopted by consensus on 28.05.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Lynparza - olaparib - EMEA/H/C/003726/II/0047	Request for supplementary information adopted with a specific timetable.

AstraZeneca AB, Rapporteur: Alexandre Moreau, "Update of sections 4.8 and 5.1 of the SmPC in order to update safety and efficacy information based on the final analysis of overall survival and safety update from study POLO, a Phase III, randomised, double-blind, placebo-controlled, multicentre study in gBRCAm patients with metastatic pancreatic adenocarcinoma whose disease had not progressed after receiving first-line platinum-based chemotherapy." Request for Supplementary Information adopted on 28.05.2021.	
Oncaspar - pegaspargase - EMEA/H/C/003789/II/0038 Les Laboratoires Servier, Rapporteur: Alexandre Moreau, "Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on the risk of osteonecrosis and to include it as an adverse drug reaction associated with pegaspargase use with an unknown frequency, following review of all available non-clinical, epidemiological and clinical data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2." Request for Supplementary Information adopted on 28.05.2021.	Request for supplementary information adopted with a specific timetable.
Phesgo - pertuzumab / trastuzumab - EMEA/H/C/005386/II/0002 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to support the safety of switching from intravenous to subcutaneous route of administration or vice versa, based on results from study MO40628; this is a Phase II, randomised, open-label, cross-over study to assess preference for intravenous or subcutaneous route of administration in patients with HER2-positive early breast cancer." Request for Supplementary Information adopted on 29.04.2021.	
Revestive - teduglutide - EMEA/H/C/002345/II/0053, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Kirstine Moll Harboe, "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."

SIRTURO - bedaquiline - EMEA/H/C/002614/II/0043, Orphan

Janssen-Cilag International NV, Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC to include reference on the use of bedaquiline as specified in the product information of other medicines used for the treatment of pulmonary tuberculosis (TB) caused by multidrug-resistant Mycobacterium tuberculosis (MDR-TB), based on recent information regarding EU approval of pretomanid, as part of a combination regimen with bedaquiline and linezolid. In addition, the MAH took the opportunity to include an editorial correction in section 5.1 of the SmPC and to update the contact details for the local representative for UK in the package leaflet, in line with QRD version 10.2."

Taltz - ixekizumab - EMEA/H/C/003943/II/0040

Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC with long-term efficacy and safety data in axial spondyloarthritis from study RHBY - A multicenter, long-term extension study of 104 weeks, including a double-blind, placebo-controlled 40-week randomized withdrawal–retreatment period, to evaluate the maintenance of treatment effect of ixekizumab in patients with axial spondyloarthritis."

Request for Supplementary Information adopted on 22.04.2021, 21.01.2021.

Ultomiris - ravulizumab - EMEA/H/C/004954/II/0018

Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa, "To update section 4.2 posology and

method of administration of the SmPC regarding the inclusion of home infusion as an alternative infusion setting for Ultomiris for approved indications (paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS)).”	
Vemlidy - tenofovir alafenamide - EMEA/H/C/004169/II/0032 Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, “Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to add new information on efficacy and safety based on final results from study GS-US-320-4035. This was a phase 2, open-label study to evaluate the safety and efficacy of switching to tenofovir alafenamide from tenofovir disoproxil fumarate and/or other oral antiviral treatment in virologically suppressed chronic hepatitis B subjects with renal and/or hepatic impairment.” Request for Supplementary Information adopted on 10.06.2021.	Request for supplementary information adopted with a specific timetable.
Votrient - pazopanib - EMEA/H/C/001141/II/0067/G Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, “C.I.4 Update of section 4.8 of the SmPC in order to add hepatic failure to the list of adverse reactions reported in patients with soft tissue sarcoma (STS) with the frequency not known. The Package Leaflet is updated accordingly. C.I.4 Update of section 4.4 of the SmPC in order to update the information on studies with pazopanib in combination with other systemic anti-cancer therapies which were terminated early due to concerns over increased toxicity and/or mortality. Type IA A.6 Update of section 5.1 of the SmPC with the updated ATC code L01EX03 released by WHO.” Opinion adopted on 10.06.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Wakix - pitolisant - EMEA/H/C/002616/II/0023/G, Orphan Bioprojet Pharma, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Kirsti Villikka, “Update of the product information based on new clinical data from the open-label, long-term treatment of EDS (with or without cataplexy) in narcolepsy P09-10 HARMONY III study, and the	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

randomised, double-blind, placebo-controlled, drug abuse potential study (P16-02)." Opinion adopted on 10.06.2021. Request for Supplementary Information adopted on 09.04.2021, 11.03.2021, 14.01.2021, 03.09.2020.	
Xarelto - rivaroxaban - EMEA/H/C/000944/II/0079 Bayer AG, Rapporteur: Kristina Dunder, "Update to SmPC section 4.4 following the submission of the final report from the CASSINI study, an interventional phase III study comparing 10 mg rivaroxaban to placebo in the prevention of venous thromboembolism in ambulatory cancer patients. The package leaflet is being updated accordingly." Request for Supplementary Information adopted on 18.02.2021, 03.09.2020.	
Xerava - eravacycline - EMEA/H/C/004237/II/0012 Paion Deutschland GmbH, Rapporteur: Filip Josephson, "Update of sections 5.3 and 6.6 of the SmPC in order to update the results of the Environmental Risk Assessment studies following their completion." Request for Supplementary Information adopted on 28.05.2021, 11.03.2021.	Request for supplementary information adopted with a specific timetable.
Yondelis - trabectedin - EMEA/H/C/000773/II/0063 Pharma Mar, S.A., Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to revise the frequency of ADRs based on a pooled safety analysis. the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2 Rev. 1"	
ZABDENO - ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005337/II/0003 Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 4.8 of the SmPC to add a new warning on febrile seizures in children and to include "febrile seizures" on the list of adverse drug reactions (ADRs) with frequency rare, based on the review of febrile seizures post-marketing cases received within the GMS Global Safety	Request for supplementary information adopted with a specific timetable.

Database. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to replace the local representative for the UK with a local representative for the territory of Northern Ireland as a consequence of the Northern Ireland Protocol." Request for Supplementary Information adopted on 28.05.2021.	
Zostavax - varicella vaccine (live) - EMEA/H/C/000674/II/0132 MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Outi Mäki-Ikola, "Submission of the final study report from the post-licensure observational study of the long-term effectiveness of Zostavax (Protocol 024) listed as category 3 study in the RMP. Consequently, section 5.1 of the SmPC was updated. With this application, the post-authorisation measure REC 23 is fulfilled. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and include editorial corrections in annex A." Opinion adopted on 03.06.2021. Request for Supplementary Information adopted on 09.04.2021.	Positive Opinion adopted by consensus on 03.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1874/G **Advagraf-EMEA/H/C/000712/WS1874/0058/G** **Modigraf-EMEA/H/C/000954/WS1874/0036/G** Astellas Pharma Europe B.V., Lead Rapporteur: Jayne Crowe, "C.I.4 Update of sections 4.4 and 4.5 of the SmPC on the drug-drug interaction with CYP3A4 based on a comprehensive review of available data. Section 4.5 of the SmPC is also updated to include impact of direct acting antiviral therapy. C.I.z Update of section 4.8 of the SmPC to add posterior reversible encephalopathy syndrome as an adverse reaction. The MAH took also the opportunity to change the SOC for febrile neutropenia from General disorders and administration site conditions to Blood and lymphatic system disorders in section 4.8 of the SmPC and to update the instruction for handling of the product in section 6.6 of the SmPC. The Package Leaflet is updated accordingly."	

Request for Supplementary Information adopted on 25.02.2021, 17.09.2020.	
WS1989 **Combivir-EMEA/H/C/000190/WS1989/0100** **Epivir-EMEA/H/C/000107/WS1989/0116** **Trizivir-EMEA/H/C/000338/WS1989/0121** ViiV Healthcare B.V., Lead Rapporteur: Jean-Michel Race, "Update of section 4.9 of the SmPC to revise the overdose information." Request for Supplementary Information adopted on 11.03.2021.	
WS2008/G **Mekinist-EMEA/H/C/002643/WS2008/0046/G** **Tafinlar-EMEA/H/C/002604/WS2008/0051/G** Novartis Europharm Limited, Lead Rapporteur: Paula Boudewina van Hennik, "C.I.4 Update of section 5.1 of the Mekinist (trametinib) and Tafinlar (dabrafenib) SmPC to include the 5-years efficacy results from study Phase III study COMBI-AD. This is a two-arm, randomized, double-blind Phase III study of dabrafenib in combination with trametinib versus two placebos in the adjuvant treatment of melanoma after surgical resection in adult patients with a BRAF V600 mutation. Type IA A.6 update the SmPC with the updated ATC codes released by WHO" Opinion adopted on 03.06.2021.	Positive Opinion adopted by consensus on 03.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2039 **Genvoya-EMEA/H/C/004042/WS2039/0076** **Stribild-EMEA/H/C/002574/WS2039/0116** **Tybost-EMEA/H/C/002572/WS2039/0058** Gilead Sciences Ireland UC, Lead Rapporteur: Bruno Sepodes, "Update of section 4.5 of the SmPC to add new information about the drug-drug interactions between cobicistat containing products (Genvoya, Tybost and Stribild) and corticosteroids, based on post-marketing data. Furthermore, the MAH took the opportunity to bring the Tybost Product Information in line with version 10.2 of the QRD template and update the list of local representatives. Moreover, minor editorial updates and corrections have been introduced throughout the Product Information of all three products."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 03.06.2021.	
WS2048 **Kalydeco-EMEA/H/C/002494/WS2048/0101** **Symkevi-EMEA/H/C/004682/WS2048/0030** Vertex Pharmaceuticals (Ireland) Limited, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Rhea Fitzgerald, "Update of the Product information to provide the final clinical study report (CSR) Part A of Study VX17- 661-116 (A Phase 3, Open-label, Rollover Study to Evaluate the Safety and Efficacy of Long-term Treatment With Tezacaftor in Combination With Ivacaftor in Subjects With Cystic Fibrosis Aged 6 Years and Older, Homozygous or Heterozygous for the F508del-CFTR Mutation). Consequently, the SmPC sections 4.2, 4.5, 4.8 and 5.1 and the package leaflet are updated accordingly. The RMP is also updated."	
WS2052/G **Stayveer-EMEA/H/C/002644/WS2052/0034/G** **Tracleer-EMEA/H/C/000401/WS2052/0099/G** Janssen-Cilag International NV, Lead Rapporteur: Alexandre Moreau, "Grouped variation application; • Type II variation C.I.4: Update of section 4.6 of the SmPC to correct the information related to male fertility based on a review of study AC-052-402 carried out by the MAH. • Type IA variation A.7 In addition, the WSA took the opportunity to update the list of local representatives in the Package Leaflet. The WSA also took the opportunity to correct some errors in the national translations." Opinion adopted on 10.06.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2054 **Enerzair Breezhaler-EMEA/H/C/005061/WS2054/0003** **Zimbus Breezhaler-EMEA/H/C/005518/WS2054/0003** Novartis Europharm Limited, Lead Rapporteur: Peter Kiely, "Update of section 5.1. Pharmacodynamic properties, based on the final	

results from the ARGON study a Phase 3b, multicenter, partially-blinded, randomized, 24-week, parallel-group, non-inferiority, open-label active controlled study comparing the efficacy and safety of QVM149 with a free triple combination of salmeterol/fluticasone + tiotropium in patients with uncontrolled asthma."	
WS2066 **Lacosamide UCB-EMEA/H/C/005243/ WS2066/0010** **Vimpat-EMEA/H/C/000863/WS2066/0092** UCB Pharma S.A., Lead Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to add dyskinesia to the list of adverse drug reactions (ADRs) with frequency uncommon following the outcome of continuous safety signal assessments of the relevant reported clinical and post-marketing cases. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the PI, to bring it in line with the latest QRD template version 10.2 and relevant guidelines and to update the details of the UK local representative in the PL." Opinion adopted on 10.06.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2085 **Kaftrio-EMEA/H/C/005269/WS2085/0014** **Kalydeco-EMEA/H/C/002494/WS2085/ 0099** Vertex Pharmaceuticals (Ireland) Limited, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Martin Huber, "Update of SmPC sections 4.4 and 4.8 following cases of liver failure in the post- marketing setting. The PL is updated accordingly. The RMP version 3.1 is submitted for Kaftrio."	

B.5.3. CHMP-PRAC assessed procedures

Accofil - filgrastim - EMEA/H/C/003956/II/0046/G Accord Healthcare S.L.U., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka"- Type II B.II.e.5.c- To introduce a new presentation, Accofil 12 MU/0.2 mL Solution for Injection or infusion in Pre-filled Syringe, to cater to low-weight patients as the clinical	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

administration of Filgrastim is based on body weight. The same concentration in mcg/ mL as for the already approved presentation of 300 mcg/ 0.5 mL (30 MU/0.5 ml) is obtained, i.e. 600 mcg/ mL. RMP and PI are updated to include this new strength.
- Type II B.II.e.5.c- To introduce a new presentation, Accofil 70 MU/0.73 mL Solution for Injection or infusion in Pre-filled Syringe, based on the dosing regimen to avoid multiple administrations. The same concentration in mcg/ mL as for the already approved presentation of 480 mcg/ 0.5 mL (48 MU/0.5 ml) is obtained, i.e. 960 mcg/ mL. RMP and PI are updated to include this new strength."
Opinion adopted on 10.06.2021.
Request for Supplementary Information adopted on 09.04.2021.

Adenuric - febuxostat - EMEA/H/C/000777/II/0061

Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop, PRAC Rapporteur: Jan Neuhauser, "C.I.4 - Update of sections 4.4, 4.8 and 5.1 of the SmPC based on the final results from study FAST (Febuxostat versus Allopurinol Streamlined Trial) listed as a category 3 study in the RMP; this is an interventional study investigating the cardiovascular safety of febuxostat in comparison with allopurinol in patients with chronic symptomatic hyperuricaemia. The Package Leaflet is updated accordingly. The RMP version 8.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to update the warning relevant to the content of sodium according to the Annex to the European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use'."

BLINCYTO - blinatumomab - EMEA/H/C/003731/II/0039, Orphan

Amgen Europe B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Eva Jirsová, "C.I.13 Submission of the final report from study 20180138 classified as category 3 PASS in the RMP. This is an observational clinical study to update the OS Kaplan-Meier probability

estimates and the plot last reported in the randomized Phase 3 blinatumomab 00103311 study." Request for Supplementary Information adopted on 11.03.2021.	
BYETTA - exenatide - EMEA/H/C/000698/II/0075 AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of sections 4.2 and 5.1 of the SmPC based on the results of study H8O-MC-GWBQ (assessed by CHMP as part of PAM P46 048); a 28-week, randomised, double-blind, placebo-controlled study to evaluate the safety and efficacy of exenatide twice daily in 120 patients aged 10 to 17 years, and study 2993-124; a randomised, single-blind, placebo-controlled, dose-rising study to evaluate the PK, PD and tolerability of exenatide in adolescent patients)." Opinion adopted on 10.06.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Caprelsa - vandetanib - EMEA/H/C/002315/II/0043 Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, "C.I.4 Update of section 5.1 of the SmPC in order to update pharmacodynamic information based on interim results from study D4200C00104, listed as a specific obligation in the Annex II. This is an observational study (including a retrospective arm to evaluate the Benefit/Risk of vandetanib (Caprelsa) 300 mg in RET mutation negative and RET mutation positive patients with symptomatic, aggressive, sporadic, unresectable, locally advanced/metastatic thyroid cancer (MTC)), to confirm the efficacy and safety of Caprelsa in RET-negative patients with the aim to fulfil SOB001 and convert Caprelsa from conditional to normal Marketing Authorization. In addition the MAH takes to opportunity to rectify the Dutch translation of the Caprelsa Product Information." Request for Supplementary Information adopted on 28.05.2020.	See 9.1
Cometriq - cabozantinib - EMEA/H/C/002640/II/0044, Orphan Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of the annex IIE and SmPC section	See 9.1

5.1 to remove the specific obligation (SOB 001) and the reference to the conditional approval based on the final results from the study XL184-401 (EXAMINER), a randomised, double-blind study to evaluate the efficacy and safety of cabozantinib (XL184) at 60 mg/day compared to a 140 mg/day in progressive, metastatic medullary thyroid cancer patients. The package leaflet is updated accordingly. The updated RMP version 5.4 has also been submitted. With this submission, the MAH is proposing to revert from conditional marketing authorisation to full marketing authorisation. Additionally, the MAH took the opportunity to bring the Product Information in line with the latest QRD template version 10.2 Rev 1, to add the sodium content in the Summary of Product Characteristics and Package Information Leaflet in line with the guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' and update details of local representatives."	
Cosentyx - secukinumab - EMEA/H/C/003729/II/0076 Novartis Europharm Limited, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Eva A. Segovia, "C.I.4 - Update of sections 4.2 and 5.1 of the SmPC in order to introduce a new posology regimen for adult plaque psoriasis patients and psoriatic arthritis patients with concomitant moderate to severe plaque psoriasis based on the final results study CAIN457A2324 and exposure-response modelling; this is a randomized, double-blind, multicenter study assessing short (16 weeks) and long-term efficacy (up to 1 year), safety, and tolerability of sub-cutaneous secukinumab in subjects of body weight 90 kg or higher with moderate to severe chronic plaque-type psoriasis; the Package Leaflet is updated accordingly. The RMP version 9.0 has also been submitted."	See 9.1
Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0016/G Sanofi Pasteur, Rapporteur: Christophe Focke, PRAC Rapporteur: Sonja Hrabcik, "Update of section 4.5. of the SmPC to include coadministration data on Gardasil/Cervarix/Adacel from CYD67, CYD71	Request for supplementary information adopted with a specific timetable.

and CYD66 final study reports respectively (final reports from 3 PAM MEA studies listed as category 3 studies in the RMP); these studies are dedicated to immunogenicity and safety of the concomitant administration; the Package Leaflet is updated accordingly. The RMP version 6.1. has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 10.06.2021, 11.02.2021.	
Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0044/G, Orphan Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Annika Folin, "C.I.4 Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include the administration of obinutuzumab as a short duration infusion (SDI) of approximately 90 minutes in patients with Follicular Lymphoma (FL), based on the end of induction safety and efficacy data from the ongoing Phase IV study MO40597 (GAZELLE); the Package Leaflet is updated accordingly. The RMP version 8.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. C.I.11.z Update of RMP version 8.0 to: - change the due date for the submission of the final CSR for Category 3 study BO21223 (GALLIUM); - remove important identified risks as per the PRAC Assessment Report for the PSUR covering period 01Nov2018 to 30Oct2019 (Procedure no. EMEA/H/C/PSUSA/00010279/201910); - correction of clinical cut-off dates and trial exposure data from previously conducted studies"	
Herceptin - trastuzumab - EMEA/H/C/000278/II/0168 Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.2 and 4.4 of the SmPC (SC formulation) in order to modify the administration instructions by shortening observation time and including mild injection-related symptoms management based on final results from study SafeHER (MO28048)	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

listed as a category 3 study in the RMP; this is a Phase III prospective, two Cohort nonrandomized, multicentre, multinational, open label study to assess the safety of assisted- and self-administered subcutaneous Herceptin as adjuvant therapy in patients with operable HER2- positive early breast cancer. The Package Leaflet is updated accordingly. Additionally, the MAH took the opportunity to introduce minor editorial updates throughout the PI. The RMP version 21.1 has also been submitted." Opinion adopted on 10.06.2021. Request for Supplementary Information adopted on 11.02.2021.	
Jakavi - ruxolitinib - EMEA/H/C/002464/II/0050 Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "Update of sections 4.2 and 5.1 of the SmPC in order to update the posology and the method of administration as well as to include the A2201/EXPAND study CINC424A2201 (referred to as A2201 or "EXPAND" study). The changes are based on final results of a category 3 clinical study, phase Ib study to fulfil an RMP post-approval commitment. This is a dose-finding study intended to establish the maximum safe starting dose (MSSD) of ruxolitinib tablets administered orally to patients with MF in the previous unstudied population of patients who had baseline platelet counts ≥50×109/L and <100×109/L. The Package Leaflet is updated accordingly. The RMP version 12 has also been submitted based on the results of study A2201 (category 3, additional pharmacovigilance activity), the review of safety concerns in compliance with the Good Pharmacovigilance Practices Module V, Revision 2, as well as recent PRAC outcome on PSUR (Procedure no.: EMEA/H/C/PSUSA/00010015/202002, CHMP Opinion dated 15-Oct-2020)." Request for Supplementary Information adopted on 28.01.2021.	
Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0055 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark,	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

"Submission of a final Clinical Study Report of study MO28231 (KAMILLA) fulfil a category 3 Additional Pharmacovigilance Activity in the Risk Management Plan to address the following safety concerns: Ventricular Dysfunction, Safety in Elderly Patients and the Use of a non-validated HER2 test. The Kadcyla EU RMP (version 13) has been updated to remove the commitment for this study and the safety concern "use of non-validated HER2 test"." Opinion adopted on 10.06.2021.	
Lorviqua - lorlatinib - EMEA/H/C/004646/II/0013 Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to include hypertension and hyperglycaemia as new adverse drug reactions (ADRs) with frequency common and very common respectively together with recommended dose modifications and warnings, based on data from Phase 3 study B7461006, comparing lorlatinib versus crizotinib for the first line treatment of advanced ALK-positive NSCLC. In addition, the pooled safety dataset has been updated to include data from studies B7461001, a Phase 1/2 open-label, multiple-dose, dose-escalation, safety, pharmacokinetic, pharmacodynamic, and anti-tumour efficacy exploration study and B7461006. As a consequence, the frequencies of ADRs have been updated in section 4.8 of the SmPC and existing warnings on Hyperlipidaemia and Lipase and amylase increase have been amended. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted." Request for Supplementary Information adopted on 25.02.2021.	
Mavenclad - cladribine - EMEA/H/C/004230/II/0020 Merck Europe B.V., Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "C.I.4 Type II Update of sections 4.2 and 4.4 of the SmPC in order to change posology recommendations by adding an advice on preventive measures to avoid liver injury and to add a new warning on liver function and liver injury based on a review of	Request for supplementary information adopted with a specific timetable.

post-approval data in MAH's safety database, non-clinical and clinical trial data and scientific literature (cladribine and liver injury and epidemiological data on hepatic injury in MS). The Package Leaflet is updated accordingly. The RMP version 1.6 has also been submitted." Request for Supplementary Information adopted on 10.06.2021.	
Natpar - parathyroid hormone - EMEA/H/C/003861/II/0029, Orphan Shire Pharmaceuticals Ireland Limited, 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."	See 9.1
Nplate - romiplostim - EMEA/H/C/000942/II/0079 Amgen Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "Update of section 4.8 of the SmPC to add Anaphylactic reaction to the list of adverse drug reactions (ADRs) with frequency to be determined in the evaluation of the variation. The package leaflet has been amended accordingly." Request for Supplementary Information adopted on 06.05.2021.	
Rinvoq - upadacitinib - EMEA/H/C/004760/II/0009 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Nikica Mirošević Skvrce, "C.I.4 - Update of sections 4.4 and 5.1 of the SmPC in order to amend the existing warning on vaccination based on the final results from vaccination substudy (within study M13-538) listed as a	

category 3 study in the RMP; this is an open-label extension to assess the impact of upadacitinib treatment with a stable background of methotrexate on immunological responses following administration of a pneumococcal vaccine in rheumatoid arthritis patients. The RMP version 5.0 has also been submitted." Request for Supplementary Information adopted on 25.03.2021.	
Rydapt - midostaurin - EMEA/H/C/004095/II/0018/G, Orphan Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "A.6 - Administrative change - Change in ATC Code/ATC Vet Code C.I.4, Update 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 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 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 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 SmPC in section 4.2 in order to amend posology instructions, section 4.4 to	

amend an existing warning and section 5.2 to update pharmacokinetic information for patients with severe hepatic impairment, based on final results from study CPKC412A2116 listed as category 3 study in the RMP. This is an open label, multiple dose study to evaluate the PK of midostaurin in subjects with mild, moderate and severe hepatic impairment compared to matched healthy subjects; (MEA010)
The RMP version 6.0 has also been submitted. In addition, MAH takes this opportunity to introduce minor changes to edit the wording related to the ethanol excipient in the Package Leaflet, according the Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (SANTE-2017-11668), by rounding the volume of alcohol to the next integer number, i.e. from 16.9 to 17 ml."

Steglujan - ertugliflozin / sitagliptin - EMEA/H/C/004313/II/0015

Merck Sharp & Dohme B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC for Steglujan in order to update clinical information following final results from the VERTIS CV study (protocol 8835-004/B1521021) listed as a category 3 study in the RMP. This is a multi-centre, multi-national, randomised, double-blind, placebo-controlled study to evaluate the effect of ertugliflozin on cardiovascular risk in adult patients with type 2 diabetes and established atherosclerotic cardiovascular disease. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to include an editorial change in section 4.1 of the SmPC."
Request for Supplementary Information adopted on 25.02.2021.

Tasigna - nilotinib - EMEA/H/C/000798/II/0109

Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, "Update of SmPC sections 4.4, 4.8 and 5.1 based on the 5-year follow up data from the study CAMN107A2203 in paediatric patients. Annex II D has been updated to reflect the fulfilment of the obligation to conduct the post-

authorisation efficacy study (PAES). The Package leaflet is updated accordingly. In addition, the Tasigna EU RMP version 24.0 has been updated to remove the corresponding additional pharmacovigilance activity and the missing information 'Long-term follow-up in paediatric patients'." Request for Supplementary Information adopted on 06.05.2021.	
Tremfya - guselkumab - EMEA/H/C/004271/II/0028 Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, "C.I.4 Update of sections 4.8 and 5.1 of the SmPC in order to update the EU product information with 5 years data from the final study reports of pivotal psoriasis studies PSO3001 and PSO3002 listed as additional PV activities (category 3 studies) in the RMP; in the long term extension part of these studies subjects received open-label guselkumab q8w, starting at Week 52 in PSO3001 and at Week 76 in PSO3002, with the last dose at Week 252 and the last safety follow-up visit at Week 264. The RMP version 8.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 10.06.2021.	Request for supplementary information adopted with a specific timetable.
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0002 AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, "Update of sections 4.8, 5.1, 6.3 and 6.6 of the SmPC in order to update the safety profile and to add the adverse drug reactions: abdominal pain and urticaria with frequency uncommon; and pain in extremity and influenza-line illness with frequency common in section 4.8; based on the primary analysis (7th December data cut-off (post data-base lock) from the pooled pivotal studies (COV001, COV002, COV003 and COV005) that supported the conditional marketing authorisation and are listed as a specific obligation in the Annex II. The update on section 5.1 is editorial. The update in sections 6.3 and 6.6 relates to a rewording of	

the information of the shelf-life for opened vials for clarity purposes. The Package Leaflet and Labelling are updated accordingly. The MAH is taking the opportunity to update the product information in relation to the "genetically modified organisms" information. The RMP version 2.1 has also been submitted." Request for Supplementary Information adopted on 22.04.2021.	
Xeljanz - tofacitinib - EMEA/H/C/004214/II/0027 Pfizer Europe MA EEIG, Rapporteur: Armando Genazzani, PRAC Rapporteur: Liana Gross-Martirosyan, "Update of sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of Xeljanz 11 mg prolonged-release tablets SmPC in order to include the treatment of active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have been intolerant to a prior disease modifying antirheumatic drug therapy; as an alternative to the immediate release film-coated tablets; section 4.2 of Xeljanz film-coated tablets is also updated to include switching with the prolonged-release tablet in the treatment of PsA. The Package Leaflet is updated accordingly. The RMP version 13.1 has also been submitted." Request for Supplementary Information adopted on 25.03.2021, 10.12.2020.	See 9.1
WS2069/G **Edistride-EMEA/H/C/004161/WS2069/0048/G** **Forxiga-EMEA/H/C/002322/WS2069/0067/G** AstraZeneca AB, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Annika Folin, "Grouped submission of final study reports of the DETERMINE studies D169EC00001 and D169EC00002, listed as category 3 PASS, assessing the risk of lower limb amputation. Both studies are international, Multicentre, parallel-group, randomised, double-blind, placebo-controlled, Phase III Study evaluating the effect of Dapagliflozin on Exercise capacity: Study D169EC00001 in patients with heart failure with preserved ejection fraction (HFpEF); Study D169EC00002 in patients with heart failure with reduced ejection fraction (HFrEF). The RMP version 25 was agreed during the	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

procedure. The studies are proposed to be removed from the Post-Authorisation Development Plan in the RMP for Forxiga and Edistride." Opinion adopted on 10.06.2021.	

B.5.4. PRAC assessed procedures

PRAC Led **Beovu - brolucizumab - EMEA/H/C/004913/II/0008** Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC in order to include the description of intraocular inflammation, based on final results from a non-interventional retrospective real-world evidence study conducted in patients with neovascular (wet) age-related macular degeneration (nAMD) to better understand the incidence of adverse events/safety signal after initiating treatment with brolucizumab for up to 6 months." Request for Supplementary Information adopted on 10.06.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0099** UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from study (RA0020 - RABBIT) listed as a category 3 study in the RMP. This is a nationwide prospective observational cohort study in Germany on the long-term safety and effectiveness of bDMARDs in rhumatoid arthritis (RA). In addition, this submission includes a safety analysis across the 4 completed RA registries (ARTIS, NDB, BSRBR and RABBIT) as requested by EMA/PRAC in the final assessment report of Procedures EMEA/H/C/001037/II/0072, EMEA/H/C/001037/II/0081, and EMA/H/C/001037/II/0087. Based on this, revisions to the RMP summary of safety concerns and consequently the pharmacovigilance plan are proposed in line	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

with GVP Module V Rev.2. An updated RMP version 19.1 is included." Opinion adopted on 10.06.2021.	
PRAC Led **Dacogen - decitabine - EMEA/H/C/002221/II/0044, Orphan** Janssen-Cilag International N.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "Update of section 4.6 of the SmPC in order to update information on fertility, pregnancy and lactation, following PSUR procedure PSUSA/00009118/202005; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives for Italy in the Package Leaflet and to include some editorial changes in the PI to align with standard English spelling." Opinion adopted on 10.06.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Faslodex - fulvestrant - EMEA/H/C/000540/II/0073** AstraZeneca AB, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Filip Josephson, "Update of the RMP version 13 for fulvestrant to remove the additional risk minimisation measures for important identified risks and reclassifiy safety concerns based on Good Pharmacovigilance Practices (GVP) module V, risk management systems (revision 2) guidelines as requested by PRAC as a part of PRAC PSUR assessment report, procedure number EMEA/H/C/PSUSA/00001489/202004 covering the period 26/04/2017 to 25/04/2020." Opinion adopted on 10.06.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **HyQvia - human normal immunoglobulin - EMEA/H/C/002491/II/0070/G** Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "C.I.4 (Type II) - Update of section 4.6 of the SmPC in order to update information on pregnancy and breast-feeding based on the final results from study 161301 listed as a category 3 study in the RMP; this is an observational study to collect long-term safety data from women treated with HyQvia.	Request for supplementary information adopted with a specific timetable.

The package leaflet has been updated accordingly. RMP version 12.0 has also been submitted. In addition, the MAH took the opportunity to implement minor corrections and editorial changes to the SmPC. C.I.11.b (Type II) – Submission of an updated RMP version 12.0 to update the educational material section Part V.2, additional Risk Minimisation Measures, for HyQvia. The change was requested by the PRAC in the outcome of the PSUSA procedure EMEA/H/C/PSUSA/00001633/202005." Request for Supplementary Information adopted on 10.06.2021.	
PRAC Led **InductOs - dibotermin alfa - EMEA/H/C/000408/II/0100** Medtronic BioPharma B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Pieter de Graeff, "C.I.11.b - Submission of an updated RMP version 2.1 in order to submit the final study report from study EUPAS32916 listed as category 3 study in the RMP. This is an observational study to evaluate the effectiveness of additional Risk Minimisation Measures for InductOs. In addition, the MAH took the opportunity to submit the study protocol for study EUPAS32916 that was agreed by PRAC." Request for Supplementary Information adopted on 10.06.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Kineret - anakinra - EMEA/H/C/000363/II/0078** Swedish Orphan Biovitrum AB (publ), Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Kirstine Moll Harboe, "Submission of the final report from study (Sobi-ANAKIN-201) listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study to evaluate the safety of Kineret in the treatment of Cryopyrin Associated Periodic Syndromes (CAPS) in routine clinical care with regard to serious infections, malignancies, injection site reactions, allergic reactions and medication errors, including reuse of syringe.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

The RMP version 5.4 has been updated to reflect completion of this study. In addition, the RMP is updated to include information about a completed paediatric study (Sobi.ANAKIN-301) assessed as per Article 46 of Reg No 1901/2006 (EMEA/H/C/000363/P46/031). This was a randomised, double-blind, placebo-controlled, multicenter, phase 3 study which evaluated the efficacy, the safety, pharmacokinetics and immunogenicity of anakinra as compared to placebo in newly diagnosed Still's disease patients (including systemic juvenile idiopathic arthritis [SJIA] and adult-onset Still's disease [AOSD]).” Opinion adopted on 10.06.2021. Request for Supplementary Information adopted on 11.02.2021.	
PRAC Led **Lojuxta - lomitapide - EMEA/H/C/002578/II/0047** Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, “To introduce 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.” Request for Supplementary Information adopted on 10.06.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Mavenclad - cladribine - EMEA/H/C/004230/II/0015** Merck Europe B.V., Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, PRAC-CHMP liaison: Bruno Sepodes, “Submission of an updated RMP version 1.5.1 in order to align to the RMP template Rev. 2. In addition, the MAH took the opportunity to include long-term safety data	Request for supplementary information adopted with a specific timetable.

from the completed PREMIERE registry and remove the completed study from the pharmacovigilance plan, update of the status of the post-approval safety studies CLARION and CLEAR and update the RMP with the most recent post-approval safety data from the PBRER." Request for Supplementary Information adopted on 10.06.2021, 06.05.2021, 14.01.2021.	
PRAC Led **Norvir - ritonavir - EMEA/H/C/000127/II/0161** AbbVie Deutschland GmbH & Co. KG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 7.1 in order to comply with revision 2 of the template. In addition, the MAH reviewed the information contained in the Norvir RMP and made the following updates: -Removal of important identified risk of toxicity of Norvir oral solution in preterm neonates -Removal of missing information regarding use of ritonavir in elderly patients -Analysis of the Antiretroviral Pregnancy Registry (APR) data will be provided with the ritonavir PSUR" Request for Supplementary Information adopted on 10.06.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Orphacol - cholic acid - EMEA/H/C/001250/II/0040, Orphan** Laboratoires CTRS, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Sofia Trantza, PRAC-CHMP liaison: Konstantinos Markopoulos, "Submission of an updated RMP version 4.0 to bring it in line with the new RMP template. At the same time, the wording of the additional risk minimisation measures has been updated and the already approved protocol for the ongoing patient surveillance database study has been included in the RMP." Opinion adopted on 10.06.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0126/G** Boehringer Ingelheim International GmbH, Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP	Request for supplementary information adopted with a specific timetable.

liaison: Kirstine Moll Harboe, "C.I.13: Submission of the final report from drug utilisation study, 1160.129, GLORIA AF. This is a three-phase, international, multicenter, prospective, observational registry program in patients with newly diagnosed non-valvular atrial fibrillation (NV AF) at risk for stroke. The objective of the registry program is to investigate patient characteristics influencing the choice of antithrombotic treatment for the prevention of stroke in NV AF patients globally and to collect data from clinical practice settings on important outcome events of antithrombotic treatments for the prevention of stroke. C.I.13: Submission of the final report from drug utilisation study, 1160.136, EU GLORIA AF listed as a category 3 study in the RMP. This is a three-phase, international, multicenter, prospective, observational registry program in patients with newly diagnosed non-valvular atrial fibrillation (NV AF) at risk for stroke. The objective of the registry program is to investigate patient characteristics influencing the choice of antithrombotic treatment for the prevention of stroke in NV AF patients from participating countries in EU/EEA Member States and to collect data from clinical practice settings on important outcome events of antithrombotic treatments for the prevention of stroke. The RMP version 39 has also been submitted." Request for Supplementary Information adopted on 10.06.2021.	
PRAC Led **Revatio - sildenafil - EMEA/H/C/000638/II/0091** Upjohn EESV, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 7.0 in order to update the summary of safety concerns in line with GVP module V rev 2 guidelines. Consequently, the educational programme for the risk of hypotension is proposed to be terminated." Opinion adopted on 10.06.2021. Request for Supplementary Information adopted on 06.05.2021, 14.01.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Shingrix - herpes zoster vaccine**	Request for supplementary information adopted with a specific timetable.

(recombinant, adjuvanted) - EMEA/H/C/004336/II/0045 GlaxoSmithkline Biologicals SA, Rapporteur: Christophe Focke, PRAC Rapporteur: Sonja Hrabcik, PRAC-CHMP liaison: Andrea Laslop, "Update of section 4.4 of the SmPC in order to add a new warning on an increased risk of Guillain-Barré Syndrome (GBS) after vaccination with Shingrix observed in a post-marketing observational study in individuals aged 65 years or older. The RMP version 5.1 has also been submitted. In addition, the MAH took the opportunity to make some editorial changes to the SmPC and to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 10.06.2021.	
PRAC Led **Zevalin - ibritumomab tiuxetan - EMEA/H/C/000547/II/0053** Ceft Biopharma s.r.o., Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "Update of the RMP in line with the new GVP module" Opinion adopted on 10.06.2021. Request for Supplementary Information adopted on 09.04.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
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 13.0) 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	Request for supplementary information adopted with a specific timetable.

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 study 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 study 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 (added as a new FDA-imposed PASS). The clinical study report (CSR) for study A0081359 is included in the submission." Request for Supplementary Information adopted on 10.06.2021, 01.10.2020.	
PRAC Led **WS2043** **OPDIVO-EMEA/H/C/003985/WS2043/0102** **Yervoy-EMEA/H/C/002213/WS2043/0087** Bristol-Myers Squibb Pharma EEIG, Lead PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "To provide an updated RMP to change the final due date for the PAES study CA2098Y8 (a Phase 3b, Randomized, Double-blind Study of Nivolumab Combined with Ipilimumab versus Nivolumab Monotherapy for Patients with Previously Untreated Advanced Renal Cell Carcinoma and Intermediate- or Poor-Risk Factors). In addition, the marketing authorisation holder has taken the opportunity to include a minor editorial revision in the French translation of the PI as previously agreed with the Agency." Opinion adopted on 10.06.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS2057** **Aerius-EMEA/H/C/000313/WS2057/0098** **Azomyr-EMEA/H/C/000310/WS2057/0102** **Neoclarityn-EMEA/H/C/000314/WS2057/0096**	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Organon N.V., Duplicate, Duplicate of Allex (SRD), Azomyr, Opulis (SRD), Lead Rapporteur: Christophe Focke, Lead PRAC Rapporteur: Laurence de Fays, PRAC-CHMP liaison: Karin Janssen van Doorn, "Submission of an updated RMP version 2.1 in order to align with GVP Module V (rev 2) template which includes updates to the list of safety concerns and reflects the completion of a post-authorisation safety study listed as category 3 (A Nordic register-based study which studied the association between the use of desloratadine and risk of seizures, supraventricular tachycardia, and atrial fribrillation or flutter: EUPAS15038) assessed in EMEA/H/WS1655." Opinion adopted on 10.06.2021.	
PRAC Led **WS2064** **Nuwiq-EMEA/H/C/002813/WS2064/0043** **Vihuma-EMEA/H/C/004459/WS2064/0024** Octapharma AB, Lead PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "To provide an updated RMP to remove the completed studies GENA-05 and GENA-15. As a consequence, in the section 'Missing Information' the following safety concerns have been removed: "Safety in previously untreated patients", "Children < 2 years" and "Immune tolerance induction". No new safety concerns were added. In addition, the RMP has been updated to GVP Module V Rev.2." Request for Supplementary Information adopted on 10.06.2021.	Request for supplementary information adopted with a specific timetable.

B.5.5. CHMP-CAT assessed procedures

Zynteglo - betibeglogene autotemcel - EMEA/H/C/003691/II/0025, Orphan, ATMP bluebird bio (Netherlands) B.V, Rapporteur: Carla Herberts, CHMP Coordinator: Paula Boudewina van Hennik	

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

WS1930 **Hexacima-EMEA/H/C/002702/WS1930/0107** **Hexaxim (SRD)-EMEA/H/W/002495/WS1930/0112** **Hexyon-EMEA/H/C/002796/WS1930/0111** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 28.05.2021. Request for Supplementary Information adopted on 25.02.2021, 03.12.2020.	Positive Opinion adopted by consensus on 28.05.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2002 **Filgrastim Hexal-EMEA/H/C/000918/WS2002/0061** **Zarzio-EMEA/H/C/000917/WS2002/0062** Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 10.06.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2033 **Hexacima-EMEA/H/C/002702/WS2033/0116** **Hexyon-EMEA/H/C/002796/WS2033/0120** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 29.04.2021.	
WS2042 **Ambirix-EMEA/H/C/000426/WS2042/0115** **Fendrix-EMEA/H/C/000550/WS2042/0075** **Infanrix hexa-EMEA/H/C/000296/WS2042/0298** **Twinrix Adult-EMEA/H/C/000112/WS2042/0150** **Twinrix Paediatric-EMEA/H/C/000129/WS2042/0151** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke Opinion adopted on 10.06.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS2053 **Infanrix hexa-EMEA/H/C/000296/ WS2053/0300** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke	
WS2055 **Actraphane-EMEA/H/C/000427/WS2055/ 0089** **Actrapid-EMEA/H/C/000424/WS2055/ 0083** **Insulatard-EMEA/H/C/000441/ WS2055/0087** **Mixtard-EMEA/H/C/000428/WS2055/ 0090** **Protaphane-EMEA/H/C/000442/ WS2055/0086** Novo Nordisk A/S, Lead Rapporteur: Kirstine Moll Harboe Opinion adopted on 28.05.2021.	Positive Opinion adopted by consensus on 28.05.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2056 **Fiasp-EMEA/H/C/004046/WS2056/0029** **NovoMix-EMEA/H/C/000308/WS2056/ 0108** **NovoRapid-EMEA/H/C/000258/WS2056/ 0140** Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder Opinion adopted on 10.06.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2060 **HyQvia-EMEA/H/C/002491/WS2060/0071** **Kiovig-EMEA/H/C/000628/WS2060/0109** Takeda Manufacturing Austria AG, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 10.06.2021.	Request for supplementary information adopted with a specific timetable.
WS2061/G **Rixathon-EMEA/H/C/003903/WS2061/ 0048/G** **Riximyo-EMEA/H/C/004729/WS2061/ 0048/G** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus, "B.II.f.1.d C.I.2.a - To align annex IIIB, Package Leaflet for Rixathon and Riximyo, with the one approved for the reference product Mabthera (procedure EMEA/H/C/000165/II/0177) i.e. addition of the side effect "tumour pain" from the 1400 mg/ml and 1600 mg/ml strength (both	Positive Opinion adopted by consensus on 03.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

subcutaneously administered) to the 100 mg/ml and 500 mg/ml (both intravenously administered) in section 4 of the package leaflet and update of the statement on sodium in section 2 of the package leaflet in line with the EC guideline Excipients in the labelling and package leaflet of medicinal products for human use (EMA/CHMP/302620/2017 Rev. 1.). Furthermore, the MAH took the opportunity to introduce editorial corrections in product information as listed in the present and proposed table and add in Annex II of the product information 'The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.'" Opinion adopted on 03.06.2021.	
WS2063 **Ryzodeg-EMEA/H/C/002499/WS2063/ 046** **Tresiba-EMEA/H/C/002498/WS2063/0052** **Xultophy-EMEA/H/C/002647/WS2063/ 041** Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder Opinion adopted on 10.06.2021.	Positive Opinion adopted by consensus on 10.06.2021. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS2072 **Abseamed-EMEA/H/C/000727/WS2072/ 094** **Binocrit-EMEA/H/C/000725/WS2072/ 093** **Epoetin alfa Hexal-EMEA/H/C/000726/ S2072/0093** Sandoz GmbH, Lead Rapporteur: Alexandre Moreau	
WS2077 **Kinzalkomb-EMEA/H/C/000415/WS2077/ 0116** **MicardisPlus-EMEA/H/C/000413/ WS2077/0119** **PritorPlus-EMEA/H/C/000414/WS2077/ 0126** Boehringer Ingelheim International GmbH, Lead Rapporteur: Armando Genazzani, "To update sections 2 (Qualitative and quantitative composition) and 4.4 (Special warnings and precautions for use) of the SmPC and sections 2 (What you need to know before you <take> <use> X) and 6 (Contents of the pack and other information) of the PL to align the wording for	

the excipients lactose, sodium and sorbitol to the "Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (SANTE-2017-11668, Rev. 1)", published in Nov. 2019. In addition, the marketing authorisation holder has taken the opportunity to: - implement minor editorial changes; - update the list of local representatives and align the PI for Kinzalkomb and PritorPlus to the QRD template v.10.1; - update the list of local representatives and align the PI for MicardiPlus to the latest QRD template v. 10.2; -."	
WS2079/G **Fluenz Tetra-EMEA/H/C/002617/ WS2079/0108/G** **Pandemic influenza vaccine H5N1 AstraZeneca-EMEA/H/C/003963/ WS2079/0041/G** AstraZeneca AB, Lead Rapporteur: Christophe Focke	
WS2084 **Cegfila-EMEA/H/C/005312/WS2084/0010** **Pelmeg-EMEA/H/C/004700/WS2084/0014** Mundipharma Corporation (Ireland) Limited, Lead Rapporteur: Karin Janssen van Doorn	

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

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

Vaborem - meropenem / vaborbactam - EMEA/H/C/004669/II/0010/G Menarini International Operations Luxembourg S.A., Rapporteur: Filip Josephson, "A grouped application including 8 type II variations (C.I.4) and 1 type II variation (C.I.13): Update of section 4.5 of the SmPC based on the results of a series of non-clinical drug-drug interaction studies undertaken with vaborbactam or meropenem. The Package Leaflet has been updated accordingly. In addition, the MAH has submitted non-clinical data on the phototoxicity potential of	Request by the applicant dated 22 April 2021 for an extension to the clock stop to respond to the request for supplementary information adopted in March 2021.

meropenem from a 3T3 neutral red uptake phototoxicity test.” Request for Supplementary Information adopted on 11.03.2021.	

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

copanlisib - EMEA/H/C/004334, Orphan Bayer AG, treatment of adult patients with relapsed marginal zone lymphoma	
dimethyl fumarate - EMEA/H/C/005956 treatment of multiple sclerosis	
budesonide, micronised - EMEA/H/C/005653, Orphan Calliditas Therapeutics AB, treatment of primary immunoglobulin A (IgA) nephropathy	**Accelerated review**
adalimumab - EMEA/H/C/005947 treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn’s disease, paediatric Crohn’s disease, ulcerative colitis, uveitis, paediatric uveitis	
maribavir - EMEA/H/C/005787, Orphan Shire Pharmaceuticals Ireland Limited, treatment of cytomegalovirus (CMV) infection	
opicapone - EMEA/H/C/005782 treatment of Parkinson’s disease and motor fluctuations	
tezepelumab - EMEA/H/C/005588 add-on maintenance treatment in adults and adolescents 12 years and older with severe asthma	
faricimab - EMEA/H/C/005642 treatment of neovascular (wet) age-related macular degeneration (nAMD) and visual impairment due to diabetic macular oedema (DME)	

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

Lyumjev - insulin lispro - EMEA/H/C/005037/X/0010
Eli Lilly Nederland B.V., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Annika Folin

Sogroya - somapacitan - EMEA/H/C/005030/X/0001/G, Orphan
Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber

Trydonis - beclometasone dipropionate / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004702/X/0015
Chiesi Farmaceutici S.p.A., Informed Consent of Trimbow, Rapporteur: Janet Koenig, PRAC Rapporteur: Jan Neuhauser, "Extension application to add a new pharmaceutical form (inhalation powder) associated with new strength (88µg / 5µg / 9µg).
The RMP (version 7.1) is updated in accordance."

Zejula - niraparib - EMEA/H/C/004249/X/0029, Orphan
GlaxoSmithKline (Ireland) Limited, Rapporteur: Bjorg Bolstad, 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."

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

arachis hypogaea extract - EMEA/H/C/004810, Article 28
treatment of peanut allergy
List of Questions adopted on 25.02.2021.

aducanumab - EMEA/H/C/005558
Alzheimer's disease
List of Questions adopted on 25.02.2021.

artesunate - EMEA/H/C/005718, Orphan
B And O Pharm, Treatment of severe malaria
List of Questions adopted on 22.04.2021.

adalimumab - EMEA/H/C/005548

treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn's disease, paediatric Crohn's disease, ulcerative colitis, uveitis,pPaediatric uveitis, treatment of rheumatoid arthritis, psoriasis, hidradenitis suppurativa, Crohn's disease, paediatric Crohn's disease, ulcerative colitis, uveitis, paediatric uveitis
List of Questions adopted on 28.01.2021.

Noxafil - posaconazole - EMEA/H/C/000610/X/0063/G
Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, "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."
List of Questions adopted on 25.03.2021.

Paliperidone Janssen-Cilag International - paliperidone - EMEA/H/C/005486/X/0002/G
Janssen-Cilag International N.V., Informed Consent of Xeplion, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Extension application to introduce two new strengths of 700 mg and 1000 mg prolonged-release suspension for injection, grouped with the following variations:
A.2.a - To change the (invented) name of the medicinal product
A.7 -
6 x C.I.7.b. - To delete the 25 mg, 50 mg, 75 mg, 100 mg and 150 mg/100 mg strengths from the Paliperidone Janssen-Cilag marketing authorisation (EU/1/20/1453/001-006)."
List of Questions adopted on 22.04.2021.

lasmiditan - EMEA/H/C/005332
acute treatment of migraine with or without aura in adults

List of Questions adopted on 25.03.2021.

rivaroxaban - EMEA/H/C/005600
Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors. Treatment of deep vein thrombosis and pulmonary embolism and prevention of recurrent DVT and PE in adults., Prevention of venous thromboembolism in adult patients undergoing elective hip or knee replacement surgery. Treatment of deep vein thrombosis and pulmonary embolism and prevention of recurrent DVT and PE in adults.
List of Questions adopted on 28.01.2021.

anifrolumab - EMEA/H/C/004975
indicated as an add-on therapy for the treatment of adult patients with moderate to severe systemic lupus erythematosus (SLE), despite standard therapy
List of Questions adopted on 25.02.2021.

sitagliptin fumarate - EMEA/H/C/005741
treatment of type 2 diabetes mellitus
List of Questions adopted on 25.03.2021.

avacopan - EMEA/H/C/005523, Orphan
Vifor Fresenius Medical Care Renal Pharma France, Treatment of granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA)
List of Questions adopted on 25.02.2021.

tecovirimat - EMEA/H/C/005248
treatment of orthopoxvirus disease
List of Questions adopted on 25.02.2021.

diroximel fumarate - EMEA/H/C/005437
treatment of relapsing remitting multiple sclerosis
List of Questions adopted on 22.04.2021.

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

DECTOVA - zanamivir - EMEA/H/C/004102/S/0011
GlaxoSmithKline Trading Services Limited, Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ulla Wändel Liminga

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

Adcetris - brentuximab vedotin -
EMEA/H/C/002455/R/0090, Orphan
Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Daptomycin Hospira - daptomycin -
EMEA/H/C/004310/R/0018
Pfizer Europe MA EEIG, Generic, Generic of Cubicin, Rapporteur: Kolbeinn Gudmundsson, PRAC Rapporteur: Pernille Harg

Jylamvo - methotrexate -
EMEA/H/C/003756/R/0015
Therakind (Europe) Limited, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Jan Neuhauser

NINLARO - ixazomib -
EMEA/H/C/003844/R/0030, Orphan
Takeda Pharma A/S, Rapporteur: Armando Genazzani, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Pregabalin Zentiva k.s. - pregabalin -
EMEA/H/C/004277/R/0019
Zentiva k.s., Generic, Generic of Lyrica, Rapporteur: Alar Irs, PRAC Rapporteur: Liana Gross-Martirosyan

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

Tadalafil Lilly - tadalafil -
EMEA/H/C/004666/R/0008
Eli Lilly Nederland B.V., Informed Consent of Cialis, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maria del Pilar Rayon

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

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

COMIRNATY - covid-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0030 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Menno van der Elst, "Extension of the existing indication from "individuals 16 years of age and older" to "individuals 12 years of age and older" for Comirnaty; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.0 of the RMP has also been submitted." Opinion adopted on 28.05.2021.	See 5.1
COVID-19 Vaccine Moderna - covid-19 mrna vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0021 Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, "Extension of indication to include use in adolescents 12 to 17 years of age for COVID-19 Vaccine Moderna; 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."	
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0073 Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "C.I.6 (Extension of indication) type II Art.29 Extension of indication to include treatment of relapsing remitting multiple sclerosis (RRMS) in paediatric patients from 10 years of age and over; as a consequence sections 4.1, 4.2, 4.8, 5.1 and 5.3 are updated. The Package Leaflet is updated in accordance. The MAH is requesting an extension of the market protection of one additional year in line with the guidance on elements required to support the significant clinical benefit in comparison with existing therapies of a new therapeutic indication in accordance with Article 14(11) of Regulation (EC) 726/2004. Version 11.4 of the RMP has also been	

submitted to update the RMP (parts I-IV) based on study 109MS306 data supporting the request for a paediatric indication and the applicant took the opportunity to update the RMP with the most updated data (Part II modules SIV, SV and SVII).” Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)	
XALKORI - crizotinib - EMEA/H/C/002489/II/0072 Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Tiphaine Vaillant, “Extension of indication to include treatment of paediatric patients (age ≥ 6 to < 18 years) with relapsed or refractory systemic anaplastic lymphoma kinase (ALK)-positive anaplastic large cell lymphoma (ALCL) and with unresectable, recurrent, or refractory ALK-positive inflammatory myofibroblastic tumour (IMT) for XALKORI based on the results from studies ADVL0912 and A8081013; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 8.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the ATC code for crizotinib. Moreover, the MAH took the opportunity to implement a minor change in the list of local representatives in the Package Leaflet.”	

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Aimovig - erenumab - EMEA/H/C/004447/II/0016 Novartis Europharm Limited, Rapporteur: Kristina Dunder	
Alprolix - eftrenonacog alfa - EMEA/H/C/004142/II/0036/G, Orphan Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop	
COMIRNATY - covid-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0039/G	See B.5.1

BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COMIRNATY - covid-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0040/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COMIRNATY - covid-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0041/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COMIRNATY - covid-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0043 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/0005 Janssen-Cilag International N.V., Rapporteur: Christophe Focke	
COVID-19 Vaccine Moderna - covid-19 mrna vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0018/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus	See B.5.1
Darzalex - daratumumab - EMEA/H/C/004077/II/0049/G, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac	
Fluad Tetra - influenza vaccine (surface antigen, inactivated, adjuvanted) - EMEA/H/C/004993/II/0017 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz	
Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0021 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz	
Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0109 AstraZeneca AB, Rapporteur: Christophe Focke	
Hemlibra - emicizumab - EMEA/H/C/004406/II/0023/G	

Roche Registration GmbH, Rapporteur: Alexandre Moreau	
IKERVIS - ciclosporin - EMEA/H/C/002066/II/0026/G Santen Oy, Rapporteur: Peter Kiely	
Nepexto - etanercept - EMEA/H/C/004711/II/0010/G Mylan IRE Healthcare Limited, Rapporteur: Martina Weise	
SARCLISA - isatuximab - EMEA/H/C/004977/II/0009/G, Orphan sanofi-aventis groupe, Rapporteur: Paula Boudewina van Hennik	
Spectrila - asparaginase - EMEA/H/C/002661/II/0025 medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Andrea Laslop	
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0020/G AstraZeneca AB, Rapporteur: Sol Ruiz	See B.5.1 and 9.1
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0021/G AstraZeneca AB, Rapporteur: Sol Ruiz	See 9.1
VEYVONDI - vonicog alfa - EMEA/H/C/004454/II/0017 Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus	
WS2080/G Hexacima-EMEA/H/C/002702/WS2080/0117/G Hexyon-EMEA/H/C/002796/WS2080/0121/G Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus	
WS2095/G Blitzima-EMEA/H/C/004723/WS2095/0043/G Truxima-EMEA/H/C/004112/WS2095/0046/G Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz	

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

Alunbrig - brigatinib / brigatinib - EMEA/H/C/004248/II/0033/G Takeda Pharma A/S, Rapporteur: Sinan B. Sarac, "Update of section 4.5 of the SmPC in order to add drug-drug interaction information about the effect of brigatinib on the pharmacokinetics of a sensitive cytochrome P450 3A substrate (midazolam) in patients with ALK-positive or ROS1-positive solid tumours based on a clinical study report (Study 1001). Update of section 4.2 of the SmPC in order to clarify the existing renal impairment dosage adjustment recommendation based on results of previously submitted studies (clinical study AP26113-15-108, Study 108). Update of section 4.2 of the SmPC in order to clarify the existing hepatic impairment dosage adjustment recommendation based on results of previously submitted studies (clinical study AP26113-15-107, Study 107). Update of sections 4.4 and 4.5 of the SmPC in order to update drug-drug interaction information regarding concomitant treatment with moderate CYP3A inhibitors or inducers based on results of previously submitted studies (physiologically-based pharmacokinetic (PBPK) report and PBPK report addendum). Update of section 5.1 of the SmPC in order to amend the ATC code; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement a statement regarding the sodium content of Alunbrig in section 4.4 of the SmPC and Package Leaflet. The MAH also took the opportunity to bring the Product Information in line with the latest QRD template (version 10.2 rev.1) and to update the list of local representatives in the Package Leaflet. Moreover, the MAH took the opportunity to introduce minor editorial changes in the PI in different languages."	
Alunbrig - brigatinib / brigatinib - EMEA/H/C/004248/II/0034 Takeda Pharma A/S, Rapporteur: Sinan B. Sarac, "Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on photosensitivity based on a report of cumulative evidence for an association between exposure to brigatinib and subsequent development of	

photosensitivity reaction; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make a minor editorial change in section 4.8 of the SmPC."

COMIRNATY - covid-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0038/G

BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst, "To update section 4.4 of the SmPC to add a new warning on "vaccine stress-related responses" following signal detection and evaluation activity in the post-authorisation setting, as a result of internal review of post-authorisation cases; the Package Leaflet is updated accordingly.
To update section 4.8 of the SmPC to add "extensive swelling of the vaccinated limb" to the list of adverse drug reactions (ADRs) with frequency "Not known" agreed by the PRAC following the outcome of the of the post Authorisation Measure PAM MEA-002.3 (EMEA/H/C/005735/MEA/002.3, dated 04. May 2021); the Package Leaflet is updated accordingly.
To update section 4.8 of the SmPC to add ("facial swelling") to the list of adverse drug reactions (ADRs) with frequency "Not known" agreed by the PRAC following the outcome of the Signal Assessment on localized swelling in patients with history of dermal filer injections with tozinameran (Comirnaty (COVID-19 mRNA vaccine), (EMEA/H/C/005735/SDA/023 (EPITT ref. 19674); the Package Leaflet is updated accordingly."

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.""

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)."

Phesgo - pertuzumab / trastuzumab - EMEA/H/C/005386/II/0004
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update in section 4.8, Undesirable Effects, to present the pooled data from Perjeta and Phesgo studies.
In addition to this, the MAH has taken the opportunity to introduce minor updates in the SmPC and the Package leaflet:
• Update in section 9 of the SmPC to reflect the date of first authorisation
• Editorial update in section 4 of the Package leaflet to add a space
• Update in Section 6 of the Package leaflet to adapt to the revised QRD Template v10.2"

Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0128
Boehringer Ingelheim International GmbH, Rapporteur: Kirstine Moll Harboe, "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."

Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0160
GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder, "Update of section 5.1 Pharmacodynamic properties of the SmPC

following submission of procedure EMEA/H/C/000973/P46/070 to include results of the study 10PN-PD-DIT-082, a phase III, controlled, partially-blind study evaluating the interchangeability of Synflorix and 13-valent pneumococcal conjugate vaccine. Section 4.2 Posology and method of administration is updated to cross reference to section 5.1. In addition, the MAH took the opportunity to add in section 4.4 Special warnings and precautions of the SmPC a statement regarding the sodium content, in line with the guideline on "Excipients in the labelling and package leaflet of medicinal product for human use" and to update the list of local representatives in the Package Leaflet."

Ultomiris - ravulizumab - EMEA/H/C/004954/II/0018

Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa, "To update section 4.2 Posology and method of administration of the SmPC regarding the inclusion of home infusion as an alternative infusion setting for Ultomiris for approved indications (paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS))."

Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0019

AstraZeneca AB, Rapporteur: Sol Ruiz, "Submission of the interim and primary reports clinical study reports from study D8111C00002, listed as a category 3 study in the RMP. This study is a Phase I/II randomised, double-blind, placebo-controlled, multicentre study in participants aged 18 years or older to determine the safety and immunogenicity of AZD1222, a nonreplicating ChAdOx1 Vector Vaccine, for the prevention of COVID-19. This submission fulfils the post-authorisation measures MEA 012 and MEA 012.1."

Vectibix - panitumumab - EMEA/H/C/000741/II/0097

Amgen Europe B.V., Rapporteur: Bjorg Bolstad, "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 was made in the PL.”	
WS2070 **Mekinist-EMEA/H/C/002643/WS2070/0047** **Tafinlar-EMEA/H/C/002604/WS2070/0052** Novartis Europharm Limited, Lead Rapporteur: Paula Boudewina van Hennik, “ Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to modify administration instructions (pyrexia dose modification guidance in the Tafinlar and Mekinist SmPC); the Package Leaflet are updated accordingly. In addition, the WSA took the opportunity to update the list of local representatives for The Netherlands in the Package Leaflet and to include minor editorial changes”	

B.6.10. CHMP-PRAC assessed procedures

COMIRNATY - covid-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005735/II/0036 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst, “Update of sections 4.8 and 5.1 of the SmPC to include new information based on updated interim results from study C4591001. This was a phase 1/2/3, placebo-controlled, observer-blind, interventional, dose-finding, study to evaluate the safety, tolerability, immunogenicity and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals. The Package Leaflet is updated accordingly. The updated RMP (version 2.1) has also been submitted.”	
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."

Qarziba - dinutuximab beta - EMEA/H/C/003918/II/0027/G, Orphan

EUSA Pharma (Netherlands) B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski, "
-A.6 - Type IA - ATC code change to L01XC16 according to the WHO
-C.I.4: Type II- Update of section 4.8 of the SmPC in order to include changes to the overall incidence of reported adverse reactions based on post-marketing data. In addition, minor changes are introduced in the Summary of Product Characteristics, Package Leaflet and Labelling in order to harmonise the Product Information with other regulatory regions.
-C.I.11.b: Type II-Submission of RMP version 10.00 in order to include an alignment to post marketing data (PSUR6) and to introduce updates on the important identified risks and important potential risks.
In addition, some linguistic corrections are included on Swedish, Finnish, Italian, Spanish, and Portuguese EMA annexes."

RAVICTI - glycerol phenylbutyrate - EMEA/H/C/003822/II/0038/G, Orphan

lmmedica Pharma AB, Rapporteur: Kirstine Moll Harboe, PRAC Rapporteur: Ilaria Baldelli, "Group of variations consisting of :
- Submission of the final study report, HPN-100-014 non interventional registry study "Long-Term Registry of Patients with Urea Cycle Disorders (UCDs) conducted in the US".
- An update to the RMP (version 7) submitted to remove the important potential risks of carcinogenicity and PAA toxicity. The update to

the RMP is based on the review of new and available data including the study report for HPN-100-014 and a new toxicological expert examination of pre-clinical carcinogenicity findings as well as a cumulative review of literature and post marketing data. In accordance with the proposed changes to the RMP, an update of Annex II is requested to waive the imposed condition related to the non-interventional post-authorisation safety study (PASS), "European Post-Authorization Registry for RAVICTI (glycerol phenylbutyrate) Oral Liquid in Partnership with the European Registry and Network for Intoxication Type Metabolic Diseases (E-IMD)". The SmPC and Package Leaflet have been updated to delete the information on additional monitoring (including the black triangle)."	
REKAMBYS - rilpivirine - EMEA/H/C/005060/II/0004 Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Liana Gross-Martirosyan, "Update of section 4.2 (to change posology recommendations) and sections 4.8, 5.1 and 5.2 of the SmPC (to update safety and efficacy information) based on week 124 results from the FLAIR study. This is a Phase III, randomized, open-label study to evaluate the efficacy, safety and tolerability of the combined treatment Cabotegravir and Rilpivirine. The Package Leaflet has been updated accordingly. Editorial changes and corrections have been carried out throughout the PI. The RMP version 3.1 has also been submitted."	
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0026 AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to include updated efficacy and safety information based on primary analysis from study D8110C00001 listed as a specific obligation in Annex II; this is a phase III randomised, double-blind, placebo-controlled, multicenter study in adults to determine the safety, efficacy and immunogenicity of Vaxzevria; the Package Leaflet and Annex II are	

updated accordingly. The updated RMP Version 3 Succession 2 has also been submitted."

Vocabria - cabotegravir - EMEA/H/C/004976/II/0004

ViiV Healthcare B.V., Rapporteur: Jean-Michel Race, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber, "Update of section 4.2 (to change posology recommendations) and sections 4.4, 4.8, 5.1 and 5.2 of the SmPC (to update safety and efficacy information) based on week 124 results from the FLAIR study. This is a Phase III, randomized, open-label study to evaluate the efficacy, safety and tolerability of the combined treatment Cabotegravir and Rilpivirine. The Package Leaflet has been updated accordingly. Editorial changes and corrections have been carried out throughout the PI. The RMP version 2 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet to bring the PI in line with the latest QRD template version 10.2."

B.6.11. PRAC assessed procedures

PRAC Led

COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0006/G

Janssen-Cilag International N.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "C.I.4-To update section 4.4 of the SmPC to add a warning for individuals who have experienced a previous cerebral venous sinus thrombosis (CVST) with thrombocytopenia or heparin-induced thrombocytopenia (HIT) to outweigh the potential risks before the administration of COVID-19 Vaccine Janssen; the Package Leaflet is updated accordingly. The updated RMP version 2.1 has also been submitted.
C.I.11.b- To update the EU-RMP for COVID-19 Vaccine Janssen to version 2.1 to include thrombosis with thrombocytopenia syndrome (TTS) in the list of the safety concerns as an

important identified risk following the PRAC recommendation, dated 6 May 2021 in the outcome of the related signal of Embolic and Thrombotic events (procedure number SDA 018.1) with COVID-19 Vaccine Janssen (Ad26.COV2-S [recombinant]). In addition, the MAH took the opportunity to update in the EU-RMP the milestone date for the submission of the VAC31518COV4003 protocol; to propose a revised frequency of data mining from the EudraVigilance database and to correct the long-term follow-up time in the VAC31518COV4001 study."	
PRAC Led **COVID-19 Vaccine Moderna - covid-19 mrna vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0015/G** Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Kirstine Moll Harboe, "Grouped variation to address PRAC requests raised in the 2nd and 3rd Moderna Monthly Safety Summary Report (MSSR) procedures (EMEA/H/C/005791/MEA/011.1 and EMEA/H/C/005791/MEA/011.2 respectively: - C.I.3.b (Type II): Update of section 4.4 of the SmPC to provide additional safety information regarding hypersensitivity and anaphylaxis, as requested by the PRAC in the 2nd Monthly Safety Summary Report. The Package Leaflet is updated accordingly. - C.I.3.b (Type II): Update of section 4.8 of the SmPC to include 'Delayed injection site reaction' as an adverse reaction, with the frequency 'Common', as requested by the PRAC in the 3rd Monthly Safety Summary. The Package Leaflet is updated accordingly. In addition, the Marketing Authorisation Holder (MAH) submitted a justification for not adding diarrhoea to the PI as an adverse reaction, as requested by the PRAC in the 3rd Monthly Safety Summary Report and took the opportunity to make minor editorial changes."	

B.6.12. CHMP-CAT assessed procedures

onasemnogene abeparvovec -

EMEA/H/C/004750/II/0015, Orphan, ATMP
Novartis Gene Therapies EU Limited, "Updates to sections 4.4, 4.8 and 5.1 of the SmPC to reflect the final study results study AVXS-101-CL-302; a Post-authorisation efficacy study intended to confirm the efficacy and safety and tolerability of a single dose of Zolgensma in patients younger than 6 months of age with SMA Type 1 with One or Two SMN2 Copies. The package leaflet has been updated accordingly and annex II has been updated to reflect completion of this Specific Obligation."

WS2071
Tecartus-EMEA/H/C/005102/WS2071/0007
Yescarta-EMEA/H/C/004480/WS2071/0039
Kite Pharma EU B.V., Lead Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

WS2076
Ambirix-EMEA/H/C/000426/WS2076/0116
Twinrix Adult-EMEA/H/C/000112/WS2076/0151
Twinrix Paediatric-EMEA/H/C/000129/WS2076/0152
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke,

WS2084
Cegfila-EMEA/H/C/005312/WS2084/0010
Pelmeg-EMEA/H/C/004700/WS2084/0014
Mundipharma Corporation (Ireland) Limited, Lead Rapporteur: Karin Janssen van Doorn

WS2087
Infanrix hexa-EMEA/H/C/000296/WS2087/0301
GlaxoSmithkline Biologicals SA, Lead

Rapporteur: Christophe Focke

WS2100/G
Prezista-EMEA/H/C/000707/WS2100/0112/G
Rezolsta-EMEA/H/C/002819/WS2100/0043/G
Symtuza-EMEA/H/C/004391/WS2100/0036/G
Janssen-Cilag International NV, Lead
Rapporteur: Johann Lodewijk Hillege

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 - EMEA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. PMF Certification Dossiers

E.1.1. Annual Update

E.1.2. Variations

E.1.3. Initial PMF Certification

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

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

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

G. ANNEX G

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

G.2. PRIME

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

G.2.1. List of procedures concluding at 21-24 June 2021 CHMP plenary:

G.2.2. List of procedures starting in June 2021 for July 2021 CHMP adoption of outcomes

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