12 December 2022
EMA/CHMP/869948/2022
Human Medicines Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 12-15 December 2022

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

12 December 2022, 09:00 – 19:30, virtual meeting/room 2C

13 December 2022, 08:30 – 19:30, virtual meeting/room 2C

14 December 2022, 08:30 – 19:30, virtual meeting/room 2C

15 December 2022, 08:30 – 15:00, virtual meeting/room 2C

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 12-15 December 2022. See December 2022 CHMP minutes (to be published post January 2023 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 12-15 December 2022.

1.3. Adoption of the minutes

CHMP minutes for 07-10 November 2022.

Minutes from PReparatory and Organisational Matters (PROM) meeting held on 05 December 2022.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. palovarotene - Orphan - EMEA/H/C/004867

Ipsen Pharma; treatment of fibrodysplasia ossificans progressiva

Scope: Oral explanation

Action: Oral explanation to be held on 13 December 2022 at 16:00

List of Outstanding Issues adopted on 15.09.2022. List of Questions adopted on 16.09.2021.

Participation of patient representative.

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

2.3.1. Kerendia - finerenone - EMEA/H/C/005200/II/0001/G

Bayer AG

Rapporteur: Kristina Dunder, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include the treatment of chronic kidney disease (CKD) and for the prevention of cardiovascular (CV) events in adults with CKD (regardless of the stage of albuminuria) associated with type 2 diabetes, based on results from study 17530 (FIGARO-DKD); a randomized, double-blind, placebo-controlled, parallel-group, multicenter, event-driven Phase III study to investigate the efficacy and safety of finerenone on the reduction of cardiovascular morbidity and mortality in subjects with type 2 diabetes mellitus and the clinical diagnosis of diabetic kidney disease in addition to standard of care.
As a consequence, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC is being updated and the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make editorial changes in the SmPC. The updated RMP version 2.1 has also been submitted.
Update of the SmPC section 5.2 based on the results of study 21429, a phase 1 drug interaction study of finerenone with rosuvastatin. The CSR PH-42032 was already submitted within the response to Day 180 List of Outstanding Issues of the initial MAA.
Submission of the results of study 21325, a phase 1 bioequivalence study assessing BE between finerenone 2 x 10 mg tablets and 20 mg tablet in Japanese healthy male adult participants (required by the Japanese PMDA)."

Scope: Oral explanation

Action: Oral explanation to be held on 12 December 2022 at 14:00

Request for Supplementary Information adopted on 15.09.2022, 23.06.2022.

See 5.1

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

GlaxoSmithKline (Ireland) Limited

Rapporteur: Ingrid Wang, PRAC Rapporteur: Jan Neuhauser

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

Scope: Oral explanation

Action: Oral explanation to be held on 13 December 2022 at 11:00

Request for Supplementary Information adopted on 19.05.2022, 10.02.2022.

See 9.1

2.4. Referral procedure oral explanations

2.4.1. Rambis - ramipril, bisoprolol fumarate - EMEA/H/A-29(4)/1519

Adamed Pharma S.A.

Rapporteur: Ewa Balkowiec Iskra, Co-Rapporteur: Ondrej Slanar

Scope: Oral explanation

Action: Oral explanation to be held on 14 December 2022 at 09:00

Decentralised procedure number: PL/H/0758/001-006/DC, notification by the Agency of Poland dated 30 May 2022 notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC

List of outstanding issues adopted on 15.09.2022. List of questions adopted on 23.06.2022.

See 10.4

3. Initial applications

3.1. Initial applications; Opinions

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

treatment of multiple sclerosis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 13.10.2022. List of Questions adopted on 22.04.2022.

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

CSL Behring GmbH; treatment of adults with Haemophilia B

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 07.10.2022. List of Questions adopted on 15.07.2022.

3.1.3. tremelimumab - Orphan - EMEA/H/C/006016

AstraZeneca AB; For use in combination with durvalumab for the treatment of adults with unresectable hepatocellular carcinoma.

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 21.07.2022.

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

Y-Mabs Therapeutics A/S; treatment of neuroblastoma

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 13.10.2022, 23.06.2022. List of Questions adopted on 16.09.2021.

3.1.5. cipaglucosidase alfa - Orphan - EMEA/H/C/005703

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

Scope: Opinion

Action: For adoption

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

3.1.6. tremelimumab - EMEA/H/C/004650

treatment of adults with metastatic NSCLC with no sensitising epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) genomic tumour aberrations

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 13.10.2022. List of Questions adopted on 22.04.2022.

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

3.2.1. niraparib / abiraterone acetate - EMEA/H/C/005932

treatment of adult patients with prostate cancer

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 15.09.2022.

3.2.2. eculizumab - EMEA/H/C/005652

treatment of paroxysmal nocturnal haemoglobinuria

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 21.07.2022.

3.2.3. mavacamten - EMEA/H/C/005457

treatment of symptomatic obstructive hypertrophic cardiomyopathy

Scope: List of outstanding issues

Action: For adoption

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

3.2.4. trastuzumab - EMEA/H/C/005769

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 19.05.2022.

3.2.5. molnupiravir - EMEA/H/C/005789

treatment of coronavirus disease 2019 (COVID-19)

Scope: List of outstanding issues

Action: For adoption

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

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

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

Scope: List of outstanding issues

Action: For information

List of Questions adopted on 19.02.2021.

3.2.7. raltegravir potassium - EMEA/H/C/005813

treatment of human immunodeficiency virus (HIV-1)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 21.07.2022.

3.2.8. deucravacitinib - EMEA/H/C/005755

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

Scope: List of outstanding issues

Action: For adoption

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

3.2.9. ivosidenib - Orphan - EMEA/H/C/005936

Les Laboratoires Servier; treatment of acute myeloid leukaemia and treatment of metastatic cholangiocarcinoma

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 21.07.2022.

3.2.10. ivosidenib - Orphan - EMEA/H/C/006174

Les Laboratoires Servier; treatment of acute myeloid leukaemia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 21.07.2022.

3.2.11. vadadustat - EMEA/H/C/005131

treatment of anaemia

Scope: List of outstanding issues

Action: For adoption

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

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

3.3.1. sparsentan - Orphan - EMEA/H/C/005783

Vifor France; for the treatment of primary immunoglobulin A nephropathy (IgAN).

Scope: List of questions

Action: For adoption

3.3.2. decitabine / cedazuridine - Orphan - EMEA/H/C/005823

Otsuka Pharmaceutical Netherlands B.V.; treatment of myeloid leukaemia

Scope: List of questions

Action: For adoption

3.3.3. catumaxomab - EMEA/H/C/005697

indicated for the treatment of malignant ascites

Scope: List of questions; Letter by the applicant requesting an extension to the clock stop to respond to the list of questions to be adopted in December 2022.

Action: For adoption

3.3.4. ritlecitinib - EMEA/H/C/006025

indicated for the treatment of severe alopecia areata in adults and adolescents 12 years of age and older.

Scope: List of questions

Action: For adoption

3.3.5. pegzilarginase - Orphan - EMEA/H/C/005484

Immedica Pharma AB; treatment of hyperargininemia

Scope: List of questions

Action: For adoption

3.3.6. masitinib - Orphan - EMEA/H/C/005897

AB Science; in combination with riluzole for the treatment of adult patients with amyotrophic lateral sclerosis (ALS)

Scope: List of questions

Action: For adoption

3.3.7. leriglitazone - Orphan - EMEA/H/C/005757

Minoryx Therapeutics S.L.; treatment of cerebral progression and myelopathy in male patients with adrenoleukodystrophy (ALD).

Scope: List of questions

Action: For adoption

3.3.8. tocilizumab - EMEA/H/C/005781

treatment of rheumatoid arthritis

Scope: List of questions

Action: For adoption

3.3.9. elacestrant - EMEA/H/C/005898

treatment of postmenopausal woman and men with breast cancer

Scope: List of questions

Action: For adoption

3.3.10. rezafungin - Orphan - EMEA/H/C/005900

Mundipharma GmbH; treatment of invasive candidiasis

Scope: List of questions

Action: For adoption

3.3.11. GBP510 - EMEA/H/C/005998

prevention of COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older

Scope: List of questions

Action: For adoption

3.3.12. sugammadex - EMEA/H/C/006115

reversal of neuromuscular blockade induced by rocuronium or vecuronium

Scope: List of questions

Action: For adoption

3.3.13. sugammadex - EMEA/H/C/006083

Reversal of neuromuscular blockade induced by rocuronium or vecuronium in adults

Scope: List of questions

Action: For adoption

3.3.14. quizartinib - Orphan - EMEA/H/C/005910

Daiichi Sankyo Europe GmbH; Treatment of adult patients with diagnosed acute myeloid leukaemia (AML)

Scope: List of questions

Action: For adoption

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

3.4.1. polihexanide - Orphan - EMEA/H/C/005858

SIFI SPA; For the treatment of acanthamoeba keratitis

Scope: Letter by the applicant dated 05 December 2022 requesting an extension to the clock stop to respond to the list of questions adopted in September 2022.

Action: For adoption

List of Questions adopted on 15.09.2022.

3.4.2. sirolimus - Orphan - EMEA/H/C/005896

Plusultra pharma GmbH; Treatment of angiofibroma associated with tuberous sclerosis complex

Scope: Letter by the applicant dated 15 November 2022 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in November 2022.

Action: For adoption

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 22.04.2022.

3.4.3. daprodustat - EMEA/H/C/005746

treatment of anaemia associated with chronic kidney disease (CKD) in adults

Scope: Letter by the applicant dated 22 November 2022 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in November 2022.

Action: For adoption

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 23.06.2022.

3.4.4. trastuzumab duocarmazine - EMEA/H/C/005654

treatment of HER2 (Human Epidermal Growth Factor Receptor 2)-positive metastatic breast cancer

Scope: Letter by the applicant dated 29 November 2022 requesting an extension to the clock stop to respond to the list of questions adopted in November 2022.

Action: For adoption

List of Questions adopted on 10.11.2022.

3.4.5. dabigatran etexilate - EMEA/H/C/006023

Prevention of venous thromboembolic events

Scope: Letter by the applicant dated 07 December 2022 requesting an extension to the clock stop to respond to the list of questions adopted in July 2022.

Action: For adoption

List of Questions adopted on 21.07.2022.

3.4.6. gadopiclenol - EMEA/H/C/005626

for diagnostic: contrast-enhanced magnetic resonance imaging (MRI) to improve detection, visualisation and assist in characterisation of lesions in the central nervous system and in other body regions (including breast, liver and prostate).

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

Action: For adoption

List of Outstanding Issues adopted on 10.11.2022. List of Questions adopted on 23.06.2022.

3.4.7. gadopiclenol - EMEA/H/C/006172

for diagnostic: contrast-enhanced magnetic resonance imaging (MRI) to improve detection, visualisation and assist in characterisation of lesions in the central nervous system and in other body regions (including breast, liver and prostate).

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

Action: For adoption

List of Outstanding Issues adopted on 10.11.2022.

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

No items

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

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

Eli Lilly Nederland B.V.

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

Scope: "Extension application to introduce a new pharmaceutical form associated with a new strength (2 mg/ml oral suspension) grouped with a type II variation (C.I.6.a) to include paediatric use (from 6 months to 17 years) based on study 4 (H6D-MC-LVHV [LVHV]) - A 24-week placebo-controlled efficacy and safety study with an open-label long-term extension phase. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The paediatric indication is applicable to the new and all existing presentations. The Package Leaflet and Labelling are updated accordingly. Furthermore, the PI is brought in line with the latest QRD template and editorial changes have been implemented. The RMP (version 9.1) is updated in accordance."

Action: For adoption

List of Outstanding Issues adopted on 13.10.2022. List of Questions adopted on 19.05.2022.

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

AstraZeneca AB

Rapporteur: Filip Josephson, PRAC Rapporteur: Željana Margan Koletić

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

Action: For adoption

List of Outstanding Issues adopted on 21.07.2022, 19.05.2022. List of Questions adopted on 24.02.2022.

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

ViiV Healthcare B.V.

Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber

Scope: "Extension application to introduce a new pharmaceutical form associated with new strength (5 mg/60 mg/30 mg dispersible tablet). The new presentation is indicated for the treatment of Human Immunodeficiency Virus (HIV) infected children weighing at least 14 kg to less than 25 kg.

This extension application is grouped with a type II variation (C.I.6.a) to include treatment of children weighing at least 25 kg for the already approved film-coated tablets for Triumeq (EU/1/14/940/001-002); as a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance.
The RMP (version 19) is updated in accordance."

Action: For adoption

List of Outstanding Issues adopted on 13.10.2022. List of Questions adopted on 19.05.2022.

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

No items

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

4.3.1. Xolair - omalizumab - EMEA/H/C/000606/X/0115/G

Novartis Europharm Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Mari Thorn

Scope: "Extension application to add a new strength of 300 mg (150 mg/ml) for Xolair solution for injection grouped with quality type II, IB and IAIN variations. The RMP (version 17.0) is updated in accordance."

Action: For adoption

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

No items

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

No items

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

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

5.1.1. Adempas - riociguat - EMEA/H/C/002737/II/0037

Bayer AG

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension of indication to include treatment of pulmonary arterial hypertension (PAH) in paediatric patients aged 6 to less than 18 years of age with WHO Functional Class (FC) I to III in combination with endothelin receptor antagonists with or without prostanoids for Adempas, based on results from pivotal study PATENT-CHILD (study 15681); this is a Phase III, Open-label, individual dose titration study to evaluate safety, tolerability and pharmacokinetics of riociguat in children from 6 to less than 18 years of age with PAH. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 8.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."

Action: For adoption

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

UCB Pharma S.A.

Rapporteur: Finbarr Leacy, Co-Rapporteur: Christophe Focke, PRAC Rapporteur: Liana Gross-Martirosyan

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

Action: For adoption

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

UCB Pharma S.A.

Rapporteur: Finbarr Leacy, Co-Rapporteur: Christophe Focke, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Extension of indication to include treatment of active psoriatic arthritis in adult patients who have had an inadequate response or who have been intolerant to one or more DMARDs for Bimzelx, based on interim results of a Phase III study in biological DMARD naïve study participants (PA0010; BE OPTIMAL) and the final results of the Phase III study in study participants who are inadequate responders (inadequate response or intolerant) to ≤2 prior TNF inhibitors (PA0011; BE COMPLETE). Both Phase III studies are interventional studies aimed to evaluate the efficacy and safety of bimekizumab. For PA0010, the Initial Treatment Period was placebo- and no inferential active reference (adalimumab)-controlled, while PA0011 was placebo-controlled. Further supportive data comprise the results of a Phase 1 study (PA0007), a Phase 2b dose-finding study (PA0008) and a Phase 2 open label extension study (PA0009). A Phase 3 open-label extension study is currently ongoing (PA0012). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 to the SmPC have been updated. The package leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.2 rev.1. As part of the application the MAH is requesting a 1-year extension of the market protection.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

5.1.4. Cosentyx - secukinumab - EMEA/H/C/003729/II/0090

Novartis Europharm Limited

Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Monica Martinez Redondo

Scope: "Extension of indication to include treatment of Hidradenitis Suppurativa (HS) for Cosentyx, based on interim results from two Phase III studies CAIN457M2301 (SUNSHINE) and CAIN457M2302 (SUNRISE); These studies are ongoing, multi-center, randomized, double-blind, placebo-controlled, parallel group Phase 3 studies conducted to assess the short (16 weeks) and long-term (up to 52 weeks) efficacy and safety of two secukinumab dose regimens (Q2W or Q4W) compared to placebo in adult subjects with moderate to severe HS; 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 11 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2022.

5.1.5. Dupixent - dupilumab - EMEA/H/C/004390/II/0062

sanofi-aventis groupe

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

Scope: "Extension of indication to include treatment of eosinophilic esophagitis (EoE) in adults and adolescents 12 years and older who are inadequately controlled by, are intolerant to, or who are not candidates for conventional medicinal therapy, based on the pivotal study R668-EE-1774. This is an ongoing phase 3, randomized, double-blind, placebo-controlled, 3-part (A, B, C) safety and efficacy study with an initial 24-week treatment period in adults (≥18 years of age) and adolescents (≥12 to <18 years of age) with EoE, and which includes an extended treatment period to a total of 52 weeks. 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."

Action: For adoption

Request for Supplementary Information adopted on 10.11.2022, 21.07.2022.

5.1.6. Enhertu - trastuzumab deruxtecan - EMEA/H/C/005124/II/0022

Daiichi Sankyo Europe GmbH

Rapporteur: Aaron Sosa Mejia, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "Extension of indication to include treatment of unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer who have received a prior systemic therapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy. Patients with hormone receptor positive (HR+) breast cancer must additionally have received or be ineligible for endocrine therapy; for Enhertu, based on final results from study DS8201-A-U303 (DESTINY-Breast04). This is a Phase III, multicentre, randomised, open-label, active-controlled trial of Trastuzumab Deruxtecan (T-DXd), an Anti-HER2-antibody Drug Conjugate (ADC), versus treatment of physician's choice for HER2-low, unresectable and/or metastatic breast cancer subjects.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.4 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.4 of the SmPC to update the dosing recommendation for corticosteroid treatment (e.g. prednisolone) with a daily dose."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2022.

5.1.7. Epidyolex - cannabidiol - Orphan - EMEA/H/C/004675/II/0020

GW Pharma (International) B.V.

Rapporteur: Thalia Marie Estrup Blicher, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: "Extension of indication to include treatment with Epidyolex (monotherapy) as adjunctive therapy of seizures associated with Lennox Gastaut syndrome (LGS) or Dravet syndrome (DS) for patients 2 years of age and older (without the restriction for use only in conjunction with clobazam), based on the previously generated data in patients treated without CLB in the LGS and DS pivotal studies re-evaluated in the context of the more recent evidence from study GWEP1521 in tuberous sclerosis complex (TSC). As a consequence, sections 4.1, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The

Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement editorial changes in the product information. Version 2.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2022.

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

Zogenix ROI Limited

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

Scope: "Extension of indication to include treatment of seizures associated with Lennox-Gastaut syndrome as an add on therapy to other anti-epileptic medicines for patients 2 years of age and older. As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.3 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 13.10.2022, 22.04.2022.

5.1.9. Hemlibra - emicizumab - EMEA/H/C/004406/II/0027

Roche Registration GmbH

Rapporteur: Alexandre Moreau, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to include treatment of adult and paediatric patients with hemophilia A without factor VIII (FVIII) inhibitors who have mild or moderate disease for whom prophylaxis is clinically indicated. Consequently, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC and section 1 of the package leaflet are updated. In addition, section 4.2 is updated to make it clear that the maintenance dose for Hemlibra applies from week 5 of dosing. The PIL is updated accordingly. Version 4.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 13.10.2022, 19.05.2022, 27.01.2022.

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

Janssen-Cilag International N.V.

Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce

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

has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 13.10.2022, 23.06.2022.

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

AstraZeneca AB

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

Scope: "Extension of indication to include first-line treatment, with Imfinzi in combination with tremelimumab and platinum-based chemotherapy, of adults with metastatic NSCLC with no sensitising epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) genomic tumour aberrations, based on final results from study D419MC00004 (POSEIDON); This was a Phase III, randomised, multicentre, open-label, comparative global study to determine the efficacy and safety of tremelimumab and durvalumab or durvalumab in combination with platinum based chemotherapy for first-line treatment in patients with metastatic NSCLC. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.2. Version 5.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 13.10.2022, 22.04.2022.

5.1.12. Imfinzi - durvalumab - EMEA/H/C/004771/II/0045

AstraZeneca AB

Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: David Olsen

Scope: "Extension of indication to include Imfinzi in combination with tremelimumab for the treatment of adults with unresectable hepatocellular carcinoma (uHCC), based on final results from study D419CC00002 (HIMALAYA); This was a randomized, open-label, multi-center phase III study of durvalumab and tremelimumab as first-line treatment in patients with unresectable hepatocellular carcinoma. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and Package Leaflet. Version 6.1 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 11.10.2022, 21.07.2022.

5.1.13. Kerendia - finerenone - EMEA/H/C/005200/II/0001/G

Bayer AG

Rapporteur: Kristina Dunder, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include the treatment of chronic kidney disease (CKD) and for the prevention of cardiovascular (CV) events in adults with CKD (regardless of the stage of albuminuria) associated with type 2 diabetes, based on results from study 17530 (FIGARO-DKD); a randomized, double-blind, placebo-controlled, parallel-group, multicenter, event-driven Phase III study to investigate the efficacy and safety of finerenone on the reduction of cardiovascular morbidity and mortality in subjects with type 2 diabetes mellitus and the clinical diagnosis of diabetic kidney disease in addition to standard of care.
As a consequence, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC is being updated and the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make editorial changes in the SmPC. The updated RMP version 2.1 has also been submitted.
Update of the SmPC section 5.2 based on the results of study 21429, a phase 1 drug interaction study of finerenone with rosuvastatin. The CSR PH-42032 was already submitted within the response to Day 180 List of Outstanding Issues of the initial MAA.
Submission of the results of study 21325, a phase 1 bioequivalence study assessing BE between finerenone 2 x 10 mg tablets and 20 mg tablet in Japanese healthy male adult participants (required by the Japanese PMDA)."

Action: For adoption

Request for Supplementary Information adopted on 15.09.2022, 23.06.2022.

See 2.3

5.1.14. Libtayo - cemiplimab - EMEA/H/C/004844/II/0028

Regeneron Ireland Designated Activity Company (DAC)

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

Scope: "Extension of indication to include Libtayo in combination with platinum-based chemotherapy for the first-line treatment of adult patients with locally advanced NSCLC who are not candidates for definitive chemoradiation or metastatic NSCLC with no EGFR, ALK or ROS1 aberrations; as a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.0 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 21.07.2022, 22.04.2022.

See 2.3

5.1.15. NexoBrid - concentrate of proteolytic enzymes enriched in bromelain - Orphan - EMEA/H/C/002246/II/0058

MediWound Germany GmbH

Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber

Scope: "Extension of current indication for removal of eschar in adults with deep partial- and full-thickness thermal burns to the paediatric population for NexoBrid based on interim results from study MW2012-01-01 (CIDS study), listed as study MW2012-01-01 is a 3-stage, multi-centre, multi-national, randomised, controlled, open label, 2 arm study aiming to demonstrate the superiority of NexoBrid treatment over SOC treatment in paediatric patients (aged 0 to 18 years) with deep partial thickness (DPT) and full thickness (FT)

thermal burns of 1% to 30% of total body surface area (TBSA).
As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated accordingly. Version 9 of the RMP has also been submitted."

Action: For adoption

5.1.16. Nubeqa - darolutamide - EMEA/H/C/004790/II/0009

Bayer AG

Rapporteur: Alexandre Moreau, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Jan Neuhauser

Scope: "Extension of indication to include treatment of adult men with metastatic hormone-sensitive prostate cancer (mHSPC) in combination with docetaxel, based on final results from study 17777 (ARASENS); this is a randomized, double-blind, placebo-controlled Phase 3 study designed to demonstrate the superiority of darolutamide in combination with docetaxel over placebo in combination with docetaxel in OS in patients with mHSPC. As a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted. As part of the application, the MAH is also requesting one additional year of market protection.", 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 15.09.2022, 23.06.2022.

5.1.17. Opdivo - nivolumab - EMEA/H/C/003985/II/0125/G

Bristol-Myers Squibb Pharma EEIG

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

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

Action: For adoption

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

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Daniela Philadelphy, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur:

Jean-Michel Dogné

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

Action: For adoption

Request for Supplementary Information adopted on 23.06.2022, 27.01.2022.

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

Roche Registration GmbH

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include treatment of new indication for slowing the rate of decline in pulmonary function in adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) for RoActemra, based on final results from the pivotal Phase III study WA29767 (focuSSced) entitled, "A Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Assess the Efficacy and Safety of Tocilizumab Versus Placebo in Patients With Systemic Sclerosis" and the supportive Phase II/III study WA27788 (faSScinate) entitled, "A Phase II/III, Multicenter, Randomized, Double-blind, Placebo-controlled Study To Assess The Efficacy And Safety Of Tocilizumab Versus Placebo In Patients With Systemic Sclerosis".
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 28 of the RMP has also been submitted."

Action: For adoption

5.1.20. Rubraca - rucaparib - EMEA/H/C/004272/II/0036

Clovis Oncology Ireland Limited

Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include maintenance treatment of adult patients with advanced (FIGO Stages III and IV) epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to first-line platinum-based chemotherapy for Rubraca, based on interim results from study CO-338-087 (ATHENA); this is a Phase III, randomized, double-blind, dual placebo controlled study of rucaparib as monotherapy and in combination with nivolumab in patients with newly diagnosed EOC, FTC or PPC who have responded to their first-line treatment (surgery and platinum-based chemotherapy). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 6.3 of the RMP has also been submitted. As part of the application the MAH is requesting a 1-year extension of the market protection.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

5.1.21. Spikevax - elasomeran - EMEA/H/C/005791/II/0083/G

Moderna Biotech Spain, S.L.

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

Scope: "Extension of indication to include a 50-µg booster dose of Spikevax bivalent Original/Omicron BA.1 in children (6 to < 12 years), based on interim results from study P204; this is a Phase 2/3, Three-Part, Open-Label, Dose-Escalation, Age De-escalation and Randomized, Observer-Blind, Placebo-Controlled Expansion Study to Evaluate the Safety, Tolerability, Reactogenicity, and Effectiveness of mRNA-1273 SARS-CoV-2 Vaccine in Healthy Children 6 Months to Less Than 12 Years of Age; As a consequence, sections 2, 4.1, 4.2, 4.4, 4.8, 5.1 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.5 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to implement editorial changes.
To update sections 4.8, 5.1 and 6.6 of the SmPC to include additional immunogenicity data for the paediatric population (6 to < 18 years) based on Real-World Safety studies."

Action: For adoption

Request for Supplementary Information adopted on 10.11.2022.

5.1.22. Tenkasi - oritavancin - EMEA/H/C/003785/II/0037

Menarini International Operations Luxembourg S.A.

Rapporteur: Janet Koenig, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension of indication to include treatment of paediatric population, aged between 3 months and less than 18 years for Tenkasi (oritavancin) 400 mg based on interim results from study TMC-ORI-11-01; this is a multicenter, open-label, dose-finding study of oritavancin single dose infusion in paediatric subjects less than 18 years of age with suspected or confirmed bacterial infections. The purpose of this Phase 1 study is to evaluate the safety, tolerability and PK of oritavancin in paediatric subjects and determine the optimal dose for a Phase 2 trial in paediatric subjects with ABSSSI. As a consequence, sections 4.1, 4.2, 4.4 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 5.0 of the RMP has also been submitted.
In addition, MAH is also taking this opportunity to update the contact details of the local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.2 rev 1."

Action: For adoption

5.1.23. Ultomiris - ravulizumab - EMEA/H/C/004954/II/0032

Alexion Europe SAS

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

Scope: "Extension of indication to include the treatment of adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin 4 (AQP4) antibody-positive,

based on interim results from study ALXN1210-NMO-307; this is a phase 3, external placebo-controlled, open-label, multicenter study to evaluate the efficacy and safety of ravulizumab in adult patients with NMOSD. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 6.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Action: For adoption

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

Novo Nordisk A/S

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Mari Thorn

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

Action: For adoption

5.1.25. WS2299
Edistride - dapagliflozin - EMEA/H/C/004161/WS2299/0055
Forxiga - dapagliflozin - EMEA/H/C/002322/WS2299/0076

AstraZeneca AB

Lead Rapporteur: Kristina Dunder, PRAC Rapporteur: Mari Thorn

Scope: "Extension of indication to include population with Heart Failure and LVEF > 40% for Forxiga and its duplicate Edistride, based on final results from study D169CC00001 (DELIVER); The DELIVER study is a category 3, Post-Authorisation Safety Study (PASS) listed in the dapagliflozin RMP to evaluate the potential risk of lower limb amputation; This was an international, multi-centre, parallel-group, event-driven, randomised, double-blind, placebo-controlled Phase III study in patients with HF and LVEF > 40%, evaluating the effect of dapagliflozin 10 mg compared with placebo, given once daily in addition to background therapy, including treatments to control co-morbidities, in reducing the composite of CV death or an HF event (hospitalisation for HF or urgent HF visit). As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet are updated in accordance. Version 27 of the RMP has also been submitted."

Action: For adoption

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

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst

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

Action: For adoption

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

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

Roche Registration GmbH

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

Scope: "Grouping of three variations as follows:
Extension of indication to include treatment of patients below 2 months of age based on interim results from study BN40703 (RAINBOWFISH). The pivotal study RAINBOWFISH is an ongoing phase II multicentre, open-label, and single-arm study designed to evaluate the efficacy, safety, tolerability, and PK/PD of risdiplam in pre-symptomatic infants below 2 months of age who were genetically diagnosed with SMA. As a consequence, SmPC sections 4.1, 4.2, 4.8, 5.1 and 5.2 have been updated and the Package Leaflet has been updated in accordance. In addition, the MAH took the opportunity to make some editorial improvements in the product information. A revised RMP version 1.1 was also submitted as part of the application.
Type IAIN, B.IV.1.a.1 variation to update Evrysdi pack configuration with the addition of a new 1 mL oral syringe into the product carton allowing precise dosing of infants below 2 months of age. As a consequence, section 6.5 of the SmPC has been updated and the labelling and Package Leaflet have been updated in accordance.
Type IAIN, B.IV.1.b variation to remove the spare unit of 12 mL oral syringe out of the two units currently provided in the product carton. As a consequence, section 6.5 of the SmPC has been updated and the labelling and Package Leaflet have been updated in accordance."

Letter by the applicant dated 28 November 2022 requesting an extension to the clock stop to respond to the request for supplementary information adopted in October 2022.

Action: For adoption

Request for Supplementary Information adopted on 13.10.2022, 21.07.2022, 22.04.2022.

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

No items

6. Medical devices

6.1. Ancillary medicinal substances - initial consultation

No items

6.2. Ancillary medicinal substances – post-consultation update

No items

6.3. Companion diagnostics - initial consultation

No items

6.4. Companion diagnostics – follow-up consultation

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. concizumab - H0005938

indicated for routine prophylaxis to prevent or reduce the frequency of bleeding in patients with
- haemophilia A (congenital factor VIII deficiency) with FVIII inhibitors ≥ 12 years of age.
- haemophilia B (congenital factor IX deficiency) with FIX inhibitors of any age.

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

Action: For adoption

8.1.2. elranatamab - Orphan - H0005908

Pfizer Europe MA EEIG; Multiple Myeloma. Indicated as monotherapy for the treatment of relapsed or refractory multiple myeloma in adult patients who have received at least 3 prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD-38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

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

Action: For adoption

8.1.3. lecanemab - H0005966

indicated as a disease modifying treatment in adult patients with Mild Cognitive Impairment due to Alzheimer's disease and Mild Alzheimer's disease (Early Alzheimer's disease)

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. COVID-19 Vaccine (inactivated, adjuvanted) Valneva - SARS-CoV-2 virus, strain Wuhan hCoV-19/Italy/INMI1-isl/2020, inactivated - EMEA/H/C/006019/II/0004

Valneva Austria GmbH

Rapporteur: Andrea Laslop

Scope: "Update of sections 4.2 and 5.1 of the SmPC in order to include a booster dose for adults 18 to 50 years of age based on the interim results from study VLA2001-301 (Booster part); this is a randomized, observer-blind, controlled, superiority study to compare the

immunogenicity of COVID-19 Vaccine (inactivated, adjuvanted) Valneva to AZD1222, where participants received a booster dose of COVID-19 vaccine Valneva; the Package Leaflet is updated accordingly."

Action: For adoption

9.1.2. Rubraca - rucaparib - EMEA/H/C/004272/II/0037

Clovis Oncology Ireland Limited

Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information and the list of adverse drug reactions (ADRs) based on the final results from study CO-338-014 (ARIEL 3) listed as a category 1 PAES in the Annex II; this is a phase 3, multicenter, randomized, double-blind, placebo-controlled study of rucaparib as switch maintenance following platinum-based chemotherapy in patients with platinum-sensitive, high grade serous or endometrioid epithelial ovarian, primary peritoneal or fallopian tube cancer. The Package Leaflet is updated accordingly. The RMP version 6.4 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Action: For adoption

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

GlaxoSmithKline (Ireland) Limited

Rapporteur: Ingrid Wang, PRAC Rapporteur: Jan Neuhauser

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

Action: For adoption

Request for Supplementary Information adopted on 19.05.2022, 10.02.2022.

See 2.3

9.1.4. JCOVDEN - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/R/0063

Janssen-Cilag International N.V.

Rapporteur: Christophe Focke, PRAC Rapporteur: Ulla Wändel Liminga

Scope: Renewal of marketing authorisation

Action: For adoption

9.1.5. Olumiant - baricitinib - EMEA/H/C/004085/II/0028

Eli Lilly Nederland B.V.

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

Scope: "C.I.6 - Extension of indication to include treatment of coronavirus disease 2019 (COVID 19) in hospitalised adult and paediatric patients aged 10 years and older who require low-flow oxygen or non-invasive ventilation/high flow oxygen for Olumiant; as a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Annex II and the Package Leaflet are updated in accordance. Version 11.1 of the RMP has also been submitted.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Withdrawal of extension of indication application.

Action: For information

Request for Supplementary Information adopted on 21.07.2022, 14.10.2021, 22.07.2021.

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. Rambis - ramipril, bisoprolol fumarate - EMEA/H/A-29(4)/1519

Adamed Pharma S.A.

Rapporteur: Ewa Balkowiec Iskra, Co-Rapporteur: Ondrej Slanar

Scope: Opinion

Action: For adoption

Decentralised procedure number: PL/H/0758/001-006/DC, notification by the Agency of Poland dated 30 May 2022 notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC

List of outstanding issues adopted on 15.09.2022. List of questions adopted on 23.06.2022.

10.4.2. Gelisia - timolol maleate - EMEA/H/A-29(4)/1522

Sifi S.p.A.

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Blanca Garcia-Ochoa

Scope: Opinion

Action: For adoption

Decentralised procedure number: NL/H/5357/001/DC, notification by the Agency of The Netherlands dated 22 October 2022 notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

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

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

No items

13.2. Innovation Task Force briefing meetings

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Vote by proxy

None

14.1.2. CHMP membership

None

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 December 2022

Action: For adoption

14.2.2. Paediatric Committee (PDCO)

PIPs reaching D30 at December 2022 PDCO

Action: For information

Report from the PDCO meeting held on 08-11 November 2022

Action: For information

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

14.3.1. Biologics Working Party (BWP)

Chair: Sol Ruiz/ Sean Barry

Reports from BWP December 2022 meeting to CHMP for adoption:

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

Action: For adoption

14.3.2. Name Review Group (NRG)

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

Action: For adoption

14.3.3. Scientific Advice Working Party (SAWP)

Chair: Paolo Foggi

Report from the SAWP meeting held on 28 November - 01 December 2022. Table of conclusions

Action: For information

Scientific advice letters:

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

14.4. 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

14.7.1. CHMP Work Plan 2023

Adoption of the CHMP Work Plan for 2023.

Action: For adoption

14.8. Planning and reporting

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

Q4-2022 initial marketing authorisation application submissions with eligibility request to central procedure

Action: For information

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Update on COVID-19

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)*

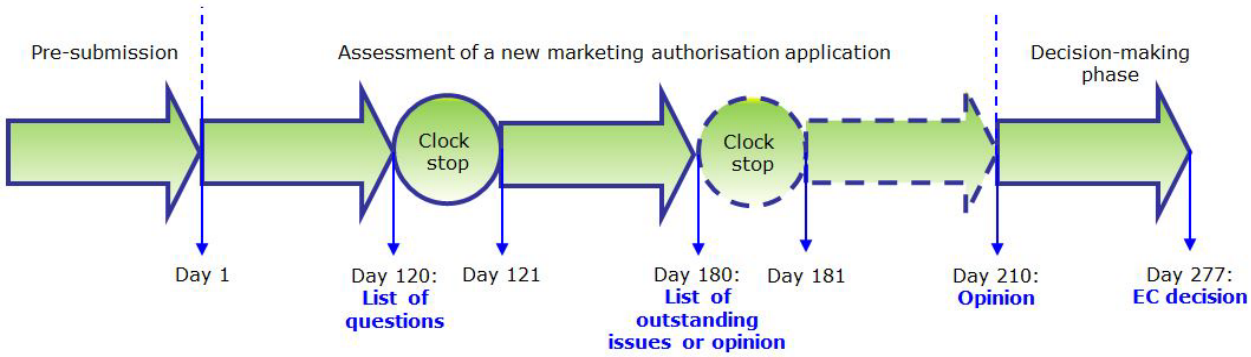
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

12 December 2022
EMA/CHMP/885263/2022

Annex to 12-15 December 2022 CHMP Agenda

Pre-submission and post-authorisations issues

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Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

A. PRE-SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

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

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

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

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

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

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

Bylvay - odevixibat - EMEA/H/C/004691/S/0008, Orphan
Albireo, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski
Request for Supplementary Information adopted on 13.10.2022.

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

Lojuxta - lomitapide - EMEA/H/C/002578/S/0052
Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Menno van der Elst

Request for Supplementary Information adopted on 10.11.2022.

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

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

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

B.2.2. Renewals of Marketing Authorisations for unlimited validity

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

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

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

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

KANJINTI - trastuzumab - EMEA/H/C/004361/R/0022
Amgen Europe B.V., BREDA, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski

Request for Supplementary Information adopted on 10.11.2022.	
Lokelma - sodium zirconium cyclosilicate - EMEA/H/C/004029/R/0027 AstraZeneca AB, Rapporteur: Silvijus Abramavicius, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Kirsti Villikka Request for Supplementary Information adopted on 13.10.2022.	
Semglee - insulin glargine - EMEA/H/C/004280/R/0040 Viatris Limited, Rapporteur: Martina Weise, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 13.10.2022.	

B.2.3. Renewals of Conditional Marketing Authorisations

Deltyba - delamanid - EMEA/H/C/002552/R/0062, Orphan Otsuka Novel Products GmbH, Rapporteur: Christophe Focke, PRAC Rapporteur: Jo Robays	
JCOVDEN - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/R/0063 Janssen-Cilag International N.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Ulla Wändel Liminga	See 9.1
JEMPERLI - dostarlimab - EMEA/H/C/005204/R/0017 GlaxoSmithKline (Ireland) Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Inês Ribeiro-Vaz	
Natpar - parathyroid hormone - EMEA/H/C/003861/R/0046, Orphan Takeda Pharmaceuticals International AG, Rapporteur: Karin Janssen van Doorn, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Rhea Fitzgerald	
Pemazyre - pemigatinib - EMEA/H/C/005266/R/0007, Orphan Incyte Biosciences Distribution B.V., Rapporteur: Alexandre Moreau, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Menno van der Elst	

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 28 November – 01 December 2022 PRAC:

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

EMEA/H/C/PSUSA/00002842/202205
(tafamidis)
CAPS:
Vyndaqel (EMEA/H/C/002294) (tafamidis), Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Tiphaine Vaillant, "16/05/2021 To: 15/05/2022"

EMEA/H/C/PSUSA/00003152/202203
(zonisamide)
CAPS:
Zonegran (EMEA/H/C/000577) (zonisamide), Amdipharm Limited, Rapporteur: Finbarr Leacy
NAPS:
NAPs - EU
PRAC Rapporteur: Ronan Grimes, "31/03/2020 To: 31/03/2022"

EMEA/H/C/PSUSA/00010644/202205
(atezolizumab)
CAPS:
Tecentriq (EMEA/H/C/004143) (atezolizumab), Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Inês Ribeiro-Vaz, "17/05/2021 To: 17/05/2022"

EMEA/H/C/PSUSA/00010918/202204
(tucatinib)
CAPS:
TUKYSA (EMEA/H/C/005263) (tucatinib), Seagen B.V., Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Jean-Michel Dogné, "16/10/2021 To: 16/04/2022"

EMEA/H/C/PSUSA/00010923/202204
(pemigatinib)
CAPS:
Pemazyre (EMEA/H/C/005266) (pemigatinib), Incyte Biosciences Distribution B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst, "16/10/2021 To: 16/04/2022"

EMEA/H/C/PSUSA/00010959/202204 (sacituzumab govitecan) CAPS: **TRODELVY** (EMEA/H/C/005182) (sacituzumab govitecan), Gilead Sciences Ireland UC, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "22/10/2021 To: 21/04/2022"	
EMEA/H/C/PSUSA/00010960/202205 (zanubrutinib) CAPS: **Brukinsa** (EMEA/H/C/004978) (zanubrutinib), BeiGene Ireland Ltd, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Menno van der Elst, "12/11/2021 To: 12/05/2022"	
EMEA/H/C/PSUSA/00010962/202205 (ripretinib) CAPS: **QINLOCK** (EMEA/H/C/005614) (ripretinib), Deciphera Pharmaceuticals (Netherlands) B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Željana Margan Koletić, "15/05/2021 To: 14/05/2022"	

B.4. EPARs / WPARs

Kauliv - teriparatide - EMEA/H/C/004932 Strides Pharma Cyprus, Treatment of osteoporosis in postmenopausal women and in men at increased risk of fracture, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Pirfenidone Viatris - pirfenidone - EMEA/H/C/005862 Viatris Limited, treatment of Idiopathic Pulmonary Fibrosis (IPF), Generic, Generic of Esbriet, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Sugammadex Amomed - sugammadex - EMEA/H/C/005935 AOP Orphan Pharmaceuticals GmbH, reversal of neuromuscular blockade induced by rocuronium or vecuronium, Generic, Generic of Bridion, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
VidPrevtyn Beta - SARS-CoV-2 prefusion spike delta TM protein, recombinant - EMEA/H/C/005754	For information only. Comments can be sent to the PL in case necessary.

Sanofi Pasteur, Active immunisation to prevent COVID-19 caused by SARS-CoV-2 prefusion Spike delta TM protein, in individuals 18 years of age and older., New active substance (Article 8(3) of Directive No 2001/83/EC)	

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

Adtralza - tralokinumab - EMEA/H/C/005255/II/0005 LEO Pharma A/S, Rapporteur: Jayne Crowe Opinion adopted on 01.12.2022. Request for Supplementary Information adopted on 01.09.2022.	Positive Opinion adopted by consensus on 01.12.2022.
Armisarte - pemetrexed - EMEA/H/C/004109/II/0030/G Actavis Group PTC ehf, Rapporteur: Alar Irs Request for Supplementary Information adopted on 22.09.2022.	
Bavencio - avelumab - EMEA/H/C/004338/II/0037/G Merck Europe B.V., Rapporteur: Filip Josephson Opinion adopted on 17.11.2022. Request for Supplementary Information adopted on 13.10.2022.	Positive Opinion adopted by consensus on 17.11.2022.
Beovu - brolucizumab - EMEA/H/C/004913/II/0019 Novartis Europharm Limited, Rapporteur: Alexandre Moreau	
Besremi - ropeginterferon alfa-2b - EMEA/H/C/004128/II/0026 AOP Orphan Pharmaceuticals GmbH, Rapporteur: Janet Koenig	
Brintellix - vortioxetine - EMEA/H/C/002717/II/0033 H. Lundbeck A/S, Rapporteur: Karin Janssen van Doorn Request for Supplementary Information adopted on 01.12.2022, 02.06.2022.	Request for supplementary information adopted with a specific timetable.
Caelyx pegylated liposomal - doxorubicin - EMEA/H/C/000089/II/0103 Baxter Holding B.V., Rapporteur: Ondřej Slanař	

Request for Supplementary Information adopted on 13.10.2022.	
CEVENFACTA - eptacog beta (activated) - EMEA/H/C/005655/II/0001 Laboratoire Francais du Fractionnement et des Biotechnologies, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 24.11.2022.	Request for supplementary information adopted with a specific timetable.
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0148/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0149/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0156/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	
Defitelio - defibrotide - EMEA/H/C/002393/II/0059, Orphan Gentium S.r.l., Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 17.11.2022.	Request for supplementary information adopted with a specific timetable.
Doptelet - avatrombopag - EMEA/H/C/004722/II/0015/G Swedish Orphan Biovitrum AB (publ), Rapporteur: Aaron Sosa Mejia Request for Supplementary Information adopted on 27.10.2022.	
Ervebo - recombinant vesicular stomatitis virus - Zaire ebolavirus vaccine (live) - EMEA/H/C/004554/II/0027 Merck Sharp & Dohme B.V., Rapporteur: Christophe Focke	
Fasturtec - rasburicase - EMEA/H/C/000331/II/0064/G sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege	
Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0029 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz Opinion adopted on 01.12.2022.	Positive Opinion adopted by consensus on 01.12.2022.

Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0031 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz	
Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0060/G Merck Sharp & Dohme B.V., Rapporteur: Kristina Dunder Opinion adopted on 01.12.2022.	Positive Opinion adopted by consensus on 01.12.2022.
Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0061 Merck Sharp & Dohme B.V., Rapporteur: Kristina Dunder	
Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0139 CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 24.11.2022. Request for Supplementary Information adopted on 01.09.2022.	Positive Opinion adopted by consensus on 24.11.2022.
Inflectra - infliximab - EMEA/H/C/002778/II/0108/G Pfizer Europe MA EEIG, Duplicate, Duplicate of Remsima, Rapporteur: Outi Mäki-Ikola Opinion adopted on 24.11.2022. Request for Supplementary Information adopted on 20.10.2022.	Positive Opinion adopted by consensus on 24.11.2022.
Insulin aspart Sanofi - insulin aspart - EMEA/H/C/005033/II/0010/G sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 17.11.2022. Request for Supplementary Information adopted on 06.10.2022.	Positive Opinion adopted by consensus on 17.11.2022.
Ivabradine Accord - ivabradine - EMEA/H/C/004241/II/0016/G Accord Healthcare S.L.U., Generic, Generic of Procoralan, Rapporteur: Anastasia Mountaki	
JCOVDEN - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0064 Janssen-Cilag International N.V., Rapporteur:	

Christophe Focke	
JCOVDEN - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0067 Janssen-Cilag International N.V., Rapporteur: Christophe Focke	
Jivi - damoctocog alfa pegol - EMEA/H/C/004054/II/0024/G Bayer AG, Rapporteur: Thalia Marie Estrup Blicher Opinion adopted on 17.11.2022. Request for Supplementary Information adopted on 08.09.2022.	Positive Opinion adopted by consensus on 17.11.2022.
Jivi - damoctocog alfa pegol - EMEA/H/C/004054/II/0025/G Bayer AG, Rapporteur: Thalia Marie Estrup Blicher Opinion adopted on 17.11.2022.	Positive Opinion adopted by consensus on 17.11.2022.
Luminity - perflutren - EMEA/H/C/000654/II/0042/G Lantheus EU Limited, Rapporteur: Finbarr Leacy	
Lyumjev - insulin lispro - EMEA/H/C/005037/II/0016 Eli Lilly Nederland B.V., Rapporteur: Outi Mäki-Ikola Opinion adopted on 17.11.2022. Request for Supplementary Information adopted on 13.10.2022, 08.09.2022.	Positive Opinion adopted by consensus on 17.11.2022.
Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0120/G Pfizer Europe MA EEIG, Rapporteur: Ingrid Wang	
Nivestim - filgrastim - EMEA/H/C/001142/II/0070/G Pfizer Europe MA EEIG, Rapporteur: Outi Mäki-Ikola	
Nuceiva - botulinum toxin type a - EMEA/H/C/004587/II/0027 Evolus Pharma B.V., Rapporteur: Finbarr Leacy Request for Supplementary Information adopted on 01.09.2022.	
Nulojix - belatacept - EMEA/H/C/002098/II/0082/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson	

Request for Supplementary Information adopted on 10.11.2022.	
NUVAXOVID - SARS-CoV-2, spike protein, recombinant, expressed in Sf9 cells derived from Spodoptera Frugiperda - EMEA/H/C/005808/II/0027 Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 17.11.2022.	Request for supplementary information adopted with a specific timetable.
NUVAXOVID - SARS-CoV-2, spike protein, recombinant, expressed in Sf9 cells derived from Spodoptera Frugiperda - EMEA/H/C/005808/II/0034 Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege	
Ozurdex - dexamethasone - EMEA/H/C/001140/II/0043/G AbbVie Deutschland GmbH & Co. KG, Rapporteur: Maria Concepcion Prieto Yerro Request for Supplementary Information adopted on 17.11.2022.	Request for supplementary information adopted with a specific timetable.
Padcev - enfortumab vedotin - EMEA/H/C/005392/II/0005/G Astellas Pharma Europe B.V., Rapporteur: Aaron Sosa Mejia	
Paxlovid - (1r,2s,5s)-n-((1s)-1-cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2s)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973/II/0028/G Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race Request for Supplementary Information adopted on 17.11.2022.	Request for supplementary information adopted with a specific timetable.
Rapiscan - regadenoson - EMEA/H/C/001176/II/0041/G GE Healthcare AS, Rapporteur: Maria Concepcion Prieto Yerro	
ReFacto AF - moroctocog alfa - EMEA/H/C/000232/II/0165/G Pfizer Europe MA EEIG, Rapporteur: Thalia Marie Estrup Blicher Opinion adopted on 24.11.2022.	Positive Opinion adopted by consensus on 24.11.2022.

Rekovelle - follitropin delta - EMEA/H/C/003994/II/0034 Ferring Pharmaceuticals A/S, Rapporteur: Jean-Michel Race Opinion adopted on 24.11.2022. Request for Supplementary Information adopted on 01.09.2022, 21.07.2022.	Positive Opinion adopted by consensus on 24.11.2022.
Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0055/G CSL Behring GmbH, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 17.02.2022.	
Ryeqo - relugolix / estradiol / norethisterone acetate - EMEA/H/C/005267/II/0012 Gedeon Richter Plc., Rapporteur: Paula Boudewina van Hennik	
SARCLISA - isatuximab - EMEA/H/C/004977/II/0017/G sanofi-aventis groupe, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 10.11.2022, 13.10.2022.	
Sogroya - somapacitan - EMEA/H/C/005030/II/0004/G, Orphan Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 24.11.2022. Request for Supplementary Information adopted on 21.07.2022.	Positive Opinion adopted by consensus on 24.11.2022.
Somavert - pegvisomant - EMEA/H/C/000409/II/0104 Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race Request for Supplementary Information adopted on 10.11.2022.	
Spectrila - asparaginase - EMEA/H/C/002661/II/0029 medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 01.09.2022, 02.06.2022.	
Spikevax - elasomeran - EMEA/H/C/005791/II/0089/G Moderna Biotech Spain, S.L., Rapporteur: Jan	

Mueller-Berghaus	
Spikevax - elasomeran - EMEA/H/C/005791/II/0090/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus	
Strensiq - asfotase alfa - EMEA/H/C/003794/II/0060/G, Orphan Alexion Europe SAS, Rapporteur: Armando Genazzani Opinion adopted on 24.11.2022.	Positive Opinion adopted by consensus on 24.11.2022.
TEZSPIRE - tezepelumab - EMEA/H/C/005588/II/0001 AstraZeneca AB, Rapporteur: Finbarr Leacy, PRAC Rapporteur: Eva Jirsová Request for Supplementary Information adopted on 01.12.2022.	Request for supplementary information adopted with a specific timetable.
Tremfya - guselkumab - EMEA/H/C/004271/II/0034/G Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics Opinion adopted on 17.11.2022. Request for Supplementary Information adopted on 13.10.2022.	Positive Opinion adopted by consensus on 17.11.2022.
TRODELVY - sacituzumab govitecan - EMEA/H/C/005182/II/0017 Gilead Sciences Ireland UC, Rapporteur: Jan Mueller-Berghaus	
Trumenba - meningococcal group b vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0042 Pfizer Europe MA EEIG, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 24.11.2022.	Request for supplementary information adopted with a specific timetable.
Ultomiris - ravulizumab - EMEA/H/C/004954/II/0033/G Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa Opinion adopted on 24.11.2022.	Positive Opinion adopted by consensus on 24.11.2022.
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0107 MCM Vaccine B.V., Rapporteur: Christophe Focke	Positive Opinion adopted by consensus on 17.11.2022.

Opinion adopted on 17.11.2022.	
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0109 MCM Vaccine B.V., Rapporteur: Christophe Focke Opinion adopted on 01.12.2022.	Positive Opinion adopted by consensus on 01.12.2022.
Vazkepa - icosapent ethyl - EMEA/H/C/005398/II/0009/G Amarin Pharmaceuticals Ireland Limited, Rapporteur: Martina Weise Request for Supplementary Information adopted on 01.09.2022.	
VidPrevtyn Beta - sars-cov-2 prefusion spike delta tm protein, recombinant - EMEA/H/C/005754/II/0001/G Sanofi Pasteur, Rapporteur: Jan Mueller-Berghaus	
Xenical - orlistat - EMEA/H/C/000154/II/0086 CHEPLAPHARM Arzneimittel GmbH, Rapporteur: Jean-Michel Race Opinion adopted on 01.12.2022. Request for Supplementary Information adopted on 01.09.2022.	Positive Opinion adopted by consensus on 01.12.2022.
Zaltrap - aflibercept - EMEA/H/C/002532/II/0067/G sanofi-aventis groupe, Rapporteur: Filip Josephson	
Zercepac - trastuzumab - EMEA/H/C/005209/II/0016 Accord Healthcare S.L.U., Rapporteur: Sol Ruiz Opinion adopted on 24.11.2022. Request for Supplementary Information adopted on 13.01.2022.	Positive Opinion adopted by consensus on 24.11.2022.
Zercepac - trastuzumab - EMEA/H/C/005209/II/0021 Accord Healthcare S.L.U., Rapporteur: Sol Ruiz Request for Supplementary Information adopted on 01.12.2022.	Request for supplementary information adopted with a specific timetable.
WS2288 Humalog- EMEA/H/C/000088/WS2288/0196 Liprolog-	Positive Opinion adopted by consensus on 17.11.2022.

EMEA/H/C/000393/WS2288/0156 Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder Opinion adopted on 17.11.2022. Request for Supplementary Information adopted on 13.10.2022, 01.09.2022.	
WS2298/G **Actraphane-EMEA/H/C/000427/WS2298/0092/G** **Actrapid-EMEA/H/C/000424/WS2298/0085/G** **Actrapid-EMEA/H/W/005779/WS2298/0001/G** **Insulatard-EMEA/H/C/000441/WS2298/0090/G** **Insulatard-EMEA/H/W/005780/WS2298/0001/G** **Levemir-EMEA/H/C/000528/WS2298/0105/G** **Mixtard-EMEA/H/C/000428/WS2298/0093/G** **Protaphane-EMEA/H/C/000442/WS2298/0089/G** **Ryzodeg-EMEA/H/C/002499/WS2298/0050/G** **Tresiba-EMEA/H/C/002498/WS2298/0057/G** **Xultophy-EMEA/H/C/002647/WS2298/0046/G** Novo Nordisk A/S, Lead Rapporteur: Thalia Marie Estrup Blicher Opinion adopted on 17.11.2022.	Positive Opinion adopted by consensus on 17.11.2022.
WS2302/G **Fiasp-EMEA/H/C/004046/WS2302/0031/G** **NovoMix-EMEA/H/C/000308/WS2302/0112/G** **NovoRapid-EMEA/H/C/000258/WS2302/0142/G** **Ryzodeg-EMEA/H/C/002499/WS2302/0049/G** Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder	
WS2303/G **Saxenda-EMEA/H/C/003780/WS2303/0033/G** **Victoza-EMEA/H/C/001026/WS2303/0064/G** **Xultophy-**	Positive Opinion adopted by consensus on 24.11.2022.

EMEA/H/C/002647/WS2303/0045/G Novo Nordisk A/S, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 24.11.2022.	
WS2326/G **Hexacima-EMEA/H/C/002702/WS2326/0138/G** **Hexyon-EMEA/H/C/002796/WS2326/0142/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus	
WS2344 **Ryzodeg-EMEA/H/C/002499/WS2344/0048** **Tresiba-EMEA/H/C/002498/WS2344/0056** **Xultophy-EMEA/H/C/002647/WS2344/0044** Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 01.12.2022, 27.10.2022.	Request for supplementary information adopted with a specific timetable.
WS2359 **HyQvia-EMEA/H/C/002491/WS2359/0085** **Kiovig-EMEA/H/C/000628/WS2359/0120** Takeda Manufacturing Austria AG, Lead Rapporteur: Jan Mueller-Berghaus	

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

ADCETRIS - brentuximab vedotin - EMEA/H/C/002455/II/0103, Orphan Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.8 and 5.1 of the SmPC to reflect new safety and efficacy information based on long-term data from the second interim analysis of OS (103 events) from study ECHELON-1, undertaken in previously untreated CD30+ Stage IV HL. In addition, following the completion of all specific obligations and considering the recent switch from a conditional to a full MA (variation II-99), the MAH takes the opportunity to propose the removal of the black triangle (regarding additional monitoring) from the SmPC and the Package Leaflet. Further, minor editorial changes are proposed in the SmPC and Package Leaflet and the contact details of the local representatives are being updated in the Package Leaflet."	Positive Opinion adopted by consensus on 17.11.2022.

Opinion adopted on 17.11.2022. Request for Supplementary Information adopted on 13.10.2022.	
Avonex - interferon beta-1A - EMEA/H/C/000102/II/0193 Biogen Netherlands B.V., Rapporteur: Maria Concepcion Prieto Yerro, "Update of sections 4.2 and 4.4 of the SmPC in order to update safety information for the paediatric population based on the final results of the Tecfidera Paediatric study (109MS306) (CONNECT - part 1), submitted as part of the PAM procedure P46/089, availability of data from published literature and post-marketing data from Biogen global safety database; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 13.10.2022, 16.06.2022.	
Benlysta - belimumab - EMEA/H/C/002015/II/0107 GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder, "Update of sections 4.4 and 5.1 of the SmPC based on final results from study 205646; this is an interventional Phase III Study to Evaluate the Efficacy and Safety of Belimumab Administered in Combination with Rituximab to Adult Subjects with Systemic Lupus Erythematosus (SLE). In addition, the MAH took the opportunity to implement editorial changes." Opinion adopted on 24.11.2022. Request for Supplementary Information adopted on 29.09.2022.	Positive Opinion adopted by consensus on 24.11.2022.
Besremi - ropeginterferon alfa-2b - EMEA/H/C/004128/II/0021 AOP Orphan Pharmaceuticals GmbH, Rapporteur: Janet Koenig, "Update of sections 4.8, 5.1 and 5.2 of the SmPC based on results from CONTINUATION-PV study. An open-label, multicentre, phase IIIb study assessing the long-term efficacy and safety of AOP2014 and standard first-line treatment (BAT) in patients with polycythaemia vera who previously participated in the PROUDPV study. The Package Leaflet is updated accordingly." Opinion adopted on 17.11.2022. Request for Supplementary Information adopted on 01.09.2022, 23.06.2022.	Positive Opinion adopted by consensus on 17.11.2022.

Betaferon - interferon beta-1B - EMEA/H/C/000081/II/0143/G

Bayer AG, Rapporteur: Martina Weise, "Update of sections 4.4 and 4.8 of the SmPC based on pooled clinical trial data from six phase II-IV studies: NASPMS (Study No. 3112), Pivotal RRMS (Study No. 13103), EUSPMS (Study No.93079), BENEFIT (Study No. 304747), BEYOND (Study No. 306440) and BEYOND pilot (Study No. 307000), post-marketing experience, scientific literature and FAERS database; the Package Leaflet is updated accordingly.
Update of section 4.8 of the SmPC in order to merge the existing two tables for ADRs, requested by the PRAC following the assessment of PSUSA procedure EMEA/H/C/PSUSA/00001759/202107), based on pooled data from four placebo controlled trials: NASPMS (Study No. 3112), Pivotal RRMS (Study No. 13103), EUSPMS (Study No. 93079), and BENEFIT (Study No. 304747); the Package Leaflet is updated accordingly.
In addition, the MAH took the opportunity to implement editorial changes and to update the list of local representatives in the Package Leaflet."
Request for Supplementary Information adopted on 06.10.2022.

Brintellix - vortioxetine - EMEA/H/C/002717/II/0038

H. Lundbeck A/S, Rapporteur: Karin Janssen van Doorn, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to include clinically relevant information on the efficacy, safety, tolerability, and PK of vortioxetine in the paediatric population based on final results from studies 12709A, 12712A and 12712B.
Study 12709A is an interventional, randomized, double-blind, placebo-controlled, active-reference (fluoxetine), fixed-dose study of vortioxetine in paediatric patients aged 7 to 11 years, with Major Depressive Disorder (MDD) to evaluate efficacy and safety. Whereas studies 12712A and 12712B are 2 open-label, long-term safety and efficacy studies in children and adolescents: one 6-month extension study (Study 12712A) to Studies 12709A and 12710A, and one 18-month extension study (Study 12712B) to Study 12712A. The Package Leaflet

is updated accordingly."	
Calquence - acalabrutinib - EMEA/H/C/005299/II/0015 AstraZeneca AB, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC based on the interim report of study ACE-CL-007; a randomized, multicenter, open-Label, 3-arm phase 3 study of obinutuzumab in combination with chlorambucil, ACP-196 in combination with obinutuzumab, and ACP-196 monotherapy in subjects with previously untreated chronic lymphocytic leukemia."	
Cotellic - cobimetinib - EMEA/H/C/003960/II/0028 Roche Registration GmbH, Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to add "Pruritus", "Dry skin" and "Oedema peripheral" to the list of adverse drug reactions (ADRs) with frequency "Very common" based on post-marketing experience and the final results from study ML29733; this is an Open-label, single-center, Phase II study evaluating the efficacy and safety of single-agent cobimetinib in patients with histiocytic disorders whose tumours were 1) BRAF V600 wildtype or 2) BRAF V600E mutant and were intolerant to, or unable to access, BRAF inhibitors. The Package Leaflet is updated accordingly." Opinion adopted on 24.11.2022.	Positive Opinion adopted by consensus on 24.11.2022.
COVID-19 Vaccine (inactivated, adjuvanted) Valneva - SARS-CoV-2 virus, strain Wuhan hCoV-19/Italy/INMI1-isl/2020, inactivated - EMEA/H/C/006019/II/0004 Valneva Austria GmbH, Rapporteur: Andrea Laslop, "Update of sections 4.2 and 5.1 of the SmPC in order to include a booster dose for adults 18 to 50 years of age based on the interim results from study VLA2001-301 (Booster part); this is a randomized, observer-blind, controlled, superiority study to compare the immunogenicity of COVID-19 Vaccine (inactivated, adjuvanted) Valneva to AZD1222, where participants received a booster dose of COVID-19 vaccine Valneva; the Package Leaflet is updated accordingly."	See 9.1
Darzalex - daratumumab -	Positive Opinion adopted by consensus on

EMEA/H/C/004077/II/0062, Orphan Janssen-Cilag International N.V., Rapporteur: Aaron Sosa Mejia, "Update of section 4.8 of the SmPC in order to add COVID-19 to the list of adverse drug reactions (ADRs) with frequency uncommon, based on a pooled dataset from the following interventional studies 4767414MMY2004, 54767414MMY3003, 54767414MMY3006, 54767414MMY3008, and 54767414MMY3013. The Package Leaflet is updated accordingly." Opinion adopted on 24.11.2022. Request for Supplementary Information adopted on 20.10.2022, 15.09.2022.	24.11.2022.
Esperoct - turoctocog alfa pegol - EMEA/H/C/004883/II/0013 Novo Nordisk A/S, Rapporteur: Andrea Laslop, "Update of section 4.2 of the SmPC in order to delete the statement in reference to previously untreated patients (PUPs) and section 5.1 of the SmPC in order to update information based on final results from study NN7088-3908; this is an open-label single-arm multicentre non-controlled phase 3a trial investigating safety and efficacy of turoctocog alfa pegol (N8-GP) in prophylaxis and treatment of bleeding episodes in previously untreated paediatric patients with severe haemophilia A. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted on 13.10.2022, 21.07.2022.	
Extavia - interferon beta-1B - EMEA/H/C/000933/II/0116/G Novartis Europharm Limited, Informed Consent of Betaferon, Rapporteur: Martina Weise, "Update of sections 4.4 and 4.8 of the SmPC in order to expand the language regarding the risk of injection site infection; the Package Leaflet is updated accordingly. Update of section 4.8 of the SmPC to merge the existing two tables for ADRs that occurred during clinical trials and those reported post-marketing, requested by PRAC following the assessment of PSUSA procedure (PSUSA/00001759/202107); the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."	

Request for Supplementary Information adopted on 13.10.2022.	
Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0030 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz, "Update of section 4.8 of the SmPC in order to add Guillain Barré syndrome (GBS), syncope and pre-syncope to the list of adverse drug reactions (ADRs) based on the assessment of the global safety database; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the Package Leaflet in order to align it with the information in the SmPC." Request for Supplementary Information adopted on 01.12.2022.	Request for supplementary information adopted with a specific timetable.
Hepcludex - bulevirtide - EMEA/H/C/004854/II/0019, Orphan Gilead Sciences Ireland Unlimited Company, Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC in order to update the list of adverse drug reactions (ADRs) and efficacy information based on interim results from study MYR301 listed as a Specific Obligation in the Annex II of the Product Information; this is a Multicenter, Open-label, Randomized Phase III Clinical Study to Assess Efficacy and Safety of Bulevirtide in Patients with Chronic Hepatitis Delta. Consequently, the MAH proposes a switch from conditional marketing authorisation to full marketing authorisation given the fulfilment of the SOB. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the SmPC."	
Imfinzi - durvalumab - EMEA/H/C/004771/II/0052 AstraZeneca AB, Rapporteur: Aaron Sosa Mejia, "Update of section 4.2 of the SmPC in order to update the recommendation for dose modification for 'other immune-mediated adverse reactions' as well as immune-mediated encephalitis, meningitis, Guillain-Barré syndrome and myasthenia gravis based on the National Comprehensive Cancer Network (NCCN) guideline recommendations (2022)."	
Leqvio - inclisiran -	Positive Opinion adopted by consensus on

EMEA/H/C/005333/II/0011 Novartis Europharm Limited, Rapporteur: Martina Weise, "Submission of the final report from non-clinical study no. 2120284 in order to address a recommendation (REC). This is an in silico assessment of the cross-tissue mRNA expression of the genes encoding for SULF1, INSYN2B (also referred to as FAM196B), ASGR1 and ASGR2 in tissues in man, monkey, rat and mouse." Opinion adopted on 01.12.2022. Request for Supplementary Information adopted on 01.09.2022.	01.12.2022.
LUTATHERA - lutetium (177Lu) oxodotreotide - EMEA/H/C/004123/II/0038, Orphan Advanced Accelerator Applications, Rapporteur: Janet Koenig, "Update of sections 2, 4.2, 4.4, 4.5, 4.6, 4.8, 4.9, 5.1, 5.2, 5.3, 6.2, 6.4, 6.5, 6.6, 11 and 12 of the SmPC to align the Lutathera product information to that of the latest Core Data Sheet (CDS) version 2.0. In addition, MAH is also taking the opportunity to propose additional corrections and changes to align with the QRD template. This application is also used as an opportunity to propose editorial updates to the product information (PI) to improve the language throughout the SmPC and patient leaflet." Request for Supplementary Information adopted on 01.12.2022.	Request for supplementary information adopted with a specific timetable.
Lysodren - mitotane - EMEA/H/C/000521/II/0026 HRA Pharma Rare Diseases, Rapporteur: Blanca Garcia-Ochoa, "Update of section 4.8 of the SmPC with new safety information regarding hypersensitivity reactions and oestrogenic-like effects based on post-marketing safety report and literature. The Package Leaflet is updated accordingly." Opinion adopted on 01.12.2022. Request for Supplementary Information adopted on 01.09.2022.	Positive Opinion adopted by consensus on 01.12.2022.
Myocet liposomal - doxorubicin hydrochloride - EMEA/H/C/000297/II/0070 Teva B.V., Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC, upon request by PRAC following the assessment of	

EMEA/H/C/PSUSA/00001172/202111, to align the wording with the published CHMP SWP advice on the duration of contraception in female patients after cessation of treatment with genotoxic drug. The Package Leaflet has been updated accordingly."	
NUVAXOVID - SARS-CoV-2, spike protein, recombinant, expressed in Sf9 cells derived from Spodoptera Frugiperda - EMEA/H/C/005808/II/0030 Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege, "Submission of 6-month efficacy and safety interim data from the ongoing randomized, observer-blinded, placebo-controlled clinical studies 2019nCoV-501, 2019nCoV-301 and 2019nCoV-302."	
Opsumit - macitentan - EMEA/H/C/002697/II/0047, Orphan Janssen-Cilag International N.V., Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 4.8 of the SmPC in order to add 'flushing' to the list of adverse drug reactions (ADRs) with frequency 'common' based on a cumulative review of cases (post-marketing, clinical studies, registry) and literature; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the SmPC." Opinion adopted on 01.12.2022.	Positive Opinion adopted by consensus on 01.12.2022.
Paxlovid - (1r,2s,5s)-n-((1s)-1-cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2s)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973/II/0010/G Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, "Update of section 4.8 of the SmPC to add hypersensitivity to the list of adverse drug reactions with frequency common, based on a cumulative search of the MAH safety database; the Package Leaflet is updated accordingly. Update of section 4.5 of the SmPC in order to add drug-drug interaction information with dabigatran (P-gp substrate) based on the clinical study results from study C4671012, a pharmacokinetic study to estimate the effect of Paxlovid on the pharmacokinetics of dabigatran; the Package Leaflet is updated accordingly. Update of section 4.5 of the SmPC in order to	

update the drug-drug interaction information of midazolam based on the clinical study results from study C4671013, a pharmacokinetic study to estimate the effect of Paxlovid on the pharmacokinetics of midazolam.
The MAH is taking the opportunity to include editorial updates in sections 4.3 and 6.1 of the SmPC."
Request for Supplementary Information adopted on 06.10.2022, 23.06.2022.

Qarziba - dinutuximab beta - EMEA/H/C/003918/II/0044, Orphan
EUSA Pharma (Netherlands) B.V., Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.2 and 4.8 of the SmPC with new safety information regarding central nervous system toxicity based on post-marketing safety report and literature."
Request for Supplementary Information adopted on 15.09.2022.

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

SARCLISA - isatuximab - EMEA/H/C/004977/II/0018/G
sanofi-aventis groupe, Rapporteur: Paula Boudewina van Hennik, "C.I.4: Update of sections 4.5, 5.1 and 5.2 of the SmPC in order to update the efficacy and pharmacokinetic data based on final progression-free survival (PFS) efficacy results from IKEMA study (EFC15246) and to introduce the Sebia Hydrashift assay, a validated assay to determine the complete response rate. IKEMA study (EFC15246) is a phase 3 randomized, open label, multicenter study assessing the clinical benefit of isatuximab combined with carfilzomib (Kyprolis) and dexamethasone versus carfilzomib with

dexamethasone in patients with relapsed and/or refractory multiple myeloma previously treated with 1 to 3 prior lines. A.6: Update of section 5.1 of the SmPC in order to update the ATC code following amendment by WHO."	
Simponi - golimumab - EMEA/H/C/000992/II/0107 Janssen Biologics B.V., Rapporteur: Kristina Dunder, "Submission of the final report from study MK-8259-038 (Go-BACK) in order to fulfil MEA/30.2. This is a phase 4, randomized, double-blind, parallel-group, withdrawal, post-authorisation efficacy study (PAES) of golimumab in adult participants, aged 18 to 45 years, with active non-radiographic axial spondyloarthritis." Request for Supplementary Information adopted on 01.09.2022.	
SIRTURO - bedaquiline - EMEA/H/C/002614/II/0051, Orphan Janssen-Cilag International N.V., Rapporteur: Filip Josephson, "Update of section 4.6 of the SmPC in order to update information on breast-feeding based on new literature."	
Skyrizi - risankizumab - EMEA/H/C/004759/II/0028 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Finbarr Leacy, "Update of section 4.8 of the SmPC in order to add eczema, rash and urticaria to the list of adverse drug reactions (ADRs) based on a thorough evaluation of all events of rash, eczema, and urticaria, including clinical trial and post-marketing data from the global safety database; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 24.11.2022.	Request for supplementary information adopted with a specific timetable.
Supemtek - quadrivalent influenza vaccine (recombinant, prepared in cell culture) - EMEA/H/C/005159/II/0009 Sanofi Pasteur, Rapporteur: Jan Mueller-Berghaus, "Update of section 5.1 of the SmPC in order to update the efficacy information based on final results from study VAP00003 listed as a category 3 study in the RMP; this is a phase 4, multi-center, modified-cluster randomized study to assess the effectiveness of Flublok	

Quadrivalent vaccine compared to standard dose inactivated influenza vaccine in adults. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."	
Tabrecta - capmatinib - EMEA/H/C/004845/II/0002 Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa, "Update of section 4.8 of the SmPC in order to add hypersensitivity to the list of adverse drug reactions (ADRs) with frequency uncommon, based on cumulative assessment of hypersensitivity cases in studies CINC280A2201, CINC280X1101, CINC280X2102, CINC280A2108, CINC280A2103 (post-DDI phase only), and CINC280A2105 (post-DDI phase only) and MAH global safety database. The Package Leaflet is updated accordingly." Opinion adopted on 01.12.2022.	Positive Opinion adopted by consensus on 01.12.2022.
Taxotere - docetaxel - EMEA/H/C/000073/II/0141 Sanofi Mature IP, Rapporteur: Alexandre Moreau, "Update of sections 4.4, 4.6 and 5.3 of the SmPC to include further information regarding genotoxicity, pregnancy/lactation exposure with associated adverse outcomes and recommendations regarding use of contraception, and update of section 5.2 of the SmPC regarding the pharmacokinetic terminal elimination half-life (t1/2). The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 13.10.2022.	
Tegsedi - inotersen - EMEA/H/C/004782/II/0034, Orphan Akcea Therapeutics Ireland Limited, Rapporteur: Martina Weise, "Submission of the final report from study ISIS 420915-CS3, listed as a category 3 in the RMP. This is an Open-Label Extension Study to Assess the Long-Term Safety and Efficacy of ISIS 420915 in Patients with Familial Amyloid Polyneuropathy (FAP)."	
Translarna - ataluren - EMEA/H/C/002720/II/0068, Orphan PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC in order to update efficacy information upon the request by the	

CHMP following the outcome of P46/026 based on final results from study PTC124-GD-045-DMD (Study 045); this is an open-label, single-arm, phase 2 study designed to evaluate the ability of ataluren treatment to increase dystrophin protein levels in muscle cells of subjects with nonsense mutation duchenne muscular dystrophy (nmDMD)." Request for Supplementary Information adopted on 06.10.2022.	
TRODELVY - sacituzumab govitecan - EMEA/H/C/005182/II/0018/G Gilead Sciences Ireland UC, Rapporteur: Jan Mueller-Berghaus, "Grouped application comprising two type II variations as follows: - To update sections 4.8 and 5.2 to address the commitment on providing bioanalytical study reports for antidrug-antibody (ADA) and neutralizing antibody (NAb) determination for both studies IMMU- 132-01 and IMMU-132-05, the NAb assay method validation report as well as an integrated summary of immunogenicity. - To update sections 4.8 and 5.2 to address the commitment to provide data on the impact of concomitant medications including UGT1A1 inhibitors/inducers on SN-38 PK based on the future PopPK model refinement."	
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0110 MCM Vaccine B.V., Rapporteur: Christophe Focke, "Update of section 4.8 of the SmPC in order to add 'hypersensitivity' and 'anaphylactic reaction' to the list of adverse drug reactions (ADRs) with frequency not known based on the safety assessment of post-marketing reports of hypersensitivity including anaphylactic reactions; the Package Leaflet is updated accordingly."	
Veklury - remdesivir - EMEA/H/C/005622/II/0043 Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, "Update of section 5.1 of the SmPC in order to update information based on the final virology report (PC-540-2040) for study GS-US-540-9012 in order to fulfil the recommendation by CHMP in the AR for	

(EMEA/H/C/005622/II/0016); this is a phase 3, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of RDV in an outpatient setting in participants with confirmed COVID-19 who were at risk for disease progression. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Velphoro - iron - EMEA/H/C/002705/II/0028

Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC, upon request by the PRAC following the assessment of PSUSA/00010296/202111, to include information on the effect on iron parameters and haemoglobin, based on results from the previously submitted post-hoc analysis of study PA-CL-05A; a Phase 3, open-label, randomised, active-controlled, parallel group, multicentre clinical study, and its extension study PA-CL-05B."

Xevudy - sotrovimab - EMEA/H/C/005676/II/0007

Glaxosmithkline Trading Services Limited, Rapporteur: Thalia Marie Estrup Blicher, "Update of sections 5.1 and 5.2 of the SmPC based on final results from study COMET-ICE (214367; VIR-7831-5001); this is a Phase II/III randomised, multi-centre, double-blind, placebo-controlled study to assess the safety and efficacy of monoclonal antibody VIR-7831 for the early treatment of coronavirus disease 2019 (COVID-19) in non-hospitalised patients." Request for Supplementary Information adopted on 15.09.2022.

Zejula - niraparib - EMEA/H/C/004249/II/0037, Orphan

GlaxoSmithKline (Ireland) Limited, Rapporteur: Ingrid Wang, "Update of section 5.2 of the SmPC in order to update information on absorption based on results from food effect study 3000-01-004; this is an Open-Label, Randomized-Sequence, Multicenter, Single-Crossover Study to Assess the Relative Bioavailability and Bioequivalence of Niraparib Tablet Formulation Compared to Niraparib Capsule Formulation in Patients with Advanced

Solid Tumours.”	
WS2321 **CONTROLOC Control-** **EMEA/H/C/001097/WS2321/0040** **PANTOZOL Control-** **EMEA/H/C/001013/WS2321/0042** **SOMAC Control-** **EMEA/H/C/001098/WS2321/0041** Takeda GmbH, Lead Rapporteur: Silvijus Abramavicius, “Update of sections 4.4 and 4.8 of the SmPC in order to add “Severe Cutaneous Adverse Reactions (SCARs)” information and to add “Acute Generalized Exanthematous Pustulosis (AGEP)” to the list of adverse drug reactions (ADRs) with frequency “not know” based on post-marketing experience, adverse reaction databases and literature; the Package Leaflet is updated accordingly. In addition, the MAH proposes to update section 4.5 of the SmPC to introduce information regarding Drug-Laboratory Interactions. Furthermore, the MAH took the opportunity to implement editorial changes and to update the list of local representatives in the Package Leaflet.” Request for Supplementary Information adopted on 24.11.2022, 06.10.2022.	Request for supplementary information adopted with a specific timetable.
WS2339/G **Keppra-** **EMEA/H/C/000277/WS2339/0198/G** UCB Pharma S.A., Lead Rapporteur: Karin Janssen van Doorn, “Grouped application comprising two type II variations as follows: C.I.4 – Update of section 4.4 of the SmPC in order to add a new warning on lack of efficacy or seizure worsening based on the cumulative review of MAH Global Safety database and published literature. C.I.4 – Update of section 4.8 of the SmPC in order to add a note on obsessive compulsive disorder in the ADR table based on the cumulative review of MAH Global Safety database, clinical studies, data from external spontaneous reporting database and published literature. The Package Leaflet is updated accordingly. In addition, the MAH proposes minor editorial changes of the Labelling.”	

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

B.5.3. CHMP-PRAC assessed procedures

Apexxnar - pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - EMEA/H/C/005451/II/0006 Pfizer Europe MA EEIG, Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Jean-Michel Dogné, "Update of sections 4.5, 4.8 and 5.1 of the SmPC based on final results from study B7471026 listed as a category 3 study in the RMP; this is a Phase III, randomized, double-blind trial to describe the safety and immunogenicity of 20-valent pneumococcal conjugate vaccine when coadministered with a booster dose of BNT162b2 in adults 65 years of age and older; the Package Leaflet is updated accordingly. The RMP version 2.1 has also been submitted to consolidate 2 RMP versions based on the outcome of current procedure and reflecting the changes in RMP v 2.0 (procedure EMEA/H/C/005451/II/0006) and RMP v1.1 (approved in procedure EMEA/H/C/005451/II/0002)." Opinion adopted on 01.12.2022. Request for Supplementary Information adopted on 01.09.2022.	Positive Opinion adopted by consensus on 01.12.2022.
Cablivi - caplacizumab - EMEA/H/C/004426/II/0040, Orphan Ablynx NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Jan Neuhauser, "Update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC in order to update information on long-term efficacy and safety based on final results from study	Request for supplementary information adopted with a specific timetable.

ALX0681-C302/LTS16371 - Prospective Follow-up Study for Patients who Completed Study ALX0681-C301 (HERCULES) to Evaluate Long-term Safety and Efficacy of Caplacizumab (Post-HERCULES), listed as a category 3 study in the RMP. The Post-HERCULES study was a Phase III, 36-month follow-up study from HERCULES (parent study) to evaluate the long-term outcomes as well as the safety and efficacy of repeat use of caplacizumab in patients who experienced a recurrence of aTTP. The RMP version 3.0 has also been submitted." Request for Supplementary Information adopted on 01.12.2022.	
Fintepla - fenfluramine - EMEA/H/C/003933/II/0011/G, Orphan Zogenix ROI Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, "- Update of sections 4.2 and 5.2 of the SmPC to include the relevant information regarding patients with renal impairment following the study 1902 (Pharmacokinetic study of fenfluramine hydrochloride in subjects with varying degrees of impaired and normal renal function) - Update of sections 4.4 and 4.5 of the SmPC in order to reflect the relevant information on CYP1A2 or CYP2B6 or CYP2D6 inducers following the study 1904 (Pharmacokinetic drug-drug interaction study of fenfluramine hydrochloride with and without fluvoxamine (CYP1A2 inhibitor), paroxetine (CYP2D6 inhibitor) and rifampin (CYP2B6 inducer) in healthy subjects). As requested, the recommendation of gastric lavage was also removed from section 4.9 of the SmPC. The RMP version 2.5 has been agreed." Opinion adopted on 17.11.2022. Request for Supplementary Information adopted on 29.09.2022, 07.07.2022, 10.03.2022.	Positive Opinion adopted by consensus on 17.11.2022.
JEMPERLI - dostarlimab - EMEA/H/C/005204/II/0013 GlaxoSmithKline (Ireland) Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Inês Ribeiro-Vaz, "Update of section 5.1 of the SmPC in order to update efficacy and safety information based on interim results from study 4010-01-001 (GARNET) listed as a specific obligation in the Annex II; This is a single-arm, open-label, phase I trial of intravenous	

dostarlimab in advanced solid tumours. In addition, the MAH took the opportunity to update section E of Annex II. The RMP version 1.2 has also been submitted. ” Request for Supplementary Information adopted on 01.09.2022.	
Kaftrio - ivacaftor / tezacaftor / elexacaftor - EMEA/H/C/005269/II/0024, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber, “Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on interim results from clinical study VX17-445-105 (study 105) listed as a category 3 study in the RMP; this is a Phase III, open label extension study to evaluate the long-term safety and efficacy of ELX/TEZ/IVA in CF subjects homozygous for F508del (F/F genotype) or heterozygous for F508del and a minimal function (MF) mutation (F/MF genotypes). The RMP version 6.1 has also been submitted. In addition, the MAH took the opportunity to implement minor corrections (section 5.3 and 6.5) as well as editorial changes to the SmPC.” Opinion adopted on 01.12.2022. Request for Supplementary Information adopted on 01.09.2022, 10.06.2022.	Positive Opinion adopted by consensus on 01.12.2022.
MenQuadfi - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/005084/II/0018/G Sanofi Pasteur, Rapporteur: Andrea Laslop, PRAC Rapporteur: Jean-Michel Dogné, “Update of sections 4.2, 4.5, 4.8 and 5.1 of the SmPC in order to add long-term antibody persistence at least 3 years after primary vaccination, immunogenicity and safety of a booster dose of MenQuadfi in adolescents, adults, and older adults, as well as co-administration data with meningococcal serogroup B vaccine in adolescents and adults, in order to fulfil ANX/002 and ANX/003 based on final results from studies MET59 and MEQ00066, respectively, listed as specific obligations in the Annex II. MET59 is a phase 3b, open-label, partially randomized, parallel-group, active-controlled, multi-center study evaluating the immunogenicity and safety of a booster dose of	

an investigational quadrivalent MenACYW conjugate vaccine in adolescents and adults, while MEQ00066 is a phase 3, two-stage, randomized, open-label, multi-center trial evaluating the safety and immunogenicity of a single dose of MenACYW conjugate vaccine at least 3 years following initial vaccination with either Menomune vaccine or MenACYW conjugate vaccine in older adults. The Annex II and Package Leaflet are updated accordingly. The RMP version 1.1 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted on 15.09.2022.	
NUBEQA - darolutamide - EMEA/H/C/004790/II/0012 Bayer AG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Jan Neuhauser, "Submission of the final report of carcinogenicity study T104877-7 listed as a category 3 study in the RMP. This is a non-clinical study to assess the carcinogenic potential in mice. The study evaluates the effects of daily oral administration of darolutamide for a period of 6 months in tg-rasH2 transgenic mouse model. The updated RMP version 3.1 has also been submitted." Request for Supplementary Information adopted on 01.12.2022, 01.09.2022.	Request for supplementary information adopted with a specific timetable.
Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0034/G Roche Registration GmbH, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Submission of the final report from study BN29739 (VELOCE) listed as a category 3 study in the RMP. This is a phase 3b, multicentre, randomized, parallel-group, open-label study to evaluate the effectiveness of vaccinations in patients with relapsing forms of multiple sclerosis (RMS) undergoing treatment with ocrelizumab. Submission of the final report from studies MA30005 (CASTING) and MN30035 (CHORDS). These are prospective, multicenter, international, interventional, open-label phase 3b studies to assess the efficacy and safety of ocrelizumab in patients with relapsing multiple sclerosis who have a suboptimal response to an	Request for supplementary information adopted with a specific timetable.

adequate course of disease-modifying treatment. The RMP version 8.0 has also been submitted." Request for Supplementary Information adopted on 01.12.2022.	
Omnitrope - somatropin - EMEA/H/C/000607/II/0073 Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, "Update of section 4.4 of the SmPC in order to add a new warning on scoliosis following PRAC recommendation from procedure EMEA/H/C/PSUSA/00002772/202003 based on final results from study EP00-401 listed as a category 3 study in the RMP; this is a prospective, open-label, non-comparative, multicenter, Phase IV study to monitor the long-term safety and efficacy of Omnitrope in short children born small for gestational age (SGA), in particular the diabetogenic potential and immunogenicity of rhGH therapy. The Package Leaflet is updated accordingly. The RMP version 12.0 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the SmPC." Opinion adopted on 01.12.2022.	Positive Opinion adopted by consensus on 01.12.2022.
Repatha - evolocumab - EMEA/H/C/003766/II/0061 Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola, "Update of sections 4.8 and 5.1 of the SmPC in order to update safety information and include long-term safety and efficacy data based on final results from study 20130295 and study 20160250 listed as category 3 studies in the RMP; these are phase 3b, multicenter, open-label extension (OLE) studies designed to assess the long-term safety of evolocumab in subjects who completed the FOURIER study (study 20110118). The RMP version 8.0 has also been submitted." Request for Supplementary Information adopted on 01.12.2022.	Request for supplementary information adopted with a specific timetable.
Rubraca - rucaparib - EMEA/H/C/004272/II/0037 Clovis Oncology Ireland Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy	See 9.1

and safety information and the list of adverse drug reactions (ADRs) based on the final results from study CO-338-014 (ARIEL 3) listed as a category 1 PAES in the Annex II; this is a phase 3, multicenter, randomized, double-blind, placebo-controlled study of rucaparib as switch maintenance following platinum-based chemotherapy in patients with platinum-sensitive, high grade serous or endometrioid epithelial ovarian, primary peritoneal or fallopian tube cancer. The Package Leaflet is updated accordingly. The RMP version 6.4 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."	
Sancuso - granisetron - EMEA/H/C/002296/II/0061 Kyowa Kirin Holdings B.V., Rapporteur: Silvijus Abramavicius, PRAC Rapporteur: Rugile Pilviniene, "Update of sections 4.4, 4.6, 4.7, 4.8, 4.10 and 5.3 of the SmPC in order to add 'Serotonin syndrome' and 'Application site Reactions' to the list of adverse drug reactions (ADRs) with frequency unknow; as well as 'Application site Irritation' with frequency 'Uncommon' based on post-marketing data and literature. The MAH also proposes to update sections 4.4 and 4.5 of the SmPC to add drug-drug interaction information with buprenorphine/Opioids and serotonergic medicinal products based on post-marketing data and literature. The Package Leaflet has been updated accordingly. The RMP version 5 has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes in the SmPC." Request for Supplementary Information adopted on 01.12.2022.	Request for supplementary information adopted with a specific timetable.
Vyndaqel - tafamidis - EMEA/H/C/002294/II/0081, Orphan Pfizer Europe MA EEIG, Rapporteur: Jean-Michel Race, PRAC Rapporteur: Tiphaine Vaillant, "Update of section 5.1 of the SmPC in order to update information based on final results from study B3461029 listed as a Specific Obligation in the Annex II of the Product Information. This is a non-interventional PASS sub-study evaluating effects of tafamidis on disease	

progression in patients with non-Val30Met mutations and symptomatic neuropathy. Consequently, the MAH proposes a switch from marketing authorisation under exceptional circumstances to full marketing authorisation given the fulfilment of the SOB. The Annex II and Package Leaflet are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet." Request for Supplementary Information adopted on 10.11.2022, 15.09.2022, 21.07.2022.	
Xenpozyme - olipudase alfa - EMEA/H/C/004850/II/0001/G, Orphan Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber, "Grouped application comprising two type II variations as follows: - To update section 4.6 of the SmPC in order to include a recommendation to conduct a pregnancy test for women of childbearing potential (WOCP) prior to treatment initiation based on embryo-foetal study in mice (study TER0694). In addition, the MAH proposes an update of section 5.3 of the SmPC based on a re-calculation of exposure margins for the embryo-foetal study. The MAH also proposes to align the SmPC with the updated CCDS. - To update sections 4.6 and 5.3 of the SmPC in order to include data in lactating mice based on final results from study MSSM-1120 - Evaluation of Olipudase alfa Transfer Into Milk of Lactating Mice. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted." Request for Supplementary Information adopted on 01.12.2022.	Request for supplementary information adopted with a specific timetable.
Zejula - niraparib - EMEA/H/C/004249/II/0033, Orphan GlaxoSmithKline (Ireland) Limited, Rapporteur: Ingrid Wang, PRAC Rapporteur: Jan Neuhauser, "Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning and add MDS/AML to the list of adverse drug reactions (ADRs) with frequency common, and update of section 5.1 based on final results from the NOVA study (213356); this is a Phase 3 Randomized Double-Blind Trial of Maintenance with Niraparib Versus Placebo in Patients with	See 9.1

Platinum Sensitive Ovarian Cancer. In addition, the MAH also took this opportunity to update sections 4.4 and 4.6 to update information on contraception based on EMA and CTFG recommendations. The Package Leaflet is updated accordingly. The RMP version 6 has also been submitted." Request for Supplementary Information adopted on 19.05.2022, 10.02.2022.	

B.5.4. PRAC assessed procedures

PRAC Led **Besremi - ropeginterferon alfa-2b - EMEA/H/C/004128/II/0025** AOP Orphan Pharmaceuticals GmbH, PRAC Rapporteur: Inês Ribeiro-Vaz, PRAC-CHMP liaison: Bruno Sepodes, "Submission of an updated RMP version 1.1 for Besremi to revise safety concerns according to GVP Module V Rev.2." Opinion adopted on 01.12.2022. Request for Supplementary Information adopted on 01.09.2022.	Positive Opinion adopted by consensus on 01.12.2022.
PRAC Led **Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0117** GlaxoSmithkline Biologicals SA, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Karin Janssen van Doorn, "Submission of the interim report from study EPI-HPV-099 (217743). This is an observational, retrospective database post-authorisation safety study (PASS) assessing trends and changes over time in incidence of anal cancer and feasibility for a case-control study in European countries that introduced Cervarix in their National Immunisation Programme. The study was set up to address the missing information on the impact and effectiveness of Cervarix against anal lesions and cancer in the Cervarix RMP. The RMP version 26 has also been submitted." Request for Supplementary Information adopted on 01.12.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Darzalex - daratumumab - EMEA/H/C/004077/II/0063, Orphan**	Request for supplementary information adopted with a specific timetable.

Janssen-Cilag International N.V., Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Inês Ribeiro-Vaz, PRAC-CHMP liaison: Bruno Sepodes, "Update of section 4.4 of the SmPC in order to update the warnings and precautions for myocardial infarction and ocular events following PSUSA/00010498/202111, based on the cumulative review of the relevant cases retrieved from the MAH's global safety database, clinical database, epidemiological evaluation and literature review. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 01.12.2022.	
PRAC Led **Deltyba - delamanid - EMEA/H/C/002552/II/0061, Orphan** Otsuka Novel Products GmbH, PRAC Rapporteur: Jo Robays, PRAC-CHMP liaison: Christophe Focke, "Update of sections 4.2 and 4.4 of the SmPC in order to update treatment duration based on final results from EU PASS (protocol no. 242-12-402), listed as a category 3 study in the RMP. This is a "A Multicentre, EU-wide, Non-Interventional Post-Authorisation Study to Assess the Safety and Usage of Delamanid in Routine Medical Practice in Multidrug-Resistant Tuberculosis (MDR-TB) Patients". This treatment registry was for monitoring and documenting Deltyba use in routine medical practice and aimed to assess compliance with the recommendations in the authorised product information when prescribed as part of an appropriate combination regimen (ACR) for the treatment of MDR-TB. The Package Leaflet is updated accordingly. The RMP version 4.2 has also been submitted. In addition, the MAH took the opportunity to update Annex II section D of the SmPC." Request for Supplementary Information adopted on 01.12.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Duavive - estrogens conjugated / bazedoxifene - EMEA/H/C/002314/II/0032** Pfizer Europe MA EEIG, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of an updated RMP version 3.2 in order to reflect the updated study	Request for supplementary information adopted with a specific timetable.

milestones and completion of the post-authorisation safety study of CE/BZA in the United States (US PASS, Study B2311060) previously assessed as part of II/0030 (MEA002.15), as well as to update the post-marketing data with the data lock point of 31 October 2021." Request for Supplementary Information adopted on 01.12.2022, 07.07.2022.	
PRAC Led **JCOVDEN - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0065** Janssen-Cilag International N.V., PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 5.1 in order to update the clinical exposure and risk sections." Request for Supplementary Information adopted on 01.12.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Mycamine - micafungin - EMEA/H/C/000734/II/0047** Astellas Pharma Europe B.V., PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "To update Annex II and the RMP to version 23.0 to include the results of the non-interventional PASS as an Effectiveness Check of the Prescriber Checklist for Mycamine (micafungin) - 9463-PV-0002." Request for Supplementary Information adopted on 01.12.2022, 01.09.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0092** Genzyme Europe BV, PRAC Rapporteur: Nathalie Gault, PRAC-CHMP liaison: Alexandre Moreau, "Update of sections 4.6 and 5.3 of the SmPC in order to update information on pregnancy, lactation and fertility following the request by PRAC in the AR for MEA/024.17 and MEA/025.17 and in PSUSA/00000086/202109; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted on 01.12.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led	Request for supplementary information adopted

Neulasta - pegfilgrastim - EMEA/H/C/000420/II/0121 Amgen Europe B.V., PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report from PASS study 20170701 listed as a category 3 study in the RMP. This is a cross-sectional survey study to Assess the Effectiveness of the Neulasta Patient Alert Card and to Measure Medication Errors Related to the Use of the Neulasta On-Body Injector. The RMP version 9.0 has also been submitted." Request for Supplementary Information adopted on 01.12.2022.	with a specific timetable.
PRAC Led **NUVAXOVID - SARS-CoV-2, spike protein, recombinant, expressed in Sf9 cells derived from Spodoptera Frugiperda - EMEA/H/C/005808/II/0028** Novavax CZ, a.s., PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 2.1 to reclassify the safety concern myocarditis and/or pericarditis from important potential risk to important identified risk. The pharmacovigilance plan and risk minimisation measures have been updated accordingly." Opinion adopted on 01.12.2022.	Positive Opinion adopted by consensus on 01.12.2022.
PRAC Led **Saxenda - liraglutide - EMEA/H/C/003780/II/0034** Novo Nordisk A/SPRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report from study NN8022-4246 listed as a category 3 study in the RMP. This is an in market utilisation non-interventional PASS of liraglutide used for weight management in the UK using the CPRD Primary Care Database. The RMP version 33.0 has also been submitted." Opinion adopted on 01.12.2022.	Positive Opinion adopted by consensus on 01.12.2022.
PRAC Led **Synagis - palivizumab - EMEA/H/C/000257/II/0131** AstraZeneca AB, PRAC Rapporteur: Marie Louise Schougaard Christiansen, PRAC-CHMP liaison: Thalia Marie Estrup Blicher, "Submission of an updated RMP version 2.0 in order to remove from the list of safety concerns "Anaphylaxis,	Request for supplementary information adopted with a specific timetable.

Anaphylactic shock, and Hypersensitivity" and "Medication error of mixing lyophilised and liquid palivizumab before injection". In addition, the MAH took the opportunity to apply the revised template." Request for Supplementary Information adopted on 01.12.2022.	
PRAC Led **TOBI Podhaler - tobramycin - EMEA/H/C/002155/II/0053, Orphan** Mylan IRE Healthcare Limited, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 8.0 following the request by PRAC in the AR for PSUSA/00009315/202106 in order to update it based on the guidance provided in the GVP and to remove the safety concerns as well as to reflect the finalisation of study CTBM100C2407 and the transfer of ownership." Request for Supplementary Information adopted on 01.12.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Zydelig - idelalisib - EMEA/H/C/003843/II/0056** Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the final report from study GS-EU-313-4172 listed as a category 3 study in the RMP. This is a non-interventional study to assess the safety profile of idelalisib in patients with refractory follicular lymphoma (FL) with primary objective to assess the overall safety profile of idelalisib monotherapy in patients with refractory FL." Request for Supplementary Information adopted on 01.12.2022.	Request for supplementary information adopted with a specific timetable.
PRAC Led **WS2306** **Aripiprazole Mylan Pharma- EMEA/H/C/003803/WS2306/0020** Mylan Pharmaceuticals Limited, Generic, Generic of Abilify, Lead Rapporteur: Eva Skovlund, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "To align the safety concerns in the RMP with the reference product. In addition, nationally authorised product has been included in the RMP for the company."	

Request for Supplementary Information adopted on 29.09.2022.	
PRAC Led **WS2369** **Filgrastim Hexal-EMEA/H/C/000918/WS2369/0066 Zarzio-EMEA/H/C/000917/WS2369/0067** Sandoz GmbH, Lead PRAC Rapporteur: Menno van der Elst, "C.I.11.z - To amend the RMP to reduce the list of safety concerns and remove risks which are well characterised and already included in the product information, following PRAC Assessment Report of PSUR P14 (EMEA/H/C/PSUSA/00001391/202109) dated 05-May-2022. Additionally, the due date of the final study report EP06-501 (MEA007) has been updated from Q3 2025 to Q1 2025. Furthermore, the MAH took the opportunity to introduce the following editorial changes: - Removal of pharmaceutical forms and strengths no longer registered in Japan; - Editorial changes in Part V "Risk minimisation measures" Request for Supplementary Information adopted on 01.12.2022.	Request for supplementary information adopted with a specific timetable.

B.5.5. CHMP-CAT assessed procedures

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0019, Orphan, ATMP Bristol-Myers Squibb Pharma EEIG, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang	
Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0020, Orphan, ATMP Bristol-Myers Squibb Pharma EEIG, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang	
Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0004, ATMP Bristol-Myers Squibb Pharma EEIG, Rapporteur: Concetta Quintarelli, CHMP Coordinator: Armando Genazzani Request for Supplementary Information adopted on 09.09.2022.	
Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel -	

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

Breyanzi - lisocabtagene maraleucel / lisocabtagene maraleucel - EMEA/H/C/004731/II/0009, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Concetta Quintarelli, CHMP Coordinator: Armando Genazzani

CARVYKTI - ciltacabtagene autoleucel - EMEA/H/C/005095/II/0005, Orphan, ATMP
Janssen-Cilag International NV, Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0050, Orphan, ATMP
Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang
Request for Supplementary Information adopted on 13.04.2022.

Upstaza - eladocagene exuparvovec - EMEA/H/C/005352/II/0004/G, Orphan, ATMP
PTC Therapeutics International Limited, Rapporteur: Maura O'Donovan, CHMP Coordinator: Finbarr Leacy

B.5.6. CHMP-PRAC-CAT assessed procedures

CARVYKTI - ciltacabtagene autoleucel - EMEA/H/C/005095/II/0003, Orphan, ATMP
Janssen-Cilag International NV, Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus, PRAC Rapporteur: Jo Robays, "Update of sections 4.4 and 4.8 of the SmPC in order to update the existing warnings on cytokine release syndrome (CRS), neurologic toxicities and grading of related events and to update the list of adverse drug reactions (ADRs) based on previously reviewed data from studies MMY2001 and MMY2003, and an additional internal characterisation of neurotoxicity risk; the Package Leaflet is updated accordingly. The RMP version 2.1 has also been submitted. In

addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

CARVYKTI - ciltacabtagene autoleucel - EMEA/H/C/005095/II/0004/G, Orphan, ATMP

Janssen-Cilag International NV, Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus, PRAC Rapporteur: Jo Robays, "Grouped application comprising two type II variations as follows:
- Update of section 4.4 of the SmPC in order to add a new warning on increased risk of severe/fatal COVID-19 infections following COVID-19 signal evaluation from the ongoing study 68284528MMY3002 (CARTITUDE-4) based on a cumulative review of all clinical trials, registries and literature.
- Update of section 4.4 of the SmPC in order to add a new warning Risk of severe bleeding in the context of hemophagocytic lymphohistiocytosis syndrome (HLH) following a signal evaluation from the ongoing study 68284528MMY3002 (CARTITUDE-4) based on cumulative review of all clinical trials, registries and literature.
The Package Leaflet is updated accordingly.
The RMP version 2.2 has also been submitted."

Libmeldy - atidarsagene autotemcel - EMEA/H/C/005321/II/0011/G, Orphan, ATMP

Orchard Therapeutics (Netherlands) B.V., Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Grouped application (Clinical & Quality) consisting of:
Type II (C.I.4): Update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC; the Package Leaflet and Labelling are updated accordingly. In addition, the MAH took the opportunity to remove ANX/002 from the Annex II and to introduce minor editorial changes to the PI. The RMP version 1.3 has also been submitted."

B.5.7. PRAC assessed ATMP procedures

PRAC Led

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0056, ATMP

Amgen Europe B.V., CHMP Coordinator:

Johanna Lähteenvuo, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from study 20120139 listed as a category 3 study in the RMP in order to fulfil MEA/004. This is a multicenter, observational registry study to evaluate the survival and long-term safety of subjects who previously received talimogene laherparepvec in Amgen or BioVEX sponsored clinical trials." Request for Supplementary Information adopted on 09.09.2022.	

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

WS2239/G **Hexacima-** **EMEA/H/C/002702/WS2239/0128/G** **Hexyon-** **EMEA/H/C/002796/WS2239/0132/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 01.12.2022. Request for Supplementary Information adopted on 21.07.2022, 12.05.2022.	Positive Opinion adopted by consensus on 01.12.2022.
WS2263 **Blitzima-** **EMEA/H/C/004723/WS2263/0060** **Truxima-** **EMEA/H/C/004112/WS2263/0063** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz Opinion adopted on 24.11.2022.	Positive Opinion adopted by consensus on 24.11.2022.
WS2325 **Adjupanrix-** **EMEA/H/C/001206/WS2325/0080** **Ambirix-** **EMEA/H/C/000426/WS2325/0123** **Bexsero-** **EMEA/H/C/002333/WS2325/0116** **Cervarix-** **EMEA/H/C/000721/WS2325/0116** **Fendrix-** **EMEA/H/C/000550/WS2325/0080** **Infanrix hexa-** **EMEA/H/C/000296/WS2325/0319** **Menveo-** **EMEA/H/C/001095/WS2325/0114** **Mosquirix-**	Positive Opinion adopted by consensus on 17.11.2022.

EMEA/H/W/002300/WS2325/0063 **Rotarix-EMEA/H/C/000639/WS2325/0126** **Shingrix-** **EMEA/H/C/004336/WS2325/0060** **Synflorix-** **EMEA/H/C/000973/WS2325/0173** **Twinrix Adult-** **EMEA/H/C/000112/WS2325/0158** **Twinrix Paediatric-** **EMEA/H/C/000129/WS2325/0159** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke Opinion adopted on 17.11.2022.	
WS2328 **HyQvia-EMEA/H/C/002491/WS2328/0082** **Kiovig-EMEA/H/C/000628/WS2328/0119** Takeda Manufacturing Austria AG, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 08.12.2022. Request for Supplementary Information adopted on 13.10.2022.	Positive Opinion adopted by consensus on 08.12.2022.
WS2333 **Ambirix-** **EMEA/H/C/000426/WS2333/0124** **Twinrix Adult-** **EMEA/H/C/000112/WS2333/0159** **Twinrix Paediatric-** **EMEA/H/C/000129/WS2333/0160** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke Opinion adopted on 24.11.2022.	Positive Opinion adopted by consensus on 24.11.2022.
WS2345 **Hexacima-** **EMEA/H/C/002702/WS2345/0137** **Hexyon-** **EMEA/H/C/002796/WS2345/0141** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 08.12.2022.	Positive Opinion adopted by consensus on 08.12.2022.
WS2352 **Mirapexin-** **EMEA/H/C/000134/WS2352/0103** **Sifrol-EMEA/H/C/000133/WS2352/0094** Boehringer Ingelheim International GmbH, Lead Rapporteur: Thalia Marie Estrup Blicher Request for Supplementary Information adopted on 13.10.2022.	
WS2360	Positive Opinion adopted by consensus on

HBVAXPRO-EMEA/H/C/000373/WS2360/0079 **Vaxelis-EMEA/H/C/003982/WS2360/0108** Merck Sharp & Dohme B.V., Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 01.12.2022.	01.12.2022.
WS2363/G **Copalia-EMEA/H/C/000774/WS2363/0127/G** **Dafiro-EMEA/H/C/000776/WS2363/0131/G** **Exforge-EMEA/H/C/000716/WS2363/0126/G** Novartis Europharm Limited, Lead Rapporteur: Thalia Marie Estrup Blicher Request for Supplementary Information adopted on 01.12.2022.	Request for supplementary information adopted with a specific timetable.
WS2364/G **Herceptin-EMEA/H/C/000278/WS2364/0185/G** **MabThera-EMEA/H/C/000165/WS2364/0194/G** Roche Registration GmbH, Lead Rapporteur: Aaron Sosa Mejia	
WS2370 **Nuwiq-EMEA/H/C/002813/WS2370/0051** **Vihuma-EMEA/H/C/004459/WS2370/0033** Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 01.12.2022.	Positive Opinion adopted by consensus on 01.12.2022.
WS2373 **Copalia HCT-EMEA/H/C/001159/WS2373/0103** **Dafiro HCT-EMEA/H/C/001160/WS2373/0105** **Exforge HCT-EMEA/H/C/001068/WS2373/0102** Novartis Europharm Limited, Lead Rapporteur: Thalia Marie Estrup Blicher, "To update Annex II to request an extension of the due date for the fulfilment of condition B. In addition, the marketing authorisation holder has taken the opportunity to implement a minor editorial change in the PI for Dafiro HCT."	
WS2380/G **Filgrastim Hexal-EMEA/H/C/000918/WS2380/0067/G**	

Zarzio- **EMEA/H/C/000917/WS2380/0068/G** Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "To update section 4.4 of the SmPC to add information about myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML) in patients with breast and lung cancer to align the PI with the PI of the reference product, Neupogen according to the update published by Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) on 4 August 2022. Sections 2 and 3 of the Package Leaflet have been updated accordingly. Additionally, a Type IA variation has been submitted as the MAH proposes to remove pre-filled syringes without a needle safety guard (NSG) from the dossier (EU/1/08/495/009-12, EU/1/08/495/013-16). Finally, some minor editorial changes were introduced to the PI, in particular the ET, FI, IT, MT and RO annexes."	

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

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

Natpar - parathyroid hormone - **EMEA/H/C/003861/II/0042, Orphan** Takeda Pharmaceuticals International AG, Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Rhea Fitzgerald, "Submission of the updated protocol from study SHP634-403 listed as a Specific Obligation in the Annex II of the Product Information with twice-daily (BID) as the proposed alternative dosing regimen to be evaluated. This is a Randomized, 2-Arm, Double-Blind, Phase 4 Study to Evaluate Once Daily (QD) Versus Twice Daily (BID) Administration of Recombinant Human Parathyroid Hormone (rhPTH[1-84]; NATPARA) for the Treatment of Adults with Hypoparathyroidism (HPT). The Annex II and the RMP (submitted version 3.4) are updated accordingly." Request for Supplementary Information adopted on 10.11.2022, 21.07.2022.	Request by the applicant for an extension to the clock stop to respond to the RSI adopted in November 2022.
Ronapreve - casirivimab / imdevimab - **EMEA/H/C/005814/II/0007** Roche Registration GmbH, Rapporteur: Jan	Request by the applicant for an extension to the clock stop to respond to the RSI adopted in October 2022.

Mueller-Berghaus, "Update of sections 4.2, 4.4, 5.1 and 5.2 of the SmPC in order to introduce the proposed dose for SARS-CoV-2 Omicron BA.2, BA.2.12.1, BA.4, and BA.5 subvariants along with dose preparation and infusion instructions for treatment of outpatients and post-exposure prophylaxis as well as to update efficacy and pharmacokinetic information based on pharmacokinetic (PK) modelling data from R10933-PK-21187-SR-01V2 and R10933-R10987-4800mgIV-KRM and in vitro viral neutralisation data from the updated virus neutralisation report R10933-PH-20091-SR-01V7 and its addendum; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI." Request for Supplementary Information adopted on 13.10.2022.

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

arpraziquantel - EMEA/H/C/004252, Article 58 treatment of schistosomiasis
aumolertinib - EMEA/H/C/006069 treatment of adult patients with locally advanced or metastatic non-small cell lung cancer
ibuprofen - EMEA/H/C/006129 Treatment of a haemodynamically significant patent ductus arteriosus in preterm newborn infants less than 34 weeks of gestational age
in vitro diagnostic medical device - EMEA/H/D/006201 to detect internal tandem duplication (ITD) and tyrosine kinase domain (TKD) mutations D835 and I836
dopamine hydrochloride - EMEA/H/C/006044, PUMA Treatment of hypotension in neonates, infants and children
momelotinib - EMEA/H/C/005768, Orphan Glaxosmithkline Trading Services Limited,

treatment of disease-related splenomegaly or symptoms and anaemia

tofersen - EMEA/H/C/005493
treatment of adults with amyotrophic lateral sclerosis (ALS), associated with a mutation in the superoxide dismutase 1 (SOD1) gene.

rozanolixizumab - EMEA/H/C/005824, Orphan
UCB Pharma, Treatment of generalised myasthenia gravis (gMG)

toripalimab - EMEA/H/C/006120
Combination treatment for metastatic or recurrent locally advanced nasopharyngeal carcinoma and for metastatic or recurrent oesophageal squamous cell carcinoma

ustekinumab - EMEA/H/C/006101
treatment of plaque psoriasis, arthritis psoriatic, Crohn's Disease and ulcerative colitis

etrasimod - EMEA/H/C/006007
treatment of patients with moderately to severely active ulcerative colitis (UC)

teriparatide - EMEA/H/C/005934, Orphan
Ascendis Pharma Bone Diseases A/S, PTH replacement therapy indicated for the treatment of hypoparathyroidism in adults.

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

Adtralza - tralokinumab - EMEA/H/C/005255/X/0007
LEO Pharma A/S, Rapporteur: Jayne Crowe, PRAC Rapporteur: Kimmo Jaakkola, "Extension application to add a new strength of 300 mg (150 mg/ml) tralokinumab solution for injection in pre-filled pen for subcutaneous administration.
The RMP (version 1.1) is updated accordingly."

Erleada - apalutamide - EMEA/H/C/004452/X/0028/G
Janssen-Cilag International N.V., Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Tiphaine Vaillant, "Extension application to add a new strength (240 mg) film-coated tablets grouped with the IB variation (C.I.z).
The RMP (version 6.1) has also been submitted.
C.I.z (IB): to align the SmPC/PL for Erleada 60

mg with the SmPC/PL proposed for the registration of the new Erleada film-coated tablet strength, 240 mg. The PL for Erleada 60 mg is proposed to be updated to ensure consistency. In addition, few minor revisions are proposed to the SmPC for Erleada 60 mg, to align the SmPC proposed for the 240 mg strength: - SmPC sections 5.1 and 5.2 Orthographic corrections - SmPC section 6.5: Further details on the description of the current packaging have been added, this change does not result from a change to the container. - SmPC section 6.6: The title of the section has been aligned with the QRD template.”	
TAKHZYRO - lanadelumab - EMEA/H/C/004806/X/0034/G, Orphan Takeda Pharmaceuticals International AG Ireland Branch, Rapporteur: Kristina Dunder, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Kirsti Villikka, “Extension application to add a new strength of 150 mg for lanadelumab solution for injection in pre-filled syringe and to extend the indication to include paediatric use (2 to <12 years). The new indication is only applicable to the new 150 mg strength presentations. The RMP (version 3.0) is updated in accordance. A type IB variation (C.I.z) has been submitted to update section 7 of the Package Leaflet (PL) for the 300 mg in 2 ml pre-filled syringe (EU/1/18/1340/004-006) in line with the proposed PL for the 150 mg in 1 ml pre-filled syringe (new strength). In addition, the MAH has requested an extension of the Orphan Market Exclusivity from 10 to 12 years. ”	
Tecentriq - atezolizumab - EMEA/H/C/004143/X/0076 Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Inês Ribeiro-Vaz, “Extension application to introduce a new pharmaceutical form (solution for injection) associated with a new strength (1875 mg) and new route of administration (subcutaneous use). The RMP (version 24.0) is updated in accordance.”	
Veltassa - patiromer -	

EMEA/H/C/004180/X/0031/G
Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Jayne Crowe, PRAC Rapporteur: Kirsti Villikka, "Extension application to introduce a new strength (1 g powder for oral suspension), grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment of population from 6 to 18 years old for Veltassa based on final results from paediatric study RLY5016-206P (EMERALD); this is a phase 2, open-label, multiple dose study to evaluate the pharmacodynamic effects, safety, and tolerability of patiromer for oral suspension in children and adolescents 2 to less than 18 years of age with chronic kidney disease and hyperkalaemia. As a consequence, sections 1, 2, 4.1, 4.2, 4.8, 4.9, 5.1 and 6.5 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 2 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes."

Vyvgart - efgartigimod alfa - EMEA/H/C/005849/X/0003, Orphan
Argenx, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Rhea Fitzgerald, "Extension application to introduce a new pharmaceutical form (solution for injection) associated with a new strength (1000 mg) and a new route of administration (subcutaneous use)."

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

aripiprazole - EMEA/H/C/005929
Maintenance treatment of schizophrenia
List of Questions adopted on 13.10.2022.

ublituximab - EMEA/H/C/005914
treatment of relapsing forms of multiple sclerosis (RMS)
List of Questions adopted on 22.04.2022.

Hefiya - adalimumab - EMEA/H/C/004865/X/0036/G
Sandoz GmbH, Duplicate, Duplicate of Hyrimoz, Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Ulla Wändel Liminga, "Extension application to add a new strength (80 mg/0.8 ml) of the solution for injection grouped with

quality variations. The Package Leaflet and Labelling are updated in accordance.
The RMP (version 9.0) has also been submitted.
Additionally, the applicant takes the opportunity to include editorial changes in the pack sizes (approved (001-003) and new presentations) in the List of All Authorised Presentations (Annex A) to differentiate packs of pre-filled syringes with or without needle safety device.
List of Questions adopted on 13.10.2022.

Hyrimoz - adalimumab - EMEA/H/C/004320/X/0036/G
Sandoz GmbH, Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Ulla Wändel Liminga,
"Extension application to add a new strength (80 mg/0.8 ml) of the solution for injection grouped with quality variations. The Package Leaflet and Labelling are updated in accordance.
The RMP (version 9.0) has also been submitted.
Additionally, the applicant takes the opportunity to include editorial changes in the pack sizes (approved (001-003) and new presentations) in the List of All Authorised Presentations (Annex A) to differentiate packs of pre-filled syringes with or without needle safety device.
List of Questions adopted on 13.10.2022.

mirikizumab - EMEA/H/C/005122
treatment of moderately to severely active ulcerative colitis
List of Questions adopted on 15.09.2022.

ganaxolone - EMEA/H/C/005825, Orphan
Marinus Pharmaceuticals Emerald Limited,
treatment of epileptic seizures associated with cyclindependent kinase-like 5 deficiency disorder (CDD)
List of Questions adopted on 25.01.2022.

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

Obiltoxaximab SFL - obiltoxaximab - EMEA/H/C/005169/S/0008, Orphan
SFL Pharmaceuticals Deutschland GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Liana Gross-Martirosyan

Orphacol - cholic acid - EMEA/H/C/001250/S/0048, Orphan
Laboratoires CTRS, Rapporteur: Anastasia

Mountaki, PRAC Rapporteur: Sofia Trantza

Raxone - idebenone -
EMEA/H/C/003834/S/0032, Orphan
Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli

Vedrop - tocofersolan -
EMEA/H/C/000920/S/0044
Recordati Rare Diseases, Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Melinda Palfi

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

Braftovi - encorafenib -
EMEA/H/C/004580/R/0029
Pierre Fabre Medicament, Rapporteur: Janet Koenig, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Rugile Pilviniene

Cablivi - caplacizumab -
EMEA/H/C/004426/R/0042, Orphan
Ablynx NV, Rapporteur: Filip Josephson, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Jan Neuhauser

CARVYKTI - ciltacabtagene autoleucel -
EMEA/H/C/005095/R/0008, Orphan, ATMP
Janssen-Cilag International NV, Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus, PRAC Rapporteur: Jo Robays,

Deferiprone Lipomed - deferiprone -
EMEA/H/C/004710/R/0011
Lipomed GmbH, Generic, Generic of Ferriprox, Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Tiphaine Vaillant

Imfinzi - durvalumab -
EMEA/H/C/004771/R/0055
AstraZeneca AB, Rapporteur: Aaron Sosa Mejia, Co-Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: David Olsen

Imnovid - pomalidomide -
EMEA/H/C/002682/R/0049, Orphan
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Monica Martinez Redondo

Kymriah - tisagenlecleucel - EMEA/H/C/004090/R/0068, Orphan, ATMP

Novartis Europharm Limited, Rapporteur: Rune Kjeken, Co-Rapporteur: Dariusz Sladowski, CHMP Coordinators: Ingrid Wang and Ewa Balkowiec Iskra, PRAC Rapporteur: Brigitte Keller-Stanislawski

Lorviqua - lorlatinib - EMEA/H/C/004646/R/0025

Pfizer Europe MA EEIG, Rapporteur: Aaron Sosa Mejia, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Nikica Mirošević Skvrce

Mektovi - binimetinib - EMEA/H/C/004579/R/0024

Pierre Fabre Medicament, Rapporteur: Janet Koenig, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Inês Ribeiro-Vaz

Ondexxya - andexanet alfa - EMEA/H/C/004108/R/0034

AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Menno van der Elst

Onpattro - patisiran - EMEA/H/C/004699/R/0031, Orphan

Alnylam Netherlands B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Rhea Fitzgerald

Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (h5n1) (live attenuated, nasal) - EMEA/H/C/003963/R/0057

AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sonja Hrabcik

VEYVONDI - vonicog alfa - EMEA/H/C/004454/R/0027

Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Ulla Wändel Liminga

Vyxeos liposomal - daunorubicin / cytarabine - EMEA/H/C/004282/R/0037, Orphan

Jazz Pharmaceuticals Ireland Limited, Rapporteur: Johanna Lähteenvuo, Co-Rapporteur: Janet Koenig, PRAC Rapporteur:

Inês Ribeiro-Vaz
WAYLIVRA - volanesorsen - EMEA/H/C/004538/R/0022, Orphan Akcea Therapeutics Ireland Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Karin Janssen van Doorn, PRAC Rapporteur: Martin Huber
Xerava - eravacycline - EMEA/H/C/004237/R/0023 Paion Deutschland GmbH, Rapporteur: Filip Josephson, Co-Rapporteur: Ingrid Wang, PRAC Rapporteur: Adam Przybylkowski
Yescarta - axicabtagene ciloleucel - EMEA/H/C/004480/R/0056, Orphan, ATMP Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Claire Beuneu, CHMP Coordinator: Jan Mueller-Berghaus, PRAC Rapporteur: Anette Kirstine Stark

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

Nordimet - methotrexate - EMEA/H/C/003983/II/0027 Nordic Group B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Martin Huber, "Extension of indication to include treatment of moderate to severe recalcitrant disabling psoriasis for Nordimet, based on literature; As a consequence, sections 4.1 and 4.2 of the SmPC were updated. The Package leaflet is updated in accordance. Version 6.0 of the RMP has also been submitted."
Ryeqo - relugolix / estradiol / norethisterone acetate - EMEA/H/C/005267/II/0013/G Gedeon Richter Plc., Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jean-Michel Race, PRAC Rapporteur: Martin Huber, "Extension of indication to include treatment of moderate to severe pain associated with endometriosis for Ryeqo in adult women of reproductive age with a history of previous medical or surgical treatment for their endometriosis, based on final results from

studies MVT-601-3101 and MVT-601-3102 and final results up to 104 weeks from study MVT-601-3103. Studies 3101 and 3102 are pivotal, phase III, randomised, double-blind, placebo-controlled, safety and efficacy studies to evaluate relugolix with E2 and NETA as a combination therapy for pain associated with endometriosis. Study 3103 is an open-label extension study including patients who completed one of the two pivotal studies and met the eligibility criteria, regardless of their treatment assignment in the pivotal studies. In the extension part all patients received relugolix combination therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC were updated. The Package Leaflet is updated in accordance. Update of section 4.5 of the SmPC to update information regarding Drug-Drug Interaction based on final results of DDI studies MVT-601-54, MVT-601-55 and MVT-601-57. Study MVT-601-54 is a 2-part interventional open-label study to assess the potential effects of erythromycin on the PK of the 3 components of Ryeqo. Study MVT-601-55 is an interventional open label fixed single sequence cross-over study to assess whether a 6-hour dose separation is sufficient to mitigate absorption mediated increased exposure to relugolix and study MVT-601-057 is a 2-part study to assess the potential effect of relugolix on the PK of total dabigatran. The updated RMP version (2.0) has also been submitted. As part of the application, the MAH also requests an extension of the market protection by one additional year." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)	
Soliris - eculizumab - EMEA/H/C/000791/II/0126, Orphan Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Monica Martinez Redondo, "Extension of indication to include treatment of paediatric patients with refractory generalised myasthenia gravis (gMG) for Soliris, based on interim results from study ECU-MG-303; this is an open-label, multicenter, phase 3 study to evaluate the efficacy, safety, pharmacokinetics and pharmacodynamics of	

intravenous (IV) eculizumab in paediatric patients aged 6 to less than 18 years with acetylcholine receptor-antibody (AChR-Ab) positive (+) refractory gMG. 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 20.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to update section 4.8 of the SmPC in order to update the frequency of the list of adverse drug reactions (ADRs) based on cumulative safety data and to introduce minor editorial changes to the PI.”

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Adjupanrix - pandemic influenza vaccine (h5n1) (split virion, inactivated, adjuvanted) - EMEA/H/C/001206/II/0081/G GlaxoSmithkline Biologicals SA, Informed Consent of Pandemrix (EXP), Rapporteur: Johann Lodewijk Hillege
Afstyla - lonoctocog alfa - EMEA/H/C/004075/II/0046/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus
Aybintio - bevacizumab - EMEA/H/C/005106/II/0016 Samsung Bioepis NL B.V., Rapporteur: Andrea Laslop
Benepali - etanercept - EMEA/H/C/004007/II/0069 Samsung Bioepis NL B.V., Rapporteur: Andrea Laslop
CEVENFACTA - eptacog beta (activated) - EMEA/H/C/005655/II/0002 Laboratoire Francais du Fractionnement et des Biotechnologies, Rapporteur: Andrea Laslop
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0159/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson
Cosentyx - secukinumab - EMEA/H/C/003729/II/0095/G Novartis Europharm Limited, Rapporteur: Outi Mäki-Ikola

Cosentyx - secukinumab - EMEA/H/C/003729/II/0096
Novartis Europharm Limited, Rapporteur: Outi Mäki-Ikola

Ervebo - recombinant vesicular stomatitis virus - zaire ebolavirus vaccine (live) - EMEA/H/C/004554/II/0030
Merck Sharp & Dohme B.V., Rapporteur: Christophe Focke

Flixabi - infliximab - EMEA/H/C/004020/II/0077/G
Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus

Fluad Tetra - influenza vaccine (surface antigen, inactivated, adjuvanted) - EMEA/H/C/004993/II/0036
Seqirus Netherlands B.V., Rapporteur: Sol Ruiz

Hemlibra - emicizumab - EMEA/H/C/004406/II/0033
Roche Registration GmbH, Rapporteur: Alexandre Moreau

Idefirix - imlifidase - EMEA/H/C/004849/II/0010, Orphan
Hansa Biopharma AB, Rapporteur: Martina Weise

Ivabradine Zentiva - ivabradine - EMEA/H/C/004117/II/0014
Zentiva k.s., Generic, Generic of Procoralan, Rapporteur: Tomas Radimersky

Kovaltry - octocog alfa - EMEA/H/C/003825/II/0040/G
Bayer AG, Rapporteur: Kristina Dunder

LifeGlobal Media - human albumin solution - EMEA/H/D/004287/II/0005/G
LifeGlobal Group LLC, Rapporteur: Maria Grazia Evandri

Lonsurf - trifluridine / tipiracil - EMEA/H/C/003897/II/0025
Les Laboratoires Servier, Rapporteur: Paula Boudewina van Hennik

LUTATHERA - lutetium (177Lu) oxodotreotide - EMEA/H/C/004123/II/0039, Orphan
Advanced Accelerator Applications, Rapporteur: Janet Koenig

Menveo - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/001095/II/0115/G
GSK Vaccines S.r.l, Rapporteur: Johann Lodewijk Hillege

Natpar - parathyroid hormone - EMEA/H/C/003861/II/0047/G, Orphan
Takeda Pharmaceuticals International AG, Rapporteur: Karin Janssen van Doorn

NUVAXOVID - SARS-CoV-2, spike protein, recombinant, expressed in Sf9 cells derived from Spodoptera Frugiperda - EMEA/H/C/005808/II/0035/G
Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege

NUVAXOVID - SARS-CoV-2, spike protein, recombinant, expressed in Sf9 cells derived from Spodoptera Frugiperda - EMEA/H/C/005808/II/0039/G
Novavax CZ, a.s., Rapporteur: Johann Lodewijk Hillege

Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0035/G
Roche Registration GmbH, Rapporteur: Thalia Marie Estrup Blicher

Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0036/G
Roche Registration GmbH, Rapporteur: Thalia Marie Estrup Blicher

Oyavas - bevacizumab - EMEA/H/C/005556/II/0019
STADA Arzneimittel AG, Duplicate, Duplicate of Alymsys, Rapporteur: Christian Gartner

Padcev - enfortumab vedotin - EMEA/H/C/005392/II/0006/G
Astellas Pharma Europe B.V., Rapporteur: Aaron Sosa Mejia

Replagal - agalsidase alfa - EMEA/H/C/000369/II/0122
Takeda Pharmaceuticals International AG Ireland Branch, Rapporteur: Johann Lodewijk Hillege

Rotarix - rotavirus vaccine (live, oral) - EMEA/H/C/000639/II/0128
GlaxoSmithKline Biologicals S.A., Rapporteur:

Christophe Focke	
Rybelsus - semaglutide - EMEA/H/C/004953/II/0030 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege	
Skyrizi - risankizumab - EMEA/H/C/004759/II/0029/G AbbVie Deutschland GmbH & Co. KG, Rapporteur: Finbarr Leacy	
Spikevax - elasomeran - EMEA/H/C/005791/II/0090/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus	See B.5.1
Supemtek - quadrivalent influenza vaccine (recombinant, prepared in cell culture) - EMEA/H/C/005159/II/0010/G Sanofi Pasteur, Rapporteur: Jan Mueller-Berghaus	
Surgiflo Haemostatic Matrix Kit - human thrombin - EMEA/H/D/002301/II/0032/G Ferrosan Medical Devices A/S, Rapporteur: Jan Mueller-Berghaus	
Tabrecta - capmatinib - EMEA/H/C/004845/II/0003/G Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa	
Taltz - ixekizumab - EMEA/H/C/003943/II/0048 Eli Lilly and Co (Ireland) Limited, Rapporteur: Kristina Dunder	
TEPADINA - thiotepa - EMEA/H/C/001046/II/0046/G ADIENNE S.r.l. S.U., Rapporteur: Alexandre Moreau	
VidPrevtyn Beta - sars-cov-2 prefusion spike delta tm protein, recombinant - EMEA/H/C/005754/II/0001/G Sanofi Pasteur, Rapporteur: Jan Mueller-Berghaus	
Xenpozyme - olipudase alfa - EMEA/H/C/004850/II/0002/G, Orphan Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege	
Zercepac - trastuzumab - EMEA/H/C/005209/II/0022	

Accord Healthcare S.L.U., Rapporteur: Sol Ruiz

WS2362
Edistride-
EMEA/H/C/004161/WS2362/0057
Forxiga-
EMEA/H/C/002322/WS2362/0078
AstraZeneca AB, Lead Rapporteur: Kristina Dunder

WS2388/G
Fluenz Tetra-
EMEA/H/C/002617/WS2388/0122/G
Pandemic influenza vaccine H5N1
AstraZeneca-
EMEA/H/C/003963/WS2388/0056/G
AstraZeneca AB, Lead Rapporteur: Christophe Focke

WS2394
Hexacima-
EMEA/H/C/002702/WS2394/0141
Hexyon-
EMEA/H/C/002796/WS2394/0145
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

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

Adtralza - tralokinumab -
EMEA/H/C/005255/II/0008
LEO Pharma A/S, Rapporteur: Jayne Crowe, "To update section 4.8 of the SmPC in order to update safety information based on interim results from the ECZTEND study, listed as a category 3 study in the RMP. This is a phase 3 open-label, single-arm, multi-centre, long-term extension trial to evaluate the safety and efficacy of tralokinumab in subjects with moderate-to-severe atopic dermatitis who participated in previous tralokinumab clinical trials. In addition, the MAH is taking this opportunity to update the list of local representatives in the Package Leaflet."

Amglidia - glibenclamide -
EMEA/H/C/004379/II/0015, Orphan
Ammtek, Rapporteur: Martina Weise, "Update of section 5.1 of the SmPC in order to update information regarding sulphonylurea effects on neurological abnormalities in children and adults with KCNJ11- and ABCC8-related neonatal

diabetes based on literature."

Beyfortus - nirsevimab - EMEA/H/C/005304/II/0001

AstraZeneca AB, Rapporteur: Thalia Marie Estrup Blicher, "Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update efficacy information based on additional results from study D5290C00004 (MELODY); this is a Phase III Randomized, Double-blind, Placebo-controlled Study to Evaluate the Safety and Efficacy of MEDI8897, for the Prevention of Medically Attended Lower Respiratory Tract Infection Due to Respiratory Syncytial Virus in Healthy Late Preterm and Term Infants."

Briviact - brivaracetam - EMEA/H/C/003898/II/0037/G

UCB Pharma S.A., Rapporteur: Filip Josephson, "Grouped application comprising two type II variations as follows:
C.I.4 - Update of section 4.6 of the SmPC in order to update information on breastfeeding following the outcome of the safety signal assessment report (SSAR).
C.I.3.a - Update of section 4.8 of the SmPC to implement the wording agreed by the CHMP following the outcome of the procedure P46/009.
In addition, the MAH took the opportunity to make editorial changes, to update the list of local representatives in the Package Leaflet and to bring the Package Leaflet in line with the current approved mock-up/specimen layout."

COMIRNATY - tozinameran - EMEA/H/C/005735/II/0160

BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC based on interim results from study C4591007 listed as a category 3 study in the RMP; this is an interventional phase I, open-label dose-finding study to evaluate safety, tolerability, and immunogenicity and phase II/III placebo-controlled, observer-blinded safety, tolerability, and immunogenicity study of a SARS-CoV-2 RNA vaccine candidate against COVID-19 in healthy children and young adults. The Package Leaflet and Labelling are updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in

the SmPC, Package Leaflet and Labelling”
Darzalex - daratumumab - EMEA/H/C/004077/II/0064, Orphan Janssen-Cilag International N.V., Rapporteur: Aaron Sosa Mejia, “Submission of the final report from study MMY3013 (54767414MMY3013). This is a Phase III, randomized, open-label study comparing daratumumab, pomalidomide and low-dose dexamethasone (DaraPomDex) with pomalidomide and low-dose dexamethasone (PomDex) in subjects with relapsed or refractory Multiple Myeloma who have received at least 1 prior treatment regimen with both lenalidomide and a proteasome inhibitor and have demonstrated disease progression.”
DuoPlavin - clopidogrel / acetylsalicylic acid - EMEA/H/C/001143/II/0065 sanofi-aventis groupe, Rapporteur: Bruno Sepodes, “Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on ‘drug reaction with eosinophilia and systemic symptoms (DRESS)’ based on a safety evaluation report; the Package Leaflet is updated accordingly.”
Dupixent - dupilumab - EMEA/H/C/004390/II/0068 sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus, “Update of sections 4.8 and 5.1 of the SmPC to include long-term safety and efficacy information in children based on final results from study LTS14424 - EXCURSION. This is an interventional one-year study, to evaluate the long-term safety and tolerability of dupilumab in children 6 to 11 years of age with asthma, who participated in a previous dupilumab asthma clinical study EFC14153.”
Eliquis - apixaban - EMEA/H/C/002148/II/0088 Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.2 and 5.1 of the SmPC in order to update efficacy and safety information in the paediatric population based on results of the paediatric studies performed in compliance with the paediatric investigation plan (PIP), including studies CV185155 and CV185362. In addition, the MAH took the opportunity to introduce

minor editorial changes to the PI."

Enbrel - etanercept - EMEA/H/C/000262/II/0249

Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 4.6 of the SmPC in order to update information on breast feeding exposure based on the cumulative review of etanercept specific pharmacology, safety database and published medical literature.
The Package Leaflet is updated accordingly.
In addition, the MAH is taking this opportunity to correct minor administrative and typographical changes to the SmPC, Labelling and Package Leaflet.
In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet."

Evrysdi - risdiplam - EMEA/H/C/005145/II/0011, Orphan

Roche Registration GmbH, Rapporteur: Bruno Sepodes, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to delete an existing warning on "Use with SMA gene therapy" and to update the safety profile and efficacy data in patients previously treated with other SMA-modifying therapies based on the 24-month primary analysis data from study BP39054 (JEWELFISH); this is a multicenter, open-label study to investigate the safety, tolerability, and pharmacokinetics/pharmacodynamics of risdiplam in adult and paediatric patients with SMA. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

IBRANCE - palbociclib - EMEA/H/C/003853/II/0040

Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to update efficacy and safety information based on final OS results from study A5481008 (PALOMA-2, "A Randomized, Multicenter, Double-blind Phase 3 Study of PD-0332991 (Oral CDK 4/6 Inhibitor) Plus Letrozole Versus Placebo Plus Letrozole for the Treatment of Postmenopausal Women with ER (+), HER2 (-) Breast Cancer Who Have Not Received Any Prior Systemic Anti-Cancer Treatment For Advanced Disease") to fulfil REC 2.
In addition, the MAH took the opportunity to

align Annex II with the current QRD template.”
Imfinzi - durvalumab - EMEA/H/C/004771/II/0054 AstraZeneca AB, Rapporteur: Aaron Sosa Mejia, “Submission of the final report from non-clinical study ONC4736-PB-0401 (Profiling of Biomarkers Relevant to Immunotherapies in Paediatric Solid Tumours).”
Kesimpta - ofatumumab - EMEA/H/C/005410/II/0006 Novartis Ireland Limited, Rapporteur: Thalia Marie Estrup Blicher, “Update of section 5.1 of the SmPC based on final results from pivotal studies G2301, G2302 and a meta-analysis of studies G2301 and G2302. G2301 and G2302 are two Phase III, randomized, double-blind, double-dummy, parallel-group studies comparing the efficacy and safety of ofatumumab versus teriflunomide in patients with relapsing multiple sclerosis.”
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0128 Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, “Update of section 5.1 of the SmPC in order to update information based on the final OS data for the overall population as well as for MMR subgroups from study 309/KEYNOTE-775 in order to fulfil the Recommendation: REC/033. This Recommendation was agreed with the approval of study 309/KEYNOTE-775; this is a multicenter, open-label, randomized, phase 3 trial to compare the efficacy and safety of lenvatinib in combination with pembrolizumab versus treatment of physician's choice in participants with advanced endometrial cancer.”
Kisplyx - lenvatinib - EMEA/H/C/004224/II/0054 Eisai GmbH, Rapporteur: Karin Janssen van Doorn, “Submission of the latest Modelling and Simulation related data (such as PopPK and PK/PD Analyses) following the assessment of procedure II/52 to fulfil MEA/FSR 008.1, MEA/FSR 007.3 and MEA/FSR 013.2.”
Lenvima - lenvatinib - EMEA/H/C/003727/II/0049 Eisai GmbH, Rapporteur: Karin Janssen van Doorn, “Update of section 5.1 of the SmPC in

order to update the efficacy information of "Endometrial carcinoma" based on the final OS analysis data for the overall population as well as for MMR subgroups from study E7080-G000-309 / KEYNOTE-775. This is a Multicenter, Open-label, Randomized, Phase III study to compare the efficacy and safety of lenvatinib in combination with pembrolizumab versus treatment of physician's choice in participants with advanced endometrial cancer.
In addition, the MAH took the opportunity to implement editorial changes in the SmPC."

Lynparza - olaparib - EMEA/H/C/003726/II/0057

AstraZeneca AB, Rapporteur: Alexandre Moreau, "Update of sections 4.8 and 5.1 of the SmPC in order to update the long-term safety data and the final OS analysis from PAOLA-1 study (D0817C00003). This is a Randomized, Double-Blind, Phase III Trial of Olaparib vs. Placebo in Patients with Advanced FIGO Stage IIIB – IV High Grade Serous or Endometrioid Ovarian, Fallopian Tube, or Peritoneal Cancer Treated with Standard First Line Treatment, Combining Platinum-Taxane Chemotherapy and Bevacizumab Concurrent with Chemotherapy and in Maintenance. The Package Leaflet is updated accordingly."

Lynparza - olaparib - EMEA/H/C/003726/II/0058

AstraZeneca AB, Rapporteur: Alexandre Moreau, "Update of section 5.1 of the SmPC in order to provide the Final Overall Survival (OS) Analysis from study D0816C00020 (OPINION). This is a Phase IIIb single-arm, open-label, multicentre study of maintenance therapy in PSR non-germline BRCA mutated ovarian cancer patients who are in complete or partial response following platinum-based chemotherapy."

Nexpovio - selinexor - EMEA/H/C/005127/II/0011

Stemline Therapeutics B.V., Rapporteur: Blanca Garcia-Ochoa, "Update of section 4.5 of the SmPC in order to add drug-drug interaction information regarding the strong CYP3A4 inhibitor, clarithromycin, based on results from the drug-drug interaction (DDI) pharmacokinetic (PK) portion of study KCP 330-017 (STOMP) following procedure

EMEA/H/C/005127/REC/003.1. This is a Phase 1b/2, multi-center, open-label, clinical study with Dose Escalation (Phase 1) and Expansion (Phase 2) to independently assess the MTD, efficacy, and safety of 10 combination therapies in 11 arms in patients with RRMM (Relapsed/Refractory Multiple Myeloma) and NDMM (Newly Diagnosed Multiple Myeloma)."

Noxafil - posaconazole - EMEA/H/C/000610/II/0077

Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau, "C.I.4. To add new in vitro study data in section 5.2 of the SmPC for gastro-resistant powder and solvent for oral suspension formulation.
The applicant took the opportunity to also include minor editorial updates to the SmPC, PI and labelling of all pharmaceutical forms."

Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0035

AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.8 of the SmPC in order to remove the information referring to healthy volunteers and to add infusion related adverse reactions in bleeding patients following an internal review of the labels and based on ANNEXA-4 study.
The Package Leaflet is updated accordingly.
In addition, the MAH would like to take this opportunity to make some corrections in the SmPC."

Orgovyx - relugolix - EMEA/H/C/005353/II/0007

Accord Healthcare S.L.U., Rapporteur: Paula Boudewina van Hennik, "Submission of the bioanalytical report of testosterone."

Orgovyx - relugolix - EMEA/H/C/005353/II/0008

Accord Healthcare S.L.U., Rapporteur: Paula Boudewina van Hennik, "Submission of the final report from study MVT-601-055; this is an open-label, fixed (single)-sequence crossover phase 1 study to assess the sufficiency of dose separation to mitigate absorption-mediated increases in exposure to relugolix resulting from inhibition of intestinal P-gp by azithromycin in healthy adult men."

Orgovyx - relugolix -

EMEA/H/C/005353/II/0009
Accord Healthcare S.L.U., Rapporteur: Paula Boudewina van Hennik, "Submission of the final report from study MVT-601-057. This is a Phase I, two-part, open-label, fixed (single)-sequence, two-treatment, two-period crossover study to assess the effects of relugolix on the pharmacokinetics of total dabigatran upon co-administration of relugolix and the P-gp substrate dabigatran etexilate in healthy adult men and women."

Piqray - alpelisib - EMEA/H/C/004804/II/0017
Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa, "Update of section 5.3 of the SmPC in order to update non-clinical information based on data from two skin toxicology studies conducted in rats: Study 1770766 and Study 1870156."

Revlimid - lenalidomide - EMEA/H/C/000717/II/0124
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Alexandre Moreau, "Update of section 5.1 of the SmPC in order to update 5-year Overall Survival data following the assessment of procedure II/107 based on study CC-5013-NHL-007, A Phase 3, Double-Blind Randomized Study To Compare The Efficacy And Safety Of Rituximab Plus Lenalidomide (Cc-5013) Versus Rituximab Plus Placebo In Subjects With Relapsed/Refractory Indolent Lymphoma."

Ronapreve - casirivimab / imdevimab - EMEA/H/C/005814/II/0009
Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning and to add convulsive syncope to the list of adverse drug reactions (ADRs) with frequency not known, following a signal assessment conducted by the MAH. The Package Leaflet is updated accordingly."

Segluromet - ertugliflozin / metformin hydrochloride - EMEA/H/C/004314/II/0017
Merck Sharp & Dohme B.V., Rapporteur: Kristina Dunder, "To include significant changes to sections 4.4 and 4.8 of the SmPC and section 4 of the Package Leaflet for the medicinal

product Segluromet containing the active substances Ertugliflozin L-pyroglutamic acid and Metformin hydrochloride in order to include a warning for vitamin B12 deficiency and to change the frequency of vitamin B12 deficiency from very rare to common, . The same wording is used for the combination product.
In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Spectrila - asparaginase - EMEA/H/C/002661/II/0032/G
medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Andrea Laslop, "Grouped Variation (Type II & Type IB): C.I.4: Update of sections 4.4 and 4.6 of the SmPC in order to include the recommendations from the SWP regarding genotoxic medicinal products and contraception duration period; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. C.I.6.b: Deletion of the indication lymphoblastic lymphoma (LBL) in section 5.3 of the SmPC, as Spectrila is not approved for LBL."

Spikevax - elasomeran - EMEA/H/C/005791/II/0088
Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, "Submission of the final report from study DMID 20-0003 listed as a category 3 study in the RMP. This is a Phase I, Open Label, Dose-ranging Study of the Safety and Immunogenicity of 2019-nCoV Vaccine (mRNA-1273) in Healthy Adults."

Taltz - ixekizumab - EMEA/H/C/003943/II/0046
Eli Lilly and Co (Ireland) Limited, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to add 'oesophageal candidiasis' to the list of adverse drug reactions (ADRs) with frequency rare based on a safety review of all associated data; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

TEPMETKO - tepotinib - EMEA/H/C/005524/II/0005
Merck Europe B.V., Rapporteur: Filip Josephson, "Update of sections 4.5 and 5.2 of the SmPC in

order to remove interactions with 'CYP and P-gp inducers' and 'dual strong CYP3A and P-gp inhibitors, and P-gp inhibitors' and to update pharmacokinetic information based on final results from the drug-drug interaction (DDI) studies MS200095-0051 and MS200095-0053. Study MS200095-0051 is a phase 1, open-label, single-sequence, cross-over study to evaluate the effect of multiple doses of carbamazepine on single-dose tepotinib pharmacokinetics in healthy participants, while study MS200095-0053 is a phase 1, open-label, single-sequence, cross-over study to evaluate the effect of multiple doses of itraconazole on single-dose tepotinib pharmacokinetics in healthy participants. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor changes to the PI."

TEZSPIRE - tezepelumab - EMEA/H/C/005588/II/0004

AstraZeneca AB, Rapporteur: Finbarr Leacy, "Submission of the final report detailing the extended follow-up data from study D5180C00018 (DESTINATION) listed as a category 3 study in the RMP; this is a multicentre, randomised, double-blind, placebo-controlled, parallel group, long term extension study designed to evaluate the safety and efficacy of 210 mg Q4W subcutaneous of tezepelumab in adults and adolescents with severe uncontrolled asthma for up to 2 continuous years of treatment."

Vargatef - nintedanib - EMEA/H/C/002569/II/0047/G

Boehringer Ingelheim International GmbH, Rapporteur: Aaron Sosa Mejia, "Grouped application containing:
C.I.4: Update of sections 4.2, 5.1 and 5.2 of the SmPC in order to update information regarding the paediatric population based on results from study 1199-0337; this is a double blind, randomised, placebo-controlled trial to evaluate the dose-exposure and safety of nintedanib on top of standard of care for 24 weeks, followed by open label treatment with nintedanib of variable duration, in children and adolescents (6 to 17 year-old) with clinically significant fibrosing interstitial lung disease. The Package

Leaflet is updated accordingly. C.I.4: Update of sections 4.2 and 5.2 of the SmPC in order to improve the recommendation for the administration of nintedanib based on food compatibility data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to introduce minor editorial changes to the PI."	
Vaxneuvance - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/005477/II/0011 Merck Sharp & Dohme B.V., Rapporteur: Johann Lodewijk Hillege, "To update sections 4.2 and 5.1 of the SmPC in order to update the information for immune response after subcutaneous administration based on final results from study V114-P033 (EudraCT: 2019-003644-68), in accordance with Article 46 of the paediatric regulation. V114-P033 is a phase 3 Active-Comparator controlled study to evaluate the Safety, Tolerability, and Immunogenicity of V114 in Healthy Japanese Infants. The Package Leaflet is updated accordingly."	
Verzenios - abemaciclib - EMEA/H/C/004302/II/0024 Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to include overall survival data based on final results from study MONARCH 2; this is a A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study of Fulvestrant with or without Abemaciclib, a CDK4/6 Inhibitor, for Women with Hormone Receptor-Positive, HER2-Negative Locally Advanced or Metastatic Breast Cancer."	
XALKORI - crizotinib - EMEA/H/C/002489/II/0078 Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, "Submission of the final report from study A8081001 (A Phase 1 Safety, Pharmacokinetic and Pharmacodynamic Study Of PF-02341066, A MET/HGFR Selective Tyrosine Kinase Inhibitor, Administered Orally to Patients with Advanced Cancer), to fulfil recommendation 8 of the Xalkori MAA to further investigate the role of c-Met status in ALK-	

negative patients.”	
WS2377 **Jentadueto-** **EMEA/H/C/002279/WS2377/0067** **Synjardy-** **EMEA/H/C/003770/WS2377/0067** Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on Vitamin B12 decrease or deficiency and to update the list of adverse drug reactions (ADRs) in accordance with the recent update of the PI for Glucophage, which is the reference label for the compound metformin, and following the request by MHRA on 20 June 2022 for all products containing metformin; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and to update the list of local representatives in the Package Leaflet.”	
WS2407 **Efficib-EMEA/H/C/000896/WS2407/0110** **Janumet-** **EMEA/H/C/000861/WS2407/0109** **Ristfor-EMEA/H/C/001235/WS2407/0098** **Velmetia-** **EMEA/H/C/000862/WS2407/0115** Merck Sharp & Dohme B.V., Lead Rapporteur: Johann Lodewijk Hillege, “To include significant changes to sections 4.4 and 4.8 of the SmPC and section 4 of the Package Leaflet for the medicinal products Janumet, Velmetia, Ristfor and Efficib, containing the active substances Metformin hydrochloride and Sitagliptin phosphate in order to include a warning for vitamin B12 deficiency and to change the frequency of vitamin B12 deficiency from very rare to common following the assessment of the medicinal product Glucophage, which also contains the active substance metformin, assessed as part of a mutual recognition procedure FR/H/0181/001-3. The same wording is used for the combination product. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet for Janumet, Ristfor and Efficib and to improve the wording in section 2 of the	

Package Leaflet.”

B.6.10. CHMP-PRAC assessed procedures

Beovu - brolucizumab - EMEA/H/C/004913/II/0021
Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to change posology recommendation in including an additional dose regimen (q16w) for DME patients during the maintenance phase, update the frequency of adverse drug reactions, update pharmacokinetic, pharmacodynamic, efficacy and safety information, following the assessment of procedure II/10, based on final results from studies CRTH258B2301 (KESTREL) and CRTH258B2302 (KITE).
The Package Leaflet is updated accordingly. The RMP version 10 has also been submitted.”

Evicel - human fibrinogen / human thrombin - EMEA/H/C/000898/II/0099
Omrix Biopharmaceuticals N. V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Update of sections 4.8 and 5.1 of the SmPC in order to update the frequency of adverse drug reactions (ADRs), add Pseudomeningocele to the list of ADRs with frequency uncommon and to update efficacy and safety information on paediatric population, following P46/0030 based on the final results from paediatric clinical study BIOS-13-006. This is a Prospective Randomized Controlled Study Evaluating the Safety and Efficacy of EVICEL used for Suture- Line Sealing in Dura-Mater Closure during Paediatric Neurosurgical Cranial Procedures.
The Package Leaflet is updated accordingly. Editorial changes are proposed to sections of the product information.
In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.3.
The RMP version 15 has also been submitted.”

Lucentis - ranibizumab - EMEA/H/C/000715/II/0101
Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel

Liminga, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update information on preterm infants based on final results from study CRFB002H2301E (RAINBOW extension), listed as a PAES in the Annex II; this is an extension study to evaluate the long term efficacy and safety of ranibizumab compared with laser therapy for the treatment of infants born prematurely with retinopathy of prematurity. The Annex II and Package Leaflet are updated accordingly. The RMP version 22.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI."

Rozlytrek - entrectinib - EMEA/H/C/004936/II/0014

Roche Registration GmbH, Rapporteur: Armando Genazzani, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2 and 5.2 of the SmPC in order to update pharmacokinetic information based on final results from study GP411174 listed as an additional pharmacovigilance activity in the RMP; this is a Phase I, non-randomized, single-dose, open-label study to investigate the effect of impaired hepatic function on the pharmacokinetics of entrectinib in volunteers with different levels of hepatic function. The RMP version 4.0 has also been submitted.
In addition, the MAH took the opportunity to update in Annex II section C and to update the list of local representatives in the Package Leaflet."

Simponi - golimumab - EMEA/H/C/000992/II/0109

Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Mari Thorn, "Update of the Package Leaflet in order to update the Instructions for Use (IFU) for the pre-filled pen."

Stelara - ustekinumab - EMEA/H/C/000958/II/0096

Janssen-Cilag International N.V., Rapporteur: Jayne Crowe, PRAC Rapporteur: Rhea Fitzgerald, "Update of section 5.1 of the SmPC in order to update information with the 4-year clinical data in patients with ulcerative colitis based on the final report from study CNTO1275UCO3001 listed as a category 3 study in the RMP; this is a phase 3, randomized,

double blind, placebo-controlled, parallel-group, multicenter study to evaluate the safety and efficacy of ustekinumab induction and maintenance therapy in subjects with moderately to severely active ulcerative colitis. The RMP version 23.1 has also been submitted. In addition, the MAH took the opportunity to introduce a correction to the PI."	
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0075 Roche Registration GmbH, Rapporteur: Aaron Sosa Mejia, PRAC Rapporteur: Inês Ribeiro-Vaz, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add 'pericardial disorders' to the list of adverse drug reactions (ADRs) with frequency common in monotherapy and uncommon in combination therapy/based on final results from Drug Safety Report (DSR 1115896) including review of available clinical trial data, post-marketing data, and literature. In addition, the MAH took the opportunity to update Annex II section D of the SmPC and to implement editorial changes in the SmPC. The Package Leaflet was updated accordingly. The RMP version 23.1 has also been submitted."	
Translarna - ataluren - EMEA/H/C/002720/II/0069, Orphan PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, "Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information following results from study PTC124-GD-041-DMD, listed as a specific obligation in the Annex II; This is a Phase 3 multicentre, randomised, double-blind, 18-month, placebo-controlled study, followed by a 18-month open label extension to confirm the efficacy and safety of ataluren in the treatment of ambulant patients with mnDMD aged 5 years or older. Annex II and Annex IIB are updated to delete the SOB and to reflect the switch from conditional to full marketing authorisation. The Package Leaflet is updated accordingly. The RMP version 11.0 has also been submitted. Minor corrections were done to align the PI with the latest QRD templates."	
Vaxneuvance - pneumococcal polysaccharide conjugate vaccine	

(adsorbed) -
EMEA/H/C/005477/II/0013/G
Merck Sharp & Dohme B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Grouped application comprising two type II variations as follows:
- To update sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to add safety data on recipients of haematopoietic stem cell transplant (HSCT) based on final results from study V114-022, listed as a category 3 study in the RMP; This is a Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of Vaxneuvance in Recipients of Allogeneic Hematopoietic Stem Cell Transplant.
- To update sections 4.2, 5.1 of the SmPC in order to update the information regarding a 3-dose regimen based on final results from study V114-026; a Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of a 3-dose Regimen of Vaxneuvance in Healthy Infants.
The Package Leaflet is updated accordingly.
The RMP version 2.1 has also been submitted."

Zeposia - ozanimod -
EMEA/H/C/004835/II/0016
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maria del Pilar Rayon, "Update of sections 4.2 and 5.2 of the SmPC in order to add a dose adjustment after completion of the dose escalation regimen in patients with mild or moderate chronic hepatic impairment (Child-Pugh class A or B) based on the final results from study RPC-1063-CP-004; this is a Phase I, multicenter, open-label study to evaluate the effect of mild or moderate hepatic impairment on the multiple-dose pharmacokinetics of ozanimod. The Package Leaflet is updated accordingly. The updated RMP version 5.0 has also been submitted."

B.6.11. PRAC assessed procedures

PRAC Led
Aldurazyme - laronidase -
EMEA/H/C/000477/II/0085
Genzyme Europe BV, PRAC Rapporteur: Nathalie Gault, PRAC-CHMP liaison: Alexandre Moreau, "To update section 4.2 of the SmPC in order to

modify the administration instructions following the assessment of procedure PSUSA/00001830/202104 based on literature review.
The Package Leaflet is updated accordingly. The RMP version 1.0 has also been submitted."

PRAC Led

Alecensa - alectinib -
EMEA/H/C/004164/II/0044

Roche Registration GmbH, PRAC Rapporteur: Jana Lukacisinova, PRAC-CHMP liaison: Ondřej Slanař, "Submission of an updated RMP version 3.2 in order to remove the important identified risks of Interstitial Lung Disease (ILD)/Pneumonitis, Hepatotoxicity, Photosensitivity, Bradycardia, Severe myalgia and Creatine Phosphokinase (CPK) elevations as safety concerns. Furthermore, template updates in line with the GVP Product or Population-Specific Considerations III: Pregnant and breastfeeding women are made."

PRAC Led

COMIRNATY - tozinameran -
EMEA/H/C/005735/II/0152

BioNTech Manufacturing GmbH, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of section 4.8 of the SmPC, upon request by PRAC following the assessment of EMEA/H/C/PSUSA/00010898/202112, to add "Dizziness" to the list of adverse drug reactions (ADRs) with frequency Uncommon. The Package Leaflet is updated accordingly."

PRAC Led

Fintepla - fenfluramine -
EMEA/H/C/003933/II/0017, Orphan

Zogenix ROI Limited, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of an updated RMP version 2.10 in order to implement a targeted follow-up questionnaire (FUQ) to further improve the collection of follow-up information on cases of vascular heart disease (VHD) and pulmonary arterial hypertension (PAH) suggested by PRAC following the assessment of procedure EMEA/H/C/PSUSA/00010907/202112."

PRAC Led

Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0063

Merck Sharp & Dohme B.V., PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Karin Janssen van Doorn, "Update of section 4.6 of the SmPC in order to include additional information on exposure during pregnancy, based on the final report of the US Pregnancy Registry, listed as a category 3 study in the RMP; the Package Leaflet is updated accordingly. The RMP version 5.1 has also been submitted."

PRAC Led

IMVANEX - smallpox vaccine (live modified vaccinia virus Ankara) - EMEA/H/C/002596/II/0081

Bavarian Nordic A/S, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 9.1 in order to update the safety specifications in line with extension of the indication to "active immunisation against smallpox, monkeypox and disease caused by vaccinia virus in adults", update the missing information from the list of safety concerns, differentiate routine pharmacovigilance activities and additional pharmacovigilance activities, addition of non-BN sponsored clinical study SEMVAc to additional pharmacovigilance activities and deletion of paediatric study POX-MVA-035 upon request by PRAC following the assessment of procedure II/76."

PRAC Led

Insuman - insulin human - EMEA/H/C/000201/II/0142

Sanofi-Aventis Deutschland GmbH, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Karin Janssen van Doorn, "Submission of the final report from study HUBIN-C-06380 listed as a category 3 study in the RMP. This is an observational prospective PASS designed to gain additional longitudinal and long-term safety data related to the use of Insuman Implantable 400 IU/mL via an IP implantable pump in a European observational cohort of patients with type 1 diabetes. The RMP version 5.0 has also been submitted."

PRAC Led

NutropinAq - somatropin - EMEA/H/C/000315/II/0077

Ipsen Pharma, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Thalia Marie Estrup Blicher, "Submission of an updated RMP version 4.0 in order to remove some of the safety concerns in compliance with GVP Module V Revision 2.
In addition, the MAH took the opportunity to add data from the final clinical study report of International Cooperative Growth Study (iNCGS) registry (non-interventional study) and exposure and safety information."

PRAC Led

Paxlovid - (1r,2s,5s)-n-((1s)-1-cyano-2-((3s)-2-oxopyrrolidin-3-yl)ethyl)-3-((2s)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide / ritonavir - EMEA/H/C/005973/II/0032

Pfizer Europe MA EEIG, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Update of section 4.8 of the SmPC in order to add 'hypertension' to the list of adverse drug reactions (ADRs) with frequency 'uncommon', following procedure EMEA/H/C/005973/LEG/006, based on review of aggregate post-marketing data. The Package Leaflet is updated accordingly."

PRAC Led

Praluent - alirocumab - EMEA/H/C/003882/II/0077

sanofi-aventis groupe, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from the PASS study ALIROC08577. This is a non-interventional drug utilisation study of alirocumab in special populations using two U.S. healthcare databases."

PRAC Led

RAVICTI - glycerol phenylbutyrate - EMEA/H/C/003822/II/0044, Orphan

Immedica Pharma AB, Rapporteur: Thalia Marie Estrup Blicher, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Armando Genazzani, "Submission of the final report from study HZNP-RAV-401 "European Post-Authorization Registry for RAVICTI (glycerol

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phenylbutyrate) Oral Liquid in Partnership with the European Registry and Network for Intoxication Type Metabolic Diseases (E-IMD)", listed as a category 3 study in the RMP.
The RMP version 7.4 has also been submitted."

PRAC Led

Sialanar - glycopyrronium - EMEA/H/C/003883/II/0026

Proveca Pharma Limited, PRAC Rapporteur: Zane Neikena, PRAC-CHMP liaison: Elita Poplavska, "Submission of an updated RMP version 3.1 in order to remove a Drug Utilisation Study (DUS)."

PRAC Led

Spikevax - elasomeran - EMEA/H/C/005791/II/0085/G

Moderna Biotech Spain, S.L., PRAC Rapporteur: Marie Louise Schougaard Christiansen, PRAC-CHMP liaison: Thalia Marie Estrup Blicher, "Grouped application comprising two type II variations as follows:
C.I.11.b - To add Spikevax bivalent Original/ Omicron BA.4-5 vaccine (mRNA-1273.222), to update studies mRNA-1273-P904, mRNA-1273-P905 and mRNA-1273-P910 in the Pharmacovigilance Plan to include exposure to Spikevax bivalent vaccines, to update the INN to elasomeran/davesomeran, and to reclassify studies mRNA-1273-P205 from category 2 to category 3 studies in the Pharmacovigilance Plan.
C.I.13 - To submit the final CSR from study mRNA-1273-P201, a Phase 2a, Randomized, Observer-Blind, Placebo-Controlled, Dose-Confirmation Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults ≥= 18 Years listed as a category 3 study including addition of clinical trial exposure data for part C of the study mRNA-1273-P201. RMP version 6.0 will be updated accordingly."

PRAC Led

Stivarga - regorafenib - EMEA/H/C/002573/II/0039

Bayer AG, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC in order to remove the disease specific precaution for hepatocellular carcinoma based on final

results from study REFINE (study number 19244) listed as a category 3 study in the RMP; this is an international, prospective, open-label, multi-center, observational study to describe the safety and effectiveness of treatment with regorafenib in real-world settings.
The RMP version 6.1 has also been submitted."

PRAC Led
Stocrin - efavirenz -
EMEA/H/C/000250/II/0130
Merck Sharp & Dohme B.V., Duplicate, Duplicate of Sustiva, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "Submission of an updated RMP version 9.0 in accordance with the new template and thereby to remove safety concerns."

PRAC Led
Tarceva - erlotinib -
EMEA/H/C/000618/II/0071
Roche Registration GmbH, PRAC Rapporteur: Marie Louise Schougaard Christiansen, PRAC-CHMP liaison: Aaron Sosa Mejia, "Update of section 4.8 of the SmPC in order to provide a single table listing all ADRs following PSUSA/00001255/202111.
The Package Leaflet is updated accordingly."

PRAC Led
Vaxzevria - covid 19 vaccine (chadox1 s [recombinant]) -
EMEA/H/C/005675/II/0084/G
AstraZeneca AB, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Christophe Focke, "Submission of an updated RMP version 6.1 in order to request the discontinuation of the category 1 study D8111C00010 and remove it from the Annex II; this is an interventional safety study of AZD1222 vaccine in immunocompromised adults.
In addition, the MAH proposes the reassessment of safety concerns and changes to due dates of additional pharmacovigilance activities."

PRAC Led
VPRIV - velaglucerase alfa -
EMEA/H/C/001249/II/0061
Takeda Pharmaceuticals International AG Ireland Branch, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of an

updated RMP version 12 in order to remove certain risks from the list of safety concerns.”	
PRAC Led **WS2356** **Epclusa-** **EMEA/H/C/004210/WS2356/0068** **Harvoni-** **EMEA/H/C/003850/WS2356/0107** **Sovaldi-EMEA/H/C/002798/WS2356/0081** **Vosevi-EMEA/H/C/004350/WS2356/0057** Gilead Sciences Ireland UC, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, “To provide an updated RMP, following finalisation of procedure EMEA/H/C/WS2222 providing the final CSR for the non-imposed joint PASS study to evaluate the risk of de novo hepatocellular carcinoma in patients with compensated cirrhosis treated with direct-acting antivirals for chronic hepatitis C (study B20-146). In particular, the list of safety concerns has been updated to remove the important potential risks: “Recurrence of hepatocellular carcinoma (HCC)” and “Emergence of HCC”, and to remove “safety in patients with previous HCC” as an area of missing information. In addition, the completed PASS studies: DAA PASS and De Novo DAA PASS have been removed from the pharmacovigilance plan.”	
PRAC Led **WS2378** **Exelon-EMEA/H/C/000169/WS2378/0140** **Prometax-** **EMEA/H/C/000255/WS2378/0141** Novartis Europharm Limited, Lead PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, “C.I.11.z - To amend the RMP to: - remove the standalone multiple patch use annual report as an additional pharmacovigilance activity from the Exelon/Prometax RMP, which was endorsed by PRAC (EMA/CHMP/PRAC/342229/2021) on 22-Jul-2021. - include the initial risks reviewed at the time of initial marketing authorisation that were agreed to within RMP Version 1.1 (final: 16-Jul-2007); and the rationale for the removal of some safety concerns from the currently approved RMP Version 10.0, following the PRAC Assessment	

Report from the currently approved RMP (version 10.0) (EMEA/H/C/XXX/WS/1773). Furthermore, the MAH took the opportunity to introduce editorial changes in the following sections of the RMP: - epidemiology literature, where relevant (Module SI, Epidemiology of the indications and target populations). - worldwide reporting rate of cases of current safety concerns for rivastigmine, as of the latest data lock point of 31-Jan-2022 (Module SV.1, Post-authorisation exposure). - editorial update of preventability of current safety concerns for rivastigmine to reflect the existing educational material (Module SVII.3, Details of important identified risks, important potential risks, and missing information). The requested worksharing procedure proposed amendments to the None and to the Risk Management Plan (RMP)."	
PRAC Led **WS2387** **Rixathon-** **EMEA/H/C/003903/WS2387/0063** **Riximyo-** **EMEA/H/C/004729/WS2387/0064** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus, Lead PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Thalia Marie Estrup Blicher, "Submission of the final report from study GP13-501 following procedure EMEA/H/C/PSUSA/00002652/201811. This is a prospective, open-label, single-arm, non-interventional, multicenter study describing the effectiveness and safety of biosimilar rituximab administered in combination with CHOP chemotherapy for the treatment of patients with previously untreated CD20-positive diffuse large B-cell lymphoma in current clinical practice."	
PRAC Led **WS2406** **Glyxambi-** **EMEA/H/C/003833/WS2406/0049** **Jardiance-** **EMEA/H/C/002677/WS2406/0075** **Synjardy-** **EMEA/H/C/003770/WS2406/0068** Boehringer Ingelheim International GmbH, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-	

CHMP liaison: Blanca Garcia-Ochoa, "Update of section 4.4 of the SmPC in order to remove an existing warning on hepatic injury based on final results from the PASS 1245-96 listed as a category 3 study in the RMP for Jardiance and Synjardy; this is a post-authorisation safety study in patients with T2DM to assess the risk of acute liver injury, acute kidney injury and chronic kidney disease, severe complications of urinary tract infection, genital infections, and diabetic ketoacidosis among patients treated with empagliflozin compared to patients treated with DPP-4 inhibitors. The RMP versions for Jardiance (RMP version 20.0), Synjardy (RMP version 13.0) and Glyxambi (RMP version 8.0) have also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet for Glyxambi."

B.6.12. CHMP-CAT assessed procedures

Upstaza - eladocagene exuparvovec - EMEA/H/C/005352/II/0005/G, Orphan, ATMP

PTC Therapeutics International Limited, Rapporteur: Maura O'Donovan, CHMP Coordinator: Finbarr Leacy

Yescarta - axicabtagene ciloleucel - EMEA/H/C/004480/II/0057, Orphan, ATMP

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

B.6.13. CHMP-PRAC-CAT assessed procedures

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0059, ATMP

Amgen Europe B.V., Rapporteur: Maija Tarkkanen, CHMP Coordinator: Johanna Lähteenvuo, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Submission of an updated RMP version 10 in order to update and reclassify identified risk of 'Disseminated herpetic infection' based on the cumulative assessment of literature review and MAH Global Safety Database and to remove studies 20180062 and 20180099 from Planned and Ongoing Studies from the list of Pharmacovigilance Plan studies

in the Annex II.”

B.6.14. PRAC assessed ATMP procedures

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

WS2276
Herceptin-
EMEA/H/C/000278/WS2276/0186
Phesgo-EMEA/H/C/005386/WS2276/0015
Roche Registration GmbH, Lead Rapporteur: Jan Mueller-Berghaus

WS2351
Fiasp-EMEA/H/C/004046/WS2351/0032
NovoMix-
EMEA/H/C/000308/WS2351/0113
NovoRapid-
EMEA/H/C/000258/WS2351/0144
Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder

WS2353
Saxenda-
EMEA/H/C/003780/WS2353/0035
Victoza-EMEA/H/C/001026/WS2353/0065
Novo Nordisk A/S, Lead Rapporteur: Johann Lodewijk Hillege

WS2357
Actraphane-
EMEA/H/C/000427/WS2357/0093
Actrapid-
EMEA/H/C/000424/WS2357/0086
Actrapid-
EMEA/H/W/005779/WS2357/0002
Insulatard-
EMEA/H/C/000441/WS2357/0091
Insulatard-
EMEA/H/W/005780/WS2357/0002
Levemir-
EMEA/H/C/000528/WS2357/0106
Mixtard-
EMEA/H/C/000428/WS2357/0094
Protaphane-
EMEA/H/C/000442/WS2357/0090
Ryzodeg-
EMEA/H/C/002499/WS2357/0051
Tresiba-EMEA/H/C/002498/WS2357/0058
Xultophy-
EMEA/H/C/002647/WS2357/0047

Novo Nordisk A/S, Lead Rapporteur: Thalia Marie Estrup Blicher

WS2361
HBVAXPRO-EMEA/H/C/000373/WS2361/0080
Vaxelis-EMEA/H/C/003982/WS2361/0112
MCM Vaccine B.V., Lead Rapporteur: Christophe Focke

WS2366
Flebogamma DIF-EMEA/H/C/000781/WS2366/0074
Instituto Grifols, S.A., Lead Rapporteur: Jan Mueller-Berghaus

WS2381
Hexacima-EMEA/H/C/002702/WS2381/0142
Hexyon-EMEA/H/C/002796/WS2381/0146
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

WS2382
Ebymect-EMEA/H/C/004162/WS2382/0060
Xigduo-EMEA/H/C/002672/WS2382/0070
AstraZeneca AB, Lead Rapporteur: Kristina Dunder, "To update sections 4.2, 4.4 and 5.1 of Xigduo and Ebymect SmPCs to harmonise the applicable dapagliflozin-specific information in the Xigduo and Ebymect QRDs with the Forxiga (dapagliflozin) product information, which has undergone several updates via procedure DAPA-HF (EMEA/H/C/002322/WS1737) and DAPA-CKD (EMEA/H/C/002322/WS1941). Wording approved for Forxiga in these procedures are proposed for the combination products. In addition, the revised QRDs also include proposals for other administrative changes. The corresponding section 2 and 4 of the PIL have also been updated."

WS2391
Fluenz Tetra-EMEA/H/C/002617/WS2391/0124
Pandemic influenza vaccine H5N1 AstraZeneca-EMEA/H/C/003963/WS2391/0059
AstraZeneca AB, Lead Rapporteur: Christophe Focke

WS2392/G
Efficib-
EMEA/H/C/000896/WS2392/0109/G
Janumet-
EMEA/H/C/000861/WS2392/0108/G
Ristfor-
EMEA/H/C/001235/WS2392/0097/G
Velmetia-
EMEA/H/C/000862/WS2392/0114/G
Merck Sharp & Dohme B.V., Lead Rapporteur: Johann Lodewijk Hillege

WS2397/G
Incresync-
EMEA/H/C/002178/WS2397/0045/G
Vipdomet-
EMEA/H/C/002654/WS2397/0042/G
Vipidia-
EMEA/H/C/002182/WS2397/0034/G
Takeda Pharma A/S, Lead Rapporteur: Johann Lodewijk Hillege

WS2399/G
Mirapexin-
EMEA/H/C/000134/WS2399/0104/G
Sifrol-
EMEA/H/C/000133/WS2399/0095/G
Boehringer Ingelheim International GmbH, Lead Rapporteur: Thalia Marie Estrup Blicher

WS2400
Lixiana-EMEA/H/C/002629/WS2400/0041
Roteas-EMEA/H/C/004339/WS2400/0028
Daiichi Sankyo Europe GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro

WS2403
Kaftrio-EMEA/H/C/005269/WS2403/0032
Symkevi-
EMEA/H/C/004682/WS2403/0036
Vertex Pharmaceuticals (Ireland) Limited, 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 - EMA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

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

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

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

G. ANNEX G

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

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

G.2. PRIME

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

G.2.1. List of procedures concluding at 12-15 December 2022 CHMP plenary

G.2.2. List of procedures starting in December 2022 for January 2023 CHMP adoption of outcomes

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