13 December 2021
EMA/CHMP/745698/2021
Human Medicines Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 13-16 December 2021

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

13 December 2021, 09:00 – 19:30, virtual meeting/ room 1C

14 December 2021, 08:30 – 19:30, virtual meeting/ room 1C

15 December 2021, 08:30 – 19:30, virtual meeting/ room 1C

16 December 2021, 08:30 – 15:00, virtual meeting/ room 1C

Disclaimers

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

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

Note on access to documents

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

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Table of contents

1. Introduction 8

1.1. Welcome and declarations of interest of members, alternates and experts 8

1.2. Adoption of agenda 8

1.3. Adoption of the minutes 8

2. Oral Explanations 8

2.1. Pre-authorisation procedure oral explanations 8

2.1.1. sodium thiosulfate - PUMA - EMEA/H/C/005130 8

2.1.2. anifrolumab - EMEA/H/C/004975 8

2.1.3. gefapixant - EMEA/H/C/005476 9

2.1.4. gefapixant - EMEA/H/C/005884 9

2.2. Re-examination procedure oral explanations 9

2.3. Post-authorisation procedure oral explanations 9

2.3.1. Tookad - padeliporfin - EMEA/H/C/004182/II/0013 9

2.3.2. Brilique - ticagrelor - EMEA/H/C/001241/II/0049 10

2.3.3. Veklury - remdesivir - EMEA/H/C/005622/II/0016 10

2.4. Referral procedure oral explanations 10

3. Initial applications 11

3.1. Initial applications; Opinions 11

3.1.1. aducanumab - EMEA/H/C/005558 11

3.1.2. pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - EMEA/H/C/005451 11

3.1.3. risperidone- EMEA/H/C/005406 11

3.1.4. finerenone - EMEA/H/C/005200 11

3.1.5. metformin hydrochloride / sitagliptin hydrochloride monohydrate - EMEA/H/C/005678 12

3.1.6. somatrogon - Orphan - EMEA/H/C/005633 12

3.1.7. opicapone - EMEA/H/C/005782 12

3.1.8. voxelotor – PRIME – Orphan - EMEA/H/C/004869 12

3.1.9. enfortumab vedotin - EMEA/H/C/005392 12

3.1.10. lasmiditan - EMEA/H/C/005332 13

3.1.11. sapropterin - EMEA/H/C/005646 13

3.1.12. tepotinib - EMEA/H/C/005524 13

3.1.13. vildagliptin / metformin hydrochloride - EMEA/H/C/005738 13

3.1.14. sotrovimab - EMEA/H/0005676 13

3.1.15. linzagolix choline - EMEA/H/C/005442 13

3.2. Initial applications; List of outstanding issues (Day 180; Day 120 for procedures with accelerated assessment timetable) 14

3.2.1. betaine anhydrous - EMEA/H/C/005637 14

3.2.2. ciltacabtagene autoleucel – PRIME – Orphan - ATMP - EMEA/H/C/005095 14
3.2.3. difelikefalin - EMEA/H/C/005612 14
3.2.4. teriparatide - EMEA/H/C/004932 14
3.2.5. lonafarnib - Orphan - EMEA/H/C/005271 14
3.2.6. arimoclomol - Orphan - EMEA/H/C/005203 15
3.2.7. relugolix - EMEA/H/C/005353 15
3.2.8. daridorexant - EMEA/H/C/005634 15
3.2.9. sitagliptin - EMEA/H/C/005598 15
3.2.10. teriparatide - EMEA/H/C/005827 15
3.3. Initial applications; List of questions (Day 120; Day 90 for procedures with accelerated assessment timetable) 16
3.3.1. germanium (68Ge) chloride / gallium (68Ga) chloride - EMEA/H/C/005165 16
3.3.2. lutetium (177lu) chloride - EMEA/H/C/005859 16
3.3.3. molnupiravir – EMEA/H/C/005789 16
3.3.4. lenacapavir - EMEA/H/C/005638 16
3.3.5. octreotide - Orphan - EMEA/H/C/005826 16
3.3.6. COVID-19 vaccine (recombinant, adjuvanted) – EMEA/H/C/005808 16
3.3.7. pemetrexed - EMEA/H/C/005848 17
3.3.8. efgartigimod alfa - Orphan - EMEA/H/C/005849 17
3.4. Update on on-going initial applications for Centralised procedure 17
3.4.1. dengue tetravalent vaccine (live, attenuated) - Article 58 - EMEA/H/W/005362 17
3.4.2. dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/005155 17
3.4.3. rimegepant - EMEA/H/C/005725 17
3.4.4. betulae cortex dry extract (5-10: 1); extraction solvent: n-heptane 95% (w/w) - Orphan - EMEA/H/C/005035 18
3.5. Re-examination of initial application procedures under Article 9(2) of Regulation no 726/2004 18
3.5.1. Ipique - bevacizumab - EMEA/H/C/005433 18
3.6. Initial applications in the decision-making phase 18
3.7. Withdrawals of initial marketing authorisation application 18
3.7.1. obeticholic acid - EMEA/H/C/005249 18
4. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008 19
4.1. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Opinion 19
4.1.1. Comirnaty - tozinameran - EMEA/H/C/005735/X/0077 19
4.1.2. Mayzent - siponimod - EMEA/H/C/004712/X/0007 19
4.1.3. Yuflyma - adalimumab - EMEA/H/C/005188/X/0005 19
4.1.4. Zejula - niraparib - Orphan - EMEA/H/C/004249/X/0029 19

4.2. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 180 list of outstanding issues 20

4.2.1. Nucala - mepolizumab - EMEA/H/C/003860/X/0042 20

4.3. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 120 List of question 20

4.4. Update on on-going extension application according to Annex I of Commission Regulation (EC) No 1234/2008 20

4.4.1. Genvoya - elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004042/X/0079/G 20

4.5. Re-examination procedure of extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008 20

5. Type II variations - variation of therapeutic indication procedure according to Annex I of Commission Regulation (EC) No 1234/2008 21

5.1. Type II variations - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008; Opinions or Requests for supplementary information 21

5.1.1. Adjupanrix - pandemic influenza vaccine (h5n1) (split virion, inactivated, adjuvanted) - EMEA/H/C/001206/II/0074 21

5.1.2. Brilique - ticagrelor - EMEA/H/C/001241/II/0049 21

5.1.3. Crysvita - burosumab - Orphan - EMEA/H/C/004275/II/0023 22

5.1.4. Entyvio - vedolizumab - EMEA/H/C/002782/II/0061 22

5.1.5. Exparel liposomal - bupivacaine - EMEA/H/C/004586/II/0005 22

5.1.6. Jakavi - ruxolitinib - EMEA/H/C/002464/II/0053 23

5.1.7. Jardiance - empagliflozin - EMEA/H/C/002677/II/0060 23

5.1.8. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0108 23

5.1.9. Kineret - anakinra - EMEA/H/C/000363/II/0086 24

5.1.10. Kymriah - tisagenlecleucel – PRIME – Orphan - ATMP - EMEA/H/C/004090/II/0044 24

5.1.11. Lorviqua - lorlatinib - EMEA/H/C/004646/II/0015 24

5.1.12. Nexpovio - selinexor - EMEA/H/C/005127/II/0001/G 25

5.1.13. Olumiant - baricitinib - EMEA/H/C/004085/II/0029/G 25

5.1.14. Senshio - ospemifene - EMEA/H/C/002780/II/0041 25

5.1.15. Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0041 26

5.1.16. Tecfidera - dimethyl fumarate - EMEA/H/C/002601/II/0073 26

5.1.17. Teysuno - tegafur / gimeracil / oteracil - EMEA/H/C/001242/II/0045 26

5.1.18. Tookad - padeliporfin - EMEA/H/C/004182/II/0013 27

5.1.19. Veklury - remdesivir - EMEA/H/C/005622/II/0016 27

5.1.20. Xeljanz - tofacitinib - EMEA/H/C/004214/II/0039 27

5.2. Update on on-going Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008 28

5.3. Re-examination of Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008 28

6. Ancillary medicinal substances in medical devices 28

6.1. Ancillary medicinal substances in medical devices; Opinions/ Day 180 list of outstanding issues / Day 120 list of questions 28

6.2. Update of Ancillary medicinal substances in medical devices 28

7. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use) 28

7.1. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use) 28

8. Pre-submission issues 28

8.1. Pre-submission issue 28

8.1.1. teclistamab - Orphan - H0005865 28

8.1.2. nirsevimab - H0005304 29

8.2. Priority Medicines (PRIME) 29

8.2.1. List of applications received 29

8.2.2. Recommendation for PRIME eligibility 29

9. Post-authorisation issues 29

9.1. Post-authorisation issues 29

9.1.1. Caprelsa - vandetanib - EMEA/H/C/002315/II/0043 29

9.1.2. Cosentyx - secukinumab - EMEA/H/C/003729/II/0076 30

9.1.3. Pemetrexed Lilly – pemetrexed – EMEA/H/C/004114 30

9.1.4. Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0042 ..30

9.1.5. COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0033 31

9.1.6. Ledaga - chlormethine – Orphan - EMEA/H/C/002826/II/0027 31

9.1.7. Bosulif - bosutinib - EMEA/H/C/002373/II/0050/G 31

9.1.8. Ravicti - glycerol phenylbutyrate – Orphan – EMEA/H/C/003822/II/0038/G 32

9.1.9. Nuceiva – botulinum toxin type A – EMEA/H/C/004587/IB/0018 32

9.1.10. Vaxzevria – COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0021/G32

10. Referral procedures 33

10.1. Procedure for Centrally Authorised products under Article 20 of Regulation (EC) No 726/2004 33

10.2. Requests for CHMP Opinion under Article 5(3) of Regulation (EC) No 726/2004.. 33

10.2.1. PF-07321332/ritonavir – EMEA/H/A-5(3)/1513 33

10.3. Procedure under Articles 5(2) and 10 of Regulation (EC) No 726/2004 33

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 33

10.4.1. Lidocain/ Prilocain IDETEC – lidocaine, prilocaine - EMEA/H/A-29(4)/1506 33

10.5. Harmonisation - Referral procedure under Article 30 of Directive 2001/83/EC.... 33

10.6. Community Interests - Referral under Article 31 of Directive 2001/83/EC 34
10.7. Re-examination Procedure under Article 32(4) of Directive 2001/83/EC 34
10.8. Procedure under Article 107(2) of Directive 2001/83/EC 34
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 34
10.10. Procedure under Article 29 of Regulation (EC) 1901/2006 34
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 34

11. Pharmacovigilance issue 34
11.1. Early Notification System 34

12. Inspections 34
12.1. GMP inspections 34
12.2. GCP inspections 35
12.3. Pharmacovigilance inspections 35
12.4. GLP inspections 35

13. Innovation Task Force 35
13.1. Minutes of Innovation Task Force 35
13.2. Innovation Task Force briefing meetings 35
13.3. Requests for CHMP Opinion under Article 57(1)J and (1)P of Regulation (EC) No 726/2004 35
13.4. Nanomedicines activities 35

14. Organisational, regulatory and methodological matters 35
14.1. Mandate and organisation of the CHMP 35
14.2. Coordination with EMA Scientific Committees 35
14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC) 35
14.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups 36
14.3.1. Biologics Working Party (BWP) 36
14.3.2. Name Review Group (NRG) 36
14.3.3. Scientific Advice Working Party (SAWP) 36
14.3.4. Election of new Scientific Advice Working Party (SAWP) Chair 36
14.3.5. Election of new Safety Working Party (SWP) Vice-Chair 37
14.3.6. Appointment of the Chair and Vice Chair of the Cardiovascular Scientific Advice Group 37
14.3.7. ITF meeting 37
14.3.8. ITF meeting 37
14.4. Cooperation within the EU regulatory network 37
14.5. Cooperation with International Regulators 37

14.6. Contacts of the CHMP with external parties and interaction with the Interested Parties to the Committee 37

14.7. CHMP work plan 37

14.7.1. CHMP Work Plan 2022 37

14.8. Planning and reporting 38

14.9. Others 38

15. Any other business 38

15.1. AOB topic 38

15.1.1. Update on COVID-19 38

15.1.2. Pregnancy labelling for COVID-19 vaccines 38

Explanatory notes 39

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 13-16 December 2021. See December 2021 CHMP minutes (to be published post January 2022 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 13-16 December 2021

1.3. Adoption of the minutes

CHMP minutes for 08-11 November 2021.

Minutes from PReparatory and Organisational Matters (PROM) meeting held on 06 December 2021.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

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

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

Scope: Oral explanation

Action: Oral explanation to be held on 14 December 2021 at 16:00

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

2.1.2. anifrolumab - EMEA/H/C/004975

indicated as an add-on therapy for the treatment of adult patients with moderate to severe systemic lupus erythematosus (SLE), despite standard therapy

Scope: Possible oral explanation

Action: Possible oral explanation to be held on 15 December 2021 at 16:00

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

2.1.3. gefapixant - EMEA/H/C/005476

treatment of refractory or unexplained chronic cough

Scope: Possible oral explanation

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

List of Outstanding Issues adopted on 14.10.2021. List of Questions adopted on 24.06.2021.

2.1.4. gefapixant - EMEA/H/C/005884

treatment of refractory or unexplained chronic cough

Scope: Possible oral explanation

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

List of Outstanding Issues adopted on 14.10.2021. List of Questions adopted on 24.06.2021.

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

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

STEBA Biotech S.A

Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maia Uusküla

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

Oral explanation

Action: Oral explanation to be held on 15 December 2021 at 11:00

Request for Supplementary Information adopted on 16.09.2021, 20.05.2021.

See 5.1

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

AstraZeneca AB

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

Scope: "Extension of indication to include, in co-administration with acetylsalicylic acid (ASA), the prevention of stroke in adult patients with acute ischaemic stroke or transient ischaemic attack (TIA), based on the final results of study D5134C00003 (THALES), a phase III, international, multicentre, randomised, double-blind, placebo-controlled study to investigate the efficacy and safety of ticagrelor and ASA compared with ASA in the prevention of stroke and death in patients with acute ischaemic stroke or transient ischaemic attack; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 13 of the RMP has also been submitted."

Oral explanation

Action: Oral explanation to be held on 15 December 2021 at 13:30

Request for Supplementary Information adopted on 24.06.2021, 28.01.2021, 17.09.2020.

See 5.1

2.3.3. Veklury - remdesivir - EMEA/H/C/005622/II/0016

Gilead Sciences Ireland UC

Rapporteur: Janet Koenig, PRAC Rapporteur: Eva Jirsová

Scope: "Extension of indication to include treatment of adults with pneumonia not requiring supplemental oxygen (moderate COVID-19), based on Part A of study GS-US-540-5774, a Phase 3, randomized, open-label, multicenter study comparing 2 RDV regimens (5 days and 10 days) versus standard of care in 584 participants with moderate COVID 19, and study CO US 540 5776 [Adaptive COVID-19 Treatment Trial (ACTT) 1, a National Institute of Allergy and Infectious Diseases (NIAID)-sponsored Phase 3, randomized, double blind, placebo controlled, multicenter study]. As a consequence, sections 4.1 and 5.1 of the SmPC are being updated, and the Package Leaflet is updated in accordance. A revised version 1.2 of the RMP has also been submitted."

Oral explanation

Action: Oral explanation to be held on 15 December 2021 at 09:00

Request for Supplementary Information adopted on 16.09.2021, 20.05.2021.

See 5.1

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. aducanumab - EMEA/H/C/005558

Alzheimer's disease

Scope: Opinion

Action: For adoption

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

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

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

Scope: Opinion

Action: For adoption

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

3.1.3. risperidone- EMEA/H/C/005406

treatment of schizophrenia

Scope: Opinion

Action: For adoption

List of outstanding issues adopted on 15.10.2020. List of questions adopted on 28.05.2020.

3.1.4. finerenone - EMEA/H/C/005200

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 11.11.2021, 16.09.2021. List of Questions adopted on 25.03.2021.

3.1.5. metformin hydrochloride / sitagliptin hydrochloride monohydrate - EMEA/H/C/005678

treatment of type 2 diabetes mellitus

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 14.10.2021. List of Questions adopted on 25.03.2021.

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

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

Scope: Opinion

Action: For adoption

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

3.1.7. opicapone - EMEA/H/C/005782

treatment of Parkinson's disease and motor fluctuations

Scope: Opinion

Action: For adoption

List of Questions adopted on 22.07.2021.

3.1.8. voxelotor – PRIME – Orphan - EMEA/H/C/004869

Global Blood Therapeutics Netherlands; Indicated for the treatment of haemolytic anaemia in adults and paediatric patients 12 years of age and older with sickle cell disease (SCD).

Scope: Opinion

Action: For adoption

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

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

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

Scope: Opinion

Action: For adoption

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

3.1.10. lasmiditan - EMEA/H/C/005332

acute treatment of migraine with or without aura in adults

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 16.09.2021, 22.07.2021. List of Questions adopted on 25.03.2021.

3.1.11. sapropterin - EMEA/H/C/005646

treatment of hyperphenylalaninemia (HPA)

Scope: Opinion

Action: For adoption

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

3.1.12. tepotinib - EMEA/H/C/005524

treatment of advanced non-small cell lung cancer

Scope: Opinion

Action: For adoption

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

3.1.13. vildagliptin / metformin hydrochloride - EMEA/H/C/005738

treatment of type 2 diabetes mellitus

Scope: Opinion

Action: For adoption

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

3.1.14. sotrovimab - EMEA/H/0005676

Treatment of coronavirus disease 2019 (COVID-19)

Scope: Opinion

Action: For adoption

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

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

Scope: Opinion

Action: For adoption

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

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

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

treatment of homocystinuria

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.04.2021.

3.2.2. ciltacabtagene autoleucel – PRIME – Orphan - ATMP - EMEA/H/C/005095

Janssen-Cilag International NV; treatment of multiple myeloma

Scope: List of outstanding issues

Action: For information

List of Questions adopted on 10.09.2021.

3.2.3. difelikefalin - EMEA/H/C/005612

treatment of pruritus

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.07.2021.

3.2.4. teriparatide - EMEA/H/C/004932

Treatment of osteoporosis in postmenopausal women and in men at increased risk of fracture

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.01.2021.

3.2.5. lonafarnib - Orphan - EMEA/H/C/005271

EigerBio Europe Limited; treatment of Hutchinson-Gilford Progeria Syndrome and Progeroid Laminopathies

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 16.09.2021, 25.02.2021. List of Questions adopted on 23.07.2020.

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

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

Scope: List of outstanding issues

Action: For adoption

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

3.2.7. relugolix - EMEA/H/C/005353

treatment of adult patients with advanced prostate cancer

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.07.2021.

3.2.8. daridorexant - EMEA/H/C/005634

treatment of insomnia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.07.2021.

3.2.9. sitagliptin - EMEA/H/C/005598

treatment of type 2 diabetes mellitus

Scope: List of outstanding issues

Action: For adoption

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

3.2.10. teriparatide - EMEA/H/C/005827

treatment of osteoporosis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.07.2021.

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

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

indicated for in vitro labelling of kits for radiopharmaceutical preparation

Scope: List of questions

Action: For adoption

3.3.2. lutetium (177lu) chloride - EMEA/H/C/005859

is a radiopharmaceutical precursor, and it is not intended for direct use in patients. It is to be used only for the radiolabelling of carrier molecules that have been specifically developed and authorised for radiolabelling with Lutetium (177Lu) chloride.

Scope: List of questions

Action: For adoption

3.3.3. molnupiravir – EMEA/H/C/005789

Treatment of coronavirus disease 2019 (COVID-19)

Scope: List of questions

Action: For adoption

3.3.4. lenacapavir - EMEA/H/C/005638

treatment of human immunodeficiency virus type 1 (HIV-1) infection

Scope: List of questions

Action: For adoption

3.3.5. octreotide - Orphan - EMEA/H/C/005826

FGK Representative Service GmbH; treatment of acromegaly

Scope: List of questions

Action: For adoption

3.3.6. COVID-19 vaccine (recombinant, adjuvanted) – EMEA/H/C/005808

prevention of coronavirus disease-2019 (COVID-19)

Scope: List of questions

Action: For adoption

3.3.7. pemetrexed - EMEA/H/C/005848

treatment of malignant pleural mesothelioma and non-small cell lung cancer

Scope: List of questions

Action: For adoption

3.3.8. efgartigimod alfa - Orphan - EMEA/H/C/005849

Argenx; treatment of generalized Myasthenia Gravis (gMG)

Scope: List of questions

Action: For adoption

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

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

prevention of dengue disease

Scope: Letter from the applicant dated 01 December 2021 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in November 2021.

Action: For adoption

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

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

prevention of dengue disease

Scope: Letter from the applicant dated 01 December 2021 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in November 2021.

Action: For adoption

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

3.4.3. rimegepant - EMEA/H/C/005725

management of migraine

Scope: Letter from the applicant dated 06 December 2021 requesting an extension to the clock stop to respond to the list of outstanding issues adopted in November 2021.

Action: For adoption

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

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

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

Scope: Letter from third party

Action: For information

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

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

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

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

Scope: Appointment of re-examination rapporteurs

Action: For adoption

Well-established use application (Article 10a of Directive No 2001/83/EC)

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

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. obeticholic acid - EMEA/H/C/005249

improvement of liver fibrosis and resolution of steatohepatitis in adult patients with significant liver fibrosis due to non-alcoholic steatohepatitis (NASH)

Scope: Withdrawal of marketing authorisation application

Action: For information

List of Outstanding Issues adopted on 25.03.2021. List of Questions adopted on 28.05.2020.

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. Comirnaty - tozinameran - EMEA/H/C/005735/X/0077

BioNTech Manufacturing GmbH

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

Scope: "Extension application to add a new strength (0.1 mg/ml). The new presentations are indicated for children from 5 to 11 years of age."

Action: For adoption

4.1.2. Mayzent - siponimod - EMEA/H/C/004712/X/0007

Novartis Europharm Limited

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Maria del Pilar Rayon

Scope: "Extension application to add a new strength of 1 mg film-coated tablet. The RMP (version 3.0) is updated in accordance."

Action: For adoption

List of Questions adopted on 16.09.2021.

4.1.3. Yuflyma - adalimumab - EMEA/H/C/005188/X/0005

Celltrion Healthcare Hungary Kft.

Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension application to introduce a new strengths of 80 mg solution for injection. Version 1.1 of the RMP has also been submitted."

Action: For adoption

List of Questions adopted on 16.09.2021.

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

GlaxoSmithKline (Ireland) Limited

Rapporteur: Ingrid Wang, PRAC Rapporteur: Jan Neuhauser

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

Action: For adoption

List of Questions adopted on 14.10.2021.

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

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

GlaxoSmithKline Trading Services Limited

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

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

Action: For adoption

List of Questions adopted on 16.09.2021.

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

No items

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

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

Gilead Sciences Ireland UC

Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ilaria Baldelli

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

Change of the timetable to respond to the list of questions adopted in November 2021.

Action: For adoption

List of questions adopted on 11.11.2021

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. Adjupanrix - pandemic influenza vaccine (h5n1) (split virion, inactivated, adjuvanted) - EMEA/H/C/001206/II/0074

GlaxoSmithkline Biologicals SA

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst

Scope: "Extension of indication to include use in children from 6 months to <18 years for Adjupanrix based on the results of the studies: study H5N1-013, a phase II, non-randomized, open-label study to evaluate the safety and immunogenicity in children aged 6 to 35 months and study H5N1-032, a phase III, randomized, open, active-controlled study to evaluate the safety and immunogenicity in children aged 3 to 17 years. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 6.6 of the SmPC are updated and the Package Leaflet is updated in accordance. Further, the MAH proposed to update section 4.4 with information on sodium and potassium content in line with the excipient guideline, as well as to add wording on traceability. In addition, the 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, the MAH performed minor editorial changes and removed information related to the withdrawal of the Prepandrix marketing authorisation. Version 13 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 22.07.2021.

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

AstraZeneca AB

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

Scope: "Extension of indication to include, in co-administration with acetylsalicylic acid (ASA), the prevention of stroke in adult patients with acute ischaemic stroke or transient ischaemic attack (TIA), based on the final results of study D5134C00003 (THALES), a phase III, international, multicentre, randomised, double-blind, placebo-controlled study to investigate the efficacy and safety of ticagrelor and ASA compared with ASA in the prevention of stroke and death in patients with acute ischaemic stroke or transient ischaemic attack; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 13 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 24.06.2021, 28.01.2021, 17.09.2020.

See 2.3

5.1.3. Crysvita - burosumab - Orphan - EMEA/H/C/004275/II/0023

Kyowa Kirin Holdings B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include treatment of FGF23-related hypophosphataemia in tumour-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumours that cannot be curatively resected or localised in patients aged 1 year and over, based on data from two ongoing open-label clinical studies, UX023T-CL201 and KRN23-002, in adults with TIO (144-week data and 88-week data are available, respectively). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated and the Package Leaflet is updated accordingly. An updated RMP version 4.0 has also been submitted. The MAH also applied for 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 22.04.2021.

5.1.4. Entyvio - vedolizumab - EMEA/H/C/002782/II/0061

Takeda Pharma A/S

Rapporteur: Armando Genazzani, PRAC Rapporteur: Adam Przybylkowski

Scope: "To add a new therapeutic indication "treatment of adult patients with pouchitis, who have undergone proctocolectomy and ileal pouch anal anastomosis for ulcerative colitis, and have had an inadequate response with, lost response to, or were intolerant to antibiotic therapy" for Entyvio 300 mg (powder for concentrate for solution for infusion), based on final results from study Vedolizumab-4004 (ERNEST). This was an interventional, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of Entyvio (intravenous) in the treatment of chronic pouchitis.
As a consequence, sections 4.1, 4.2, 4.5, 5.1 and 5.2 of the SmPC for Entyvio 300 mg are updated. The Package Leaflet are updated in accordance. Version 7.0 of the RMP is also submitted.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 14.10.2021.

5.1.5. Exparel liposomal - bupivacaine - EMEA/H/C/004586/II/0005

Pacira Ireland Limited

Rapporteur: Elita Poplavska, Co-Rapporteur: Margareta Bego, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Extension of indication to include children over 6 years old."

Action: For adoption

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

Novartis Europharm Limited

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

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

Action: For adoption

Request for Supplementary Information adopted on 24.06.2021.

5.1.7. Jardiance - empagliflozin - EMEA/H/C/002677/II/0060

Boehringer Ingelheim International GmbH

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia

Scope: "Extension of indication to add the treatment of patients with Heart Failure with preserved ejection fraction based on the results from the clinical study 1245.110 EMPEROR-preserved. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC and sections 1 and 4 of the PIL are updated accordingly. Further, the MAH applied for an additional year of market protection. The updated RMP v 16.0 has also been submitted.
In addition, the statement 'sodium free' was re-located from section 2 of the SmPC to section 4.4. to comply with EMA'S QRD guidance and minor linguistic changes to the national translations are included in this submission", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

5.1.8. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0108

Merck Sharp & Dohme B.V.

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

Scope: "C.I.6.a
Update of sections 4.1, 4.2 and 5.1 of the SmPC in order to extend the existing therapeutic indications for Keytruda to include the adjuvant treatment in monotherapy of adults with renal cell carcinoma (RCC) at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions. The Package Leaflet are updated accordingly. The RMP version 35.1 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 14.10.2021.

5.1.9. Kineret - anakinra - EMEA/H/C/000363/II/0086

Swedish Orphan Biovitrum AB (publ)

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Fátima Ventura, PRAC Rapporteur: Anette Kirstine Stark

Scope: "C.I.6 - Extension of indication to include treatment of coronavirus disease 2019 (COVID-19) in adult patients with pneumonia who are at risk of developing severe respiratory failure for Kineret; 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 5.6 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 14.10.2021.

5.1.10. Kymriah - tisagenlecleucel – PRIME – Orphan - ATMP - EMEA/H/C/004090/II/0044

Novartis Europharm Limited

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

Scope: "Extension of indication to include treatment of adult patients with follicular lymphoma (FL) after two or more lines of therapy who are refractory or relapsed during or within 6 months after completion of anti-CD20 antibody maintenance or relapsed after autologous haematopoietic stem cell transplantation (HSCT) for Kymriah. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and corresponding sections in the Package Leaflet are updated accordingly. The RMP has been updated to version 4.0 to align with the indication extension. Lastly, the minor editorial corrections are made throughout the SmPC and package leaflet to align with the current QRD template version 10.2.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

5.1.11. Lorviqua - lorlatinib - EMEA/H/C/004646/II/0015

Pfizer Europe MA EEIG

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication to include the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously not treated with an ALK inhibitor based on results from the phase III randomised CROWN (1006) study listed as a specific obligation (SOB) in the Annex II; 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 accordingly. Version 3.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to include minor editorial changes in the PI."

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021, 20.05.2021.

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

Karyopharm Europe GmbH

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

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

Action: For adoption

Request for Supplementary Information adopted on 22.07.2021.

5.1.13. Olumiant - baricitinib - EMEA/H/C/004085/II/0029/G

Eli Lilly Nederland B.V.

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski

Scope: "Grouping of the following variations:
C.I.6 - Extension of indication to include treatment of severe alopecia areata in adult patients for Olumiant; 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 12.1 of the RMP has also been submitted.
C.I.11.z - Update of RMP (version 12.1) to change the category 3 study PASS I4V-MC-B011 end of data collection for the Atopic Dermatitis cohort and the subsequent final study report milestone.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

5.1.14. Senshio - ospemifene - EMEA/H/C/002780/II/0041

Shionogi B.V.

Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Kirsti Villikka

Scope: "Extension of indication by deletion of information on specific subset of patients for Senshio. This is supported by the submission of the final study report of the imposed non-interventional post-authorisation safety study. As mentioned in Annex IID, this is an observational retrospective cohort study of ospemifene to assess the incidence of venous thromboembolism and other safety concerns as agreed in the Risk Management Plan (RMP), in vulvar and vaginal atrophy (VVA) patients treated with ospemifene compared to 1) patients newly prescribed SERMs for oestrogen-deficiency conditions or breast cancer prevention, and 2) the incidence in untreated VVA patients. As a consequence, sections 4.1 and 4.4 of the SmPC are updated. The Package Leaflet and Annex IID are updated in

accordance. Version 2 of the RMP has also been submitted. In addition, the Marketing authorisation holder took the opportunity to update the list of local representatives in the Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 14.10.2021.

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

Moderna Biotech Spain, S.L.

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

Scope: "Extension of indication to include use in children 6-11 years of age for Spikevax, based on data from study mRNA-1273-P204, an ongoing Phase 2/3, 2-part, open-label, dose-escalation, age de-escalation and subsequent randomized, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of mRNA-1273 in healthy children; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance."

Action: For adoption

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

Biogen Netherlands B.V.

Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber

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

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021.

5.1.17. Teysuno - tegafur / gimeracil / oteracil - EMEA/H/C/001242/II/0045

Nordic Group B.V.

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

Scope: "Extension of indication to include treatment of metastatic colorectal cancer in adult

patients where it is not possible to initiate or continue treatment with another fluoropyrimidine. As a consequence, sections 4.1, 4.2, 4.3, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 10 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021, 28.01.2021.

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

STEBA Biotech S.A

Rapporteur: Bruno Sepodes, PRAC Rapporteur: Maia Uusküla

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

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021, 20.05.2021.

See 2.3

5.1.19. Veklury - remdesivir - EMEA/H/C/005622/II/0016

Gilead Sciences Ireland UC

Rapporteur: Janet Koenig, PRAC Rapporteur: Eva Jirsová

Scope: "Extension of indication to include treatment of adults with pneumonia not requiring supplemental oxygen (moderate COVID-19), based on Part A of study GS-US-540-5774, a Phase 3, randomized, open-label, multicenter study comparing 2 RDV regimens (5 days and 10 days) versus standard of care in 584 participants with moderate COVID 19, and study CO US 540 5776 [Adaptive COVID-19 Treatment Trial (ACTT) 1, a National Institute of Allergy and Infectious Diseases (NIAID)-sponsored Phase 3, randomized, double blind, placebo controlled, multicenter study]. As a consequence, sections 4.1 and 5.1 of the SmPC are being updated, and the Package Leaflet is updated in accordance. A revised version 1.2 of the RMP has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021, 20.05.2021.

See 2.3

5.1.20. Xeljanz - tofacitinib - EMEA/H/C/004214/II/0039

Pfizer Europe MA EEIG

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

Scope: "Extension of indication to include treatment of active ankylosing spondylitis for

Xeljanz prolonged release; 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 18.1 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

No items

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

No items

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. teclistamab - Orphan - H0005865

Janssen-Cilag International N.V.; indicated for the treatment of adult patients with relapsed

or refractory multiple myeloma, who previously received ≥3 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 monoclonal antibody.

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

Action: For adoption

8.1.2. nirsevimab - H0005304

Prevention of lower respiratory tract infection caused by respiratory syncytial virus in all infants entering their first RSV season and children with Chronic Lung Disease or Congenital Heart Disease entering their first and second RSV season

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

Action: For adoption

8.2. Priority Medicines (PRIME)

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

8.2.1. List of applications received

Action: For information

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

9. Post-authorisation issues

9.1. Post-authorisation issues

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

Genzyme Europe BV

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant

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

conditional to normal Marketing Authorisation.
In addition the MAH takes to opportunity to rectify the Dutch translation of the Caprelsa Product Information."

Action: For adoption

Request for Supplementary Information adopted on 24.06.2021, 28.05.2020.

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

Novartis Europharm Limited

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

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

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021, 24.06.2021.

9.1.3. Pemetrexed Lilly – pemetrexed – EMEA/H/C/004114

Eli Lilly Nederland B.V.; treatment of malignant pleural mesothelioma and non-small cell lung cancer

Rapporteur: Alar Irs

Scope: Expiry of Marketing authorisation due to the application of the sunset clause

Action: For information

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

Moderna Biotech Spain, S.L.,

Rapporteur: Jan Mueller-Berghaus

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

Action: For adoption

9.1.5. COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0033

Janssen-Cilag International N.V.

Rapporteur: Christophe Focke

Scope: "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to introduce an homologous booster dose (second dose) of COVID-19 vaccine Janssen based on interim efficacy, immunogenicity and safety results from different clinical studies including the two randomised, double blind, placebo-controlled Phase 3 studies COV3001 and COV3009. In addition, an update to introduce an heterologous booster dose of COVID-19 vaccine Janssen following completion of a primary vaccination with an approved mRNA COVID-19 vaccine is introduced based on immunogenicity and safety interim results from the phase 1/2 study DMID 21-0012. In addition, the MAH took the opportunity to update the efficacy data for the primary vaccination schedule based on final analysis from study COV3001. The Package Leaflet is updated accordingly."

Action: For adoption

9.1.6. Ledaga - chlormethine – Orphan - EMEA/H/C/002826/II/0027

Helsinn Birex Pharmaceuticals Limited

Rapporteur: Sinan B. Sarac

Scope: "Update of sections 4.2 of the SmPC in order to allow flexibility in the starting frequency of the treatment based on current clinical practice; the Package Leaflet is updated accordingly."

Action: For adoption

Request for Supplementary Information adopted on 20.05.2021.

9.1.7. Bosulif - bosutinib - EMEA/H/C/002373/II/0050/G

Pfizer Europe MA EEIG

Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber

Scope: "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to reflect results from the studies B1871039 (SOB) and B1871040 (category 3); study B1871039 is A Phase 4 Safety and Efficacy Study of Bosutinib in Patients With Philadelphia Chromosome Positive Chronic Myeloid Leukemia Previously Treated With One or More Tyrosine Kinase Inhibitors and study B1871040 is An Open-Label Bosutinib Treatment Extension Study for Subjects With Chronic Myeloid Leukemia (CML) who Have Previously Participated in Bosutinib Studies B1871006 or B1871008. The Package Leaflet is updated accordingly. The MAH request deletion of the SOB from annex II of the PI and request consideration for switch of the Conditional Marketing Authorisation to a full Marketing Authorisation. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives for Belgium, Luxemburg, Germany and Northern Island in the Package Leaflet. The MAH is also asking the deletion of the product from the additional monitoring list."

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021.

9.1.8. Ravicti - glycerol phenylbutyrate – Orphan – EMEA/H/C/003822/II/0038/G

Immedica Pharma AB

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Ilaria Baldelli

Scope: "Group of variations consisting of:
- Submission of the final study report, HPN-100-014 non interventional registry study "Long-Term Registry of Patients with Urea Cycle Disorders (UCDs) conducted in the US".
- An update to the RMP (version 7) submitted to remove the important potential risks of carcinogenicity and PAA toxicity. The update to the RMP is based on the review of new and available data including the study report for HPN-100-014 and a new toxicological expert examination of pre-clinical carcinogenicity findings as well as a cumulative review of literature and post-marketing data. In accordance with the proposed changes to the RMP, an update of Annex II is requested to waive the imposed condition related to the non-interventional post authorisation safety study (PASS), "European Post-Authorization Registry for RAVICTI (glycerol phenylbutyrate) Oral Liquid in Partnership with the European Registry and Network for Intoxication Type Metabolic Diseases (E-IMD)". The SmPC and Package Leaflet have been updated to delete the information on additional monitoring (including the black triangle)."

Action: For adoption

Request for Supplementary Information adopted on 22.07.2021.

9.1.9. Nuceiva – botulinum toxin type A – EMEA/H/C/004587/IB/0018

Evolus Pharma Limited

Rapporteur: Peter Kiely

Scope: An extension to the introduction of an in vitro method as replacement for the potency assay of Nuceiva finished product.

Action: For adoption

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

AstraZeneca AB

Rapporteur: Sol Ruiz

Scope: Quality variation

Action: For adoption

Request for Supplementary Information adopted on 16.09.2021, 24.06.2021, 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

10.2.1. PF-07321332/ritonavir – EMEA/H/A-5(3)/1513

Pfizer Europe MA EEIG; Treatment for adult patients with symptomatic COVID-19

Rapporteur: Jean-Michel Race, Co-Rapporteur: Fatima Ventura

Scope: Opinion

Action: For adoption

Request for CHMP opinion under Article 5(3) of Regulation (EC) No 726/2004 on potential use of PF-07321332 for the treatment of COVID-19 in adult patients

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

No items

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

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

International Drug Development France

Re-examination Referral Rapporteur: Ewa Balkwiec Iskra, Re-examination Co-Rapporteur: Janet Koenig

Scope: Proposal to involve QWP; List of questions to QWP

Action: For adoption

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

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

No items

13.2. Innovation Task Force briefing meetings

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

No items

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

List of Union Reference Dates and frequency of submission of Periodic Safety Update

Reports (EURD list) for December 2021

Action: For adoption

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

14.3.1. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP December 2021 meeting to CHMP for adoption:

- 19 reports on products in scientific advice and protocol assistance
- 10 reports on products in pre-authorisation procedures
- 1 report on products in post-authorisation procedures
- 2 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 09-10 November 2021.

Action: For adoption

14.3.3. Scientific Advice Working Party (SAWP)

Chair: Anja Schiel

Report from the SAWP meeting held on 29 November - 02 December 2021. Table of conclusions

Action: For information

Scientific advice letters:

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

14.3.4. Election of new Scientific Advice Working Party (SAWP) Chair

Election of new SAWP chair. The mandate of Scientific Advice Working Party Chair Anja Schiel will expire on 28 February 2022.

Action: For election

Nomination(s) received

14.3.5. Election of new Safety Working Party (SWP) Vice-Chair

Susanne Brendler-Schwaab (DE) left her position as SWP vice-chair to undertake the SWP chair position following election at the October 2021 CHMP meeting.

Action: For election

Nomination(s) received

14.3.6. Appointment of the Chair and Vice Chair of the Cardiovascular Scientific Advice Group

Formal appointment of the Chair and Vice Chair of the SAG Cardiovascular following the elections

Action: For endorsement

14.3.7. ITF meeting

Meeting date: 10th December 2021

Action: For adoption

14.3.8. ITF meeting

Meeting date: 15th December 2021

Action: For adoption

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 2022

Adoption of CHMP Work Plan for 2022.

Action: For adoption

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Update on COVID-19

Action: For information

15.1.2. Pregnancy labelling for COVID-19 vaccines

Action: For discussion

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)*

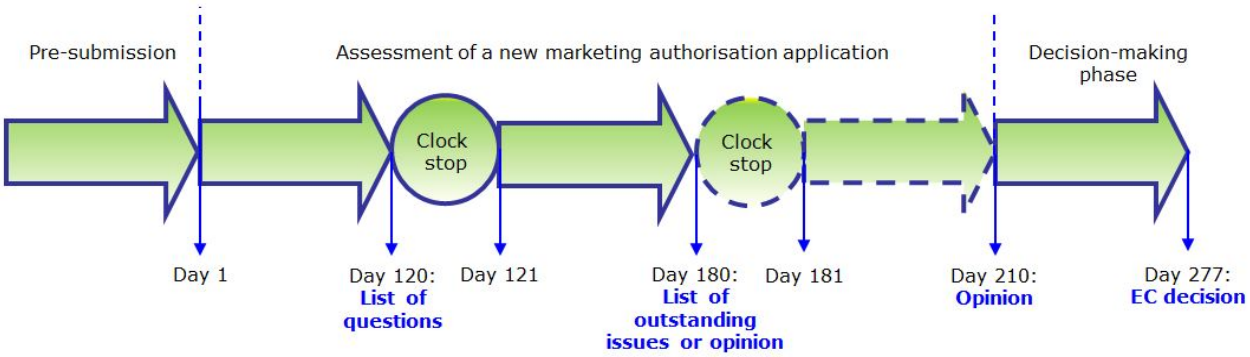
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

13 December 2021
EMA/CHMP/746909/2021

Annex to 13-16 December 2021 CHMP Agenda

Pre-submission and post-authorisations issues

A. PRE-SUBMISSION ISSUES 3
A.1. ELIGIBILITY REQUESTS 3
A.2. Appointment of Rapporteur / Co-Rapporteur Full Applications 3
A.3. PRE-SUBMISSION ISSUES FOR INFORMATION 3

B. POST-AUTHORISATION PROCEDURES OUTCOMES 3
B.1. Annual re-assessment outcomes 3
B.1.1. Annual reassessment for products authorised under exceptional circumstances 3
B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES 4
B.2.1. Renewals of Marketing Authorisations requiring 2nd Renewal 4
B.2.2. Renewals of Marketing Authorisations for unlimited validity 4
B.2.3. Renewals of Conditional Marketing Authorisations 6
B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES 7
B.4. EPARs / WPARs 10
B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES 11
B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects 12
B.5.2. CHMP assessed procedures scope: Non-Clinical and Clinical aspects 21
B.5.3. CHMP-PRAC assessed procedures 38
B.5.4. PRAC assessed procedures 48
B.5.5. CHMP-CAT assessed procedures 57
B.5.6. CHMP-PRAC-CAT assessed procedures 58
B.5.7. PRAC assessed ATMP procedures 59
B.5.8. Unclassified procedures and worksharing procedures of type I variations 59
B.5.9. Information on withdrawn type II variation / WS procedure 62
B.5.10. Information on type II variation / WS procedure with revised timetable 63
B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION 63
B.6.1. Start of procedure for New Applications: timetables for information 63
B.6.2. Start of procedure for Extension application according to Annex I of Reg. 1234/2008): timetables for information 64

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000
An agency of the European Union

B.6.3. Restart of procedure - responses received to Day 120 List of Questions timetables: for information....64
B.6.4. Annual Re-assessments: timetables for adoption....65
B.6.5. Renewals of Marketing Authorisations: timetables for adoption provided only if the validation has been completed....65
B.6.6. VARIATIONS – START OF THE PROCEDURE....67
B.6.7. Type II Variations scope of the Variations: Extension of indication....67
B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects....69
B.6.9. CHMP assessed procedures scope: Non-Clinical and Clinical aspects....74
B.6.10. CHMP-PRAC assessed procedures....82
B.6.11. PRAC assessed procedures....86
B.6.12. CHMP-CAT assessed procedures....93
B.6.13. CHMP-PRAC-CAT assessed procedures....94
B.6.14. PRAC assessed ATMP procedures....95
B.6.15. Unclassified procedures and worksharing procedures of type I variations....95
B.7. DOCUMENTS TABLED IN MMD AFTER THE CHMP PLENARY....98
B.7.1. Yearly Line listing for Type I and II variations....98
B.7.2. Monthly Line listing for Type I variations....98
B.7.3. Opinion on Marketing Authorisation transfer (MMD only)....98
B.7.4. Notifications in accordance with Article 61(3) of Council Directive 2001/83/EC (MMD only)....98
B.7.5. Request for supplementary information relating to Notification of Type I variation (MMD only)....98
B.7.6. Notifications of Type I Variations (MMD only)....98

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)....98

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)....98

E. Annex E - EMA CERTIFICATION OF PLASMA MASTER FILES....98
E.1. Timetables – starting & ongoing procedures: For information....98

F. ANNEX F - Decision of the Granting of a Fee Reduction/Fee Waiver....98

G. ANNEX G....98
G.1. Final Scientific Advice (Reports and Scientific Advice letters):....98
List of procedures concluding at 13-16 December 2021 CHMP plenary....99
G.1.1. List of procedures starting in December 2021 for January 2022 CHMP adoption of outcomes....99

H. ANNEX H - Product Shared Mailboxes – e-mail address....99

A. PRE-SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

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

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

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

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

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

Brineura - cerliponase alfa - EMEA/H/C/004065/S/0035, Orphan
BioMarin International Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga

Increlex - mecasermin - EMEA/H/C/000704/S/0070
Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka

Lojuxta - lomitapide - EMEA/H/C/002578/S/0048
Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst

Strensiq - asfotase alfa - EMEA/H/C/003794/S/0056, 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

Rixathon - rituximab -
EMEA/H/C/003903/R/0053
Sandoz GmbH, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Anette Kirstine Stark

Riximyo - rituximab -
EMEA/H/C/004729/R/0054
Sandoz GmbH, Duplicate, Duplicate of Rixathon, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Anette Kirstine Stark

Xeljanz - tofacitinib -
EMEA/H/C/004214/R/0040
Pfizer Europe MA EEIG, Rapporteur: Armando Genazzani, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan
Request for Supplementary Information adopted on 14.10.2021.

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Axumin - fluciclovine (18f) -
EMEA/H/C/004197/R/0027
Blue Earth Diagnostics Ireland Limited, Rapporteur: Janet Koenig, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Rugile Pilviniene

BESPONSA - inotuzumab ozogamicin -
EMEA/H/C/004119/R/0023, Orphan
Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, Co-Rapporteur: Konstantina Alexopoulou, PRAC Rapporteur: Brigitte Keller-Stanislawski

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

Febuxostat Mylan - febuxostat -
EMEA/H/C/004374/R/0011
Mylan Pharmaceuticals Limited, Generic, Generic of Adenuric, Rapporteur: Elita

Poplavska, PRAC Rapporteur: Jan Neuhauser

Ivabradine Accord - ivabradine - EMEA/H/C/004241/R/0010
Accord Healthcare S.L.U., Generic, Generic of Procoralan, Rapporteur: Konstantina Alexopoulou, PRAC Rapporteur: Menno van der Elst

Kalydeco - ivacaftor - EMEA/H/C/002494/R/0106, Orphan
Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Maria Concepcion Prieto Yerro, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Maria del Pilar Rayon

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

Refixia - nonacog beta pegol - EMEA/H/C/004178/R/0025
Novo Nordisk A/S, Rapporteur: Andrea Laslop, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski
Request for Supplementary Information adopted on 11.11.2021.

Skilarence - dimethyl fumarate - EMEA/H/C/002157/R/0030
Almirall S.A, Rapporteur: Janet Koenig, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin
Request for Supplementary Information adopted on 11.11.2021.

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

Trimbow - beclometasone / formoterol / glycopyrronium bromide - EMEA/H/C/004257/R/0025
Chiesi Farmaceutici S.p.A., Rapporteur: Janet Koenig, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Jan Neuhauser

Veltassa - patiromer -

EMEA/H/C/004180/R/0028
Vifor Fresenius Medical Care Renal Pharma France, Rapporteur: Jayne Crowe, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Kirsti Villikka

Zykadia - ceritinib - EMEA/H/C/003819/R/0042
Novartis Europharm Limited, Rapporteur: Blanca Garcia-Ochoa, Co-Rapporteur: Ingrid Wang, PRAC Rapporteur: Annika Folin

B.2.3. Renewals of Conditional Marketing Authorisations

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

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

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

Natpar - parathyroid hormone - EMEA/H/C/003861/R/0034, Orphan
Takeda Pharmaceuticals International AG, Rapporteur: Karin Janssen van Doorn, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Rhea Fitzgerald

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

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

Huber

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 29 November – 02 December 2021 PRAC:

Signal of Myocarditis and pericarditis

Comirnaty - COVID-19 mRNA vaccine (nucleoside-modified)

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

PRAC recommendation on a variation adopted via written procedure on 03.12.2021.
Action: For information

Signal of Myocarditis and pericarditis

Spikevax - COVID-19 mRNA vaccine (nucleoside-modified)

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Hans Christian Siersted

PRAC recommendation on a variation adopted via written procedure on 03.12.2021.
Action: For information

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

Fexinidazole Winthrop - fexinidazole - EMEA/H/W/002320/PSUV/0008 (without RMP)
sanofi-aventis groupe, Rapporteur: Fátima Ventura, PRAC Rapporteur: Liana Gross-Martirosyan, "16-Nov-2020 to 15-May-2021"

EMEA/H/C/PSUSA/00000226/202105
(apixaban)
CAPS:
Eliquis (EMEA/H/C/002148) (apixaban), Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van

der Elst, "17/05/2020 To: 17/05/2021"

EMEA/H/C/PSUSA/00001267/202104
(eslicarbazepine acetate)
CAPS:
Zebinix (EMEA/H/C/000988) (eslicarbazepine acetate), Bial - Portela & Cª, S.A., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "22/10/2018 To: 21/04/2021"

EMEA/H/C/PSUSA/00002839/202103
(tacrolimus (systemic formulations))
CAPS:
Advagraf (EMEA/H/C/000712) (tacrolimus), Astellas Pharma Europe B.V., Rapporteur: Jayne Crowe
Envarsus (EMEA/H/C/002655) (tacrolimus), Chiesi Farmaceutici S.p.A., Rapporteur: John Joseph Borg
Modigraf (EMEA/H/C/000954) (tacrolimus), Astellas Pharma Europe B.V., Rapporteur: Kristina Dunder
NAPS:
NAPs - EU, PRAC Rapporteur: Ronan Grimes, "01/04/2018 To: 31/03/2021"

EMEA/H/C/PSUSA/00003074/202105
(ulipristal (female emergency contraceptive))
CAPS:
ellaOne (EMEA/H/C/001027) (ulipristal acetate), Laboratoire HRA Pharma, Rapporteur: Paula Boudewina van Hennik
NAPS:
NAPs - LABORATOIRE HRA PHARMA, PRAC Rapporteur: Menno van der Elst, "15/05/2020 To: 14/05/2021"

EMEA/H/C/PSUSA/00010044/202104
(meningococcal group a, c, w135, y conjugate vaccine (conjugated to tetanus toxoid carrier protein))
CAPS:
MenQuadfi (EMEA/H/C/005084) (meningococcal group a, c, w135 and y conjugate vaccine), Sanofi Pasteur, Rapporteur: Andrea Laslop
Nimenrix (EMEA/H/C/002226) (meningococcal group a, c, w135 and y conjugate vaccine), Pfizer Europe MA EEIG, Rapporteur: Ingrid Wang, PRAC Rapporteur: David Olsen, "20/04/2020 To: 19/04/2021"

EMEA/H/C/PSUSA/00010213/202104
(delamanid)
CAPS:
Deltyba (EMEA/H/C/002552) (delamanid), Otsuka Novel Products GmbH, Rapporteur: Christophe Focke, PRAC Rapporteur: Laurence de Fays, "27/04/2020 To: 27/04/2021"

EMEA/H/C/PSUSA/00010388/202104
(empagliflozin, empagliflozin / metformin)
CAPS:
Jardiance (EMEA/H/C/002677) (empagliflozin), Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege
Synjardy (EMEA/H/C/003770) (empagliflozin / metformin), Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Eva A. Segovia, "17/04/2019 To: 17/04/2021"

EMEA/H/C/PSUSA/00010550/202105
(mycophenolate mofetil, mycophenolic acid)
CAPS:
CellCept (EMEA/H/C/000082) (mycophenolate mofetil), Roche Registration GmbH, Rapporteur: Sinan B. Sarac
Myclausen (EMEA/H/C/001218) (mycophenolate mofetil), Passauer Pharma GmbH, Rapporteur: Andrea Laslop
Mycophenolate mofetil Teva (EMEA/H/C/000882) (mycophenolate mofetil), Teva B.V., Rapporteur: Ondřej Slanař
Myfenax (EMEA/H/C/000884) (mycophenolate mofetil), Teva B.V., Rapporteur: Ondřej Slanař
NAPS:
NAP - EU, PRAC Rapporteur: Anette Kirstine Stark, "03/05/2020 To: 02/05/2021"

EMEA/H/C/PSUSA/00010644/202105
(atezolizumab)
CAPS:
Tecentriq (EMEA/H/C/004143) (atezolizumab), Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "17/05/2020 To: 17/05/2021"

EMEA/H/C/PSUSA/00010723/202104
(durvalumab)
CAPS:
Imfinzi (EMEA/H/C/004771) (durvalumab), AstraZeneca AB, Rapporteur: Sinan B. Sarac,

PRAC Rapporteur: David Olsen, "01/05/2020 To: 30/04/2021"	
EMEA/H/C/PSUSA/00010917/202105 (selpercatinib) CAPS: **RETSEVMO** (EMEA/H/C/005375) (selpercatinib), Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst, "08/11/2020 To: 08/05/2021"	

B.4. EPARs / WPARs

Lonapegsomatropin Ascendis Pharma - lonapegsomatropin - EMEA/H/C/005367, Orphan Ascendis Pharma Endocrinology Division A/S, Treatment of growth hormone deficiency, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Lumykras - sotorasib - EMEA/H/C/005522 Amgen Europe B.V., treatment of locally advanced or metastatic non-small cell lung cancer, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Nexviadyme - avalglucosidase alfa - EMEA/H/C/005501, Orphan Genzyme Europe BV, for long-term enzyme replacement therapy for the treatment of patients with Pompe disease., New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Nouryant - istradefylline - EMEA/H/C/005308 Kyowa Kirin Holdings B.V., indicated as an adjunctive treatment to levodopa-based regimens in patients with Parkinson's disease, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Regkirona - regdanvimab - EMEA/H/C/005854 Celltrion Healthcare Hungary Kft., treatment of COVID 19, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Riltrava Aerosphere - formoterol fumarate dihydrate / glycopyrronium / budesonide - EMEA/H/C/005311	For information only. Comments can be sent to the PL in case necessary.

AstraZeneca AB, maintenance treatment of chronic obstructive pulmonary disease (COPD), Informed Consent of Trixeo Aerosphere, Informed consent application (Article 10c of Directive No 2001/83/EC)	
Ronapreve - casirivimab / imdevimab - EMEA/H/C/005814 Roche Registration GmbH, prevention and treatment of COVID-19, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
TAVNEOS - avacopan - EMEA/H/C/005523, Orphan Vifor Fresenius Medical Care Renal Pharma France, Treatment of granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Tecovirimat SIGA - tecovirimat - EMEA/H/C/005248 SIGA Technologies Netherlands B.V., treatment of orthopoxvirus disease, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Uplizna - inebilizumab - EMEA/H/C/005818, Orphan Viela Bio, indicated for the treatment of adults with neuromyelitis optica spectrum disorders, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Voraxaze - glucarpidase - EMEA/H/C/005467, Orphan Serb, treatment of patients at risk of methotrexate toxicity, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Vyepti - eptinezumab - EMEA/H/C/005287 H. Lundbeck A/S, Indicated for the prophylaxis of migraine in adults, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Wegovy - semaglutide - EMEA/H/C/005422 Novo Nordisk A/S, treatment for weight loss and weight maintenance, Known active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.

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

ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0024 Baxalta Innovations GmbH, Rapporteur: Andrea Laslop	
Ceprotin - human protein C - EMEA/H/C/000334/II/0121/G Takeda Manufacturing Austria AG, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 09.09.2021.	
Ceprotin - human protein C - EMEA/H/C/000334/II/0122 Takeda Manufacturing Austria AG, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 09.09.2021.	
Ceprotin - human protein C - EMEA/H/C/000334/II/0124/G Takeda Manufacturing Austria AG, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 25.11.2021. Request for Supplementary Information adopted on 21.10.2021.	Positive Opinion adopted by consensus on 25.11.2021.
Cinacalcet Mylan - cinacalcet - EMEA/H/C/004014/II/0016 Mylan Pharmaceuticals Limited, Generic, Generic of Mimpara, Rapporteur: Tomas Radimersky Request for Supplementary Information adopted on 23.09.2021.	
Cinryze - human c1-esterase inhibitor - EMEA/H/C/001207/II/0089 Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 02.12.2021. Request for Supplementary Information adopted on 28.10.2021.	Positive Opinion adopted by consensus on 02.12.2021.
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0054/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, "Grouped Variation: · Type II C.I.11.b, To update Annex II to implement changes and provision of data to fulfill specific obligations SO2f, SO4, and SO5. Request for Supplementary Information adopted	

on 14.10.2021.	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0056/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, " C.I.11.b, (Type II)- To submit additional data to complete characterisation of the active substance and finished product, which are a condition to the Marketing Authorisation (Special Obligation SO1) C.I.11.b, (Type II)- To submit additional data to enhance the control strategy, including the active substance and finished product specifications, which are a condition to the Marketing Authorisation (Special Obligation SO2) Request for Supplementary Information adopted on 14.10.2021.	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0083/G BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 17.11.2021.	Positive Opinion adopted by consensus on 17.11.2021.
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0086 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Opinion adopted on 26.11.2021.	Positive Opinion adopted by consensus on 26.11.2021.
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0089 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson Request for Supplementary Information adopted on 09.12.2021.	Request for supplementary information adopted with a specific timetable.
COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0026/G Janssen-Cilag International N.V., Rapporteur: Christophe Focke	
Cyramza - ramucirumab - EMEA/H/C/002829/II/0044 Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik	
Drovelis - drospirenone / estetrol - EMEA/H/C/005336/II/0001/G Chemical Works of Gedeon Richter Plc. (Gedeon	

Richter Plc.), Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 16.09.2021.	
Drovelis - drospirenone / estetrol - EMEA/H/C/005336/II/0004/G Chemical Works of Gedeon Richter Plc. (Gedeon Richter Plc.), Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 23.09.2021.	
Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0062 Organon N.V., Rapporteur: Paula Boudewina van Hennik	
Emtricitabine/Tenofovir disoproxil Mylan - emtricitabine / tenofovir disoproxil - EMEA/H/C/004050/II/0019 Mylan Pharmaceuticals Limited, Generic, Generic of Truvada, Rapporteur: Romaldas Mačiulaitis	
Enbrel - etanercept - EMEA/H/C/000262/II/0243/G Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro Request for Supplementary Information adopted on 02.09.2021.	
Enhertu - trastuzumab deruxtecan - EMEA/H/C/005124/II/0010 Daiichi Sankyo Europe GmbH, Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 28.10.2021.	
Entyvio - vedolizumab - EMEA/H/C/002782/II/0063/G Takeda Pharma A/S, Rapporteur: Armando Genazzani Opinion adopted on 09.12.2021. Request for Supplementary Information adopted on 28.10.2021.	Positive Opinion adopted by consensus on 09.12.2021.
Erelzi - etanercept - EMEA/H/C/004192/II/0038/G Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 02.12.2021.	Request for supplementary information adopted with a specific timetable.
Fasenra - benralizumab - EMEA/H/C/004433/II/0038/G	

AstraZeneca AB, Rapporteur: Fátima Ventura	
Fasenra - benralizumab - EMEA/H/C/004433/II/0040 AstraZeneca AB, Rapporteur: Fátima Ventura	
Fendrix - hepatitis B (rDNA) vaccine (adjuvanted, adsorbed) - EMEA/H/C/000550/II/0076/G GlaxoSmithKline Biologicals, Rapporteur: Christophe Focke Opinion adopted on 09.12.2021.	Positive Opinion adopted by consensus on 09.12.2021.
Herceptin - trastuzumab - EMEA/H/C/000278/II/0174/G Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 07.10.2021.	
Herzuma - trastuzumab - EMEA/H/C/002575/II/0041/G Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 09.12.2021. Request for Supplementary Information adopted on 21.10.2021.	Positive Opinion adopted by consensus on 09.12.2021.
IKERVIS - ciclosporin - EMEA/H/C/002066/II/0026/G Santen Oy, Rapporteur: Peter Kiely Request for Supplementary Information adopted on 11.11.2021, 22.07.2021.	
Imfinzi - durvalumab - EMEA/H/C/004771/II/0036 AstraZeneca AB, Rapporteur: Sinan B. Sarac	
Intrarosa - prasterone - EMEA/H/C/004138/II/0015 Endoceutics S.A., Rapporteur: Jean-Michel Race Request for Supplementary Information adopted on 22.07.2021, 11.03.2021.	
Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0061/G Roche Registration GmbH, Rapporteur: Sinan B. Sarac Request for Supplementary Information adopted on 09.12.2021.	Request for supplementary information adopted with a specific timetable.
Kirsty - insulin aspart - EMEA/H/C/004965/II/0003/G Mylan IRE Healthcare Limited, Rapporteur: Sinan B. Sarac	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 09.12.2021.	
Levetiracetam SUN - levetiracetam - EMEA/H/C/002051/II/0026 Sun Pharmaceutical Industries Europe B.V., Generic, Generic of Keppra, Rapporteur: Konstantina Alexopoulou Request for Supplementary Information adopted on 21.10.2021.	
Lydisilka - drospirenone / estetrol - EMEA/H/C/005382/II/0001/G Estetra SRL, Duplicate, Duplicate of Drovelis, Rapporteur: Kristina Dunder Opinion adopted on 09.12.2021. Request for Supplementary Information adopted on 16.09.2021.	Positive Opinion adopted by consensus on 09.12.2021.
Lydisilka - drospirenone / estetrol - EMEA/H/C/005382/II/0004/G Estetra SRL, Duplicate, Duplicate of Drovelis, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 23.09.2021.	
Mepsevii - vestronidase alfa - EMEA/H/C/004438/II/0024, Orphan Ultragenyx Germany GmbH, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 02.12.2021. Request for Supplementary Information adopted on 02.09.2021.	Positive Opinion adopted by consensus on 02.12.2021.
Mycamine - micafungin - EMEA/H/C/000734/II/0044/G Astellas Pharma Europe B.V., Rapporteur: Janet Koenig Request for Supplementary Information adopted on 09.12.2021.	Request for supplementary information adopted with a specific timetable.
Myocet liposomal - doxorubicin hydrochloride - EMEA/H/C/000297/II/0066 Teva B.V., Rapporteur: Filip Josephson Opinion adopted on 25.11.2021.	Positive Opinion adopted by consensus on 25.11.2021.
Natpar - parathyroid hormone - EMEA/H/C/003861/II/0033/G, Orphan Takeda Pharmaceuticals International AG, Rapporteur: Karin Janssen van Doorn Request for Supplementary Information adopted on 02.12.2021.	Request for supplementary information adopted with a specific timetable.

Nepexto - etanercept - EMEA/H/C/004711/II/0011 Mylan IRE Healthcare Limited, Rapporteur: Martina Weise Opinion adopted on 02.12.2021. Request for Supplementary Information adopted on 02.09.2021.	Positive Opinion adopted by consensus on 02.12.2021.
Neulasta - pegfilgrastim - EMEA/H/C/000420/II/0117 Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege Opinion adopted on 18.11.2021. Request for Supplementary Information adopted on 07.10.2021.	Positive Opinion adopted by consensus on 18.11.2021.
Nimenrix - meningococcal group a, c, w135 and y conjugate vaccine - EMEA/H/C/002226/II/0112 Pfizer Europe MA EEIG, Rapporteur: Ingrid Wang Opinion adopted on 18.11.2021.	Positive Opinion adopted by consensus on 18.11.2021.
Palynziq - pegvaliase - EMEA/H/C/004744/II/0024, Orphan BioMarin International Limited, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 25.11.2021.	Positive Opinion adopted by consensus on 25.11.2021.
ProQuad - measles, mumps, rubella and varicella vaccine (live) - EMEA/H/C/000622/II/0154 MSD Vaccins, Rapporteur: Jan Mueller-Berghaus	
Reagila - cariprazine - EMEA/H/C/002770/II/0020/G Gedeon Richter Plc., Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 30.09.2021.	
Reagila - cariprazine - EMEA/H/C/002770/II/0022 Gedeon Richter Plc., Rapporteur: Kristina Dunder Opinion adopted on 18.11.2021. Request for Supplementary Information adopted on 30.09.2021.	Positive Opinion adopted by consensus on 18.11.2021.
Remsima - infliximab - EMEA/H/C/002576/II/0101/G Celltrion Healthcare Hungary Kft., Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 18.11.2021, 02.09.2021, 03.06.2021.	
Revestive - teduglutide - EMEA/H/C/002345/II/0055, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Sinan B. Sarac	
RoActemra - tocilizumab - EMEA/H/C/000955/II/0104/G Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus	
Spectrila - asparaginase - EMEA/H/C/002661/II/0026 medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 25.11.2021.	Request for supplementary information adopted with a specific timetable.
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0024/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 25.11.2021. Request for Supplementary Information adopted on 16.09.2021.	Positive Opinion adopted by consensus on 25.11.2021.
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0043/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus	
Supemtek - quadrivalent influenza vaccine (recombinant, prepared in cell culture) - EMEA/H/C/005159/II/0005/G Sanofi Pasteur, Rapporteur: Jan Mueller-Berghaus	
Synagis - palivizumab - EMEA/H/C/000257/II/0127/G AstraZeneca AB, Rapporteur: Sinan B. Sarac	
Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0166/G GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder Opinion adopted on 18.11.2021.	Positive Opinion adopted by consensus on 18.11.2021.
Taltz - ixekizumab - EMEA/H/C/003943/II/0045/G Eli Lilly and Co (Ireland) Limited, Rapporteur:	

Kristina Dunder Request for Supplementary Information adopted on 14.10.2021.	
Thyrogen - thyrotropin alfa - EMEA/H/C/000220/II/0109/G Genzyme Europe BV, Rapporteur: Peter Kiely	
Trogarzo - ibalizumab - EMEA/H/C/004961/II/0016/G Theratechnologies Europe Limited, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 25.11.2021.	Request for supplementary information adopted with a specific timetable.
Vaxchora - cholera vaccine, oral, live - EMEA/H/C/003876/II/0009 Emergent Netherlands B.V., Rapporteur: Ingrid Wang	
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0021/G AstraZeneca AB, Rapporteur: Sol Ruiz Request for Supplementary Information adopted on 16.09.2021, 22.07.2021, 24.06.2021.	See 9.1
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0050 AstraZeneca AB, Rapporteur: Sol Ruiz Opinion adopted on 18.11.2021.	Positive Opinion adopted by consensus on 18.11.2021.
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0051/G AstraZeneca AB, Rapporteur: Sol Ruiz Opinion adopted on 18.11.2021.	Positive Opinion adopted by consensus on 18.11.2021.
VEYVONDI - vonicog alfa - EMEA/H/C/004454/II/0019/G Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 02.09.2021.	
VEYVONDI - vonicog alfa - EMEA/H/C/004454/II/0020 Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus	
Yuflyma - adalimumab - EMEA/H/C/005188/II/0009/G Celltrion Healthcare Hungary Kft., Rapporteur:	

Outi Mäki-Ikola	
ZABDENO - ebola vaccine (rDNA, replication-incompetent) - EMEA/H/C/005337/II/0006/G Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege	
Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/II/0027/G Pfizer Ireland Pharmaceuticals, Rapporteur: Ingrid Wang Request for Supplementary Information adopted on 02.12.2021, 28.10.2021, 09.09.2021.	Request for supplementary information adopted with a specific timetable.
Zutectra - human hepatitis b immunoglobulin - EMEA/H/C/001089/II/0050 Biotest Pharma GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 02.12.2021.	Request for supplementary information adopted with a specific timetable.
WS2118/G **Blitzima-EMEA/H/C/004723/WS2118/0044/G** **Truxima-EMEA/H/C/004112/WS2118/0048/G** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz Opinion adopted on 02.12.2021. Request for Supplementary Information adopted on 16.09.2021.	Positive Opinion adopted by consensus on 02.12.2021.
WS2119/G **M-M-RVAXPRO-EMEA/H/C/000604/WS2119/0110/G** **ProQuad-EMEA/H/C/000622/WS2119/0152/G** MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 18.11.2021.	Positive Opinion adopted by consensus on 18.11.2021.
WS2120 **Nuwiq-EMEA/H/C/002813/WS2120/0045** **Vihuma-EMEA/H/C/004459/WS2120/0027** Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 02.09.2021.	
WS2132 **Infanrix hexa-EMEA/H/C/000296/**	Positive Opinion adopted by consensus on

WS2132/0305 GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke Opinion adopted on 02.12.2021.	02.12.2021.
WS2138/G **Hexacima-EMEA/H/C/002702/WS2138/0120/G** **Hexyon-EMEA/H/C/002796/WS2138/0124/G** Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 02.12.2021.	Request for supplementary information adopted with a specific timetable.
WS2142 **M-M-RVAXPRO-EMEA/H/C/000604/WS2142/0111** **ProQuad-EMEA/H/C/000622/WS2142/0153** MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 09.12.2021.	Positive Opinion adopted by consensus on 09.12.2021.
WS2165/G **Blitzima-EMEA/H/C/004723/WS2165/0048/G** **Truxima-EMEA/H/C/004112/WS2165/0052/G** Celltrion Healthcare Hungary Kft., Duplicate, Duplicate of Truxima, Lead Rapporteur: Sol Ruiz Opinion adopted on 25.11.2021.	Positive Opinion adopted by consensus on 25.11.2021.
WS2182/G **Fluenz Tetra-EMEA/H/C/002617/WS2182/0110/G** **Pandemic influenza vaccine H5N1 AstraZeneca-EMEA/H/C/003963/WS2182/0045/G** AstraZeneca AB, Lead Rapporteur: Christophe Focke	

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

Adtralza - tralokinumab - EMEA/H/C/005255/II/0001 LEO Pharma A/S, Rapporteur: Jayne Crowe, "C.I.4 Update of sections 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information	

with cytochrome P450 and CYP substrates based on final results from study ECZTRA 4 (LP0162-1342). This is an open-label drug–drug interaction trial to investigate the effects of tralokinumab on the pharmacokinetics of selected CYP substrates in adult subjects with moderate-to-severe atopic dermatitis. In addition, the MAH took the opportunity make editorial changes to sections 4.8, 6.5 and 9 of SmPC."	
Bimzelx - bimekizumab - EMEA/H/C/005316/II/0002 UCB Pharma S.A., Rapporteur: Peter Kiely, "C.I.4 - Update of section 5.1 of the SmPC in order to update efficacy information based on interim results from study PS0015; this is a multicenter, randomized, double-blind, active comparator controlled, parallel group study to evaluate the efficacy and safety of bimekizumab compared with secukinumab in adult study participants with moderate to severe plaque psoriasis. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2."	
COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0033 Janssen-Cilag International N.V., Rapporteur: Christophe Focke, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to introduce a homologous booster dose (second dose) of COVID-19 vaccine Janssen based on interim efficacy, immunogenicity and safety results from different clinical studies including the two randomised, double blind, placebo-controlled Phase 3 studies COV3001 and COV3009. In addition, an update to introduce an heterologous booster dose of COVID-19 vaccine Janssen following completion of a primary vaccination with an approved mRNA COVID-19 vaccine is introduced based on immunogenicity and safety interim results from the phase 1/2 study DMID 21-0012. In addition, the MAH took the opportunity to update the efficacy data for the primary vaccination schedule based on final analysis from study COV3001. The Package Leaflet is updated accordingly."	See 9.1
Cyramza - ramucirumab - EMEA/H/C/002829/II/0043	

Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik, "Update of section 4.4 of the SmPC in order to add a new warning on heart failure following a detailed cumulative review of post-marketing data. The Package Leaflet and Labelling are updated accordingly. In addition, the MAH took the opportunity to update the package leaflet to include hypothyroidism as a common side effect."	
Dapivirine Vaginal Ring 25 mg - dapivirine - EMEA/H/W/002168/II/0012/G International Partnership for Microbicides Belgium AISBL, Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information with vaginal products (e.g. vaginal miconazole) that are metabolised by CYP and UGT enzymes and to update pharmacokinetic information based on the final study reports of 3 in vitro enzyme/transporter studies evaluating the interactions between dapivirine and transporters (study NPK/0025), dapivirine-miconazole interactions on CYP (study NPK/0026) and UGT enzymes (study NPK/0027). Submission of the final report from study evaluating the impact of dapivirine and miconazole on cellular tight junctions and assessing the impact of miconazole on dapivirine tissue permeability (study NPK/0028). These 4 in vitro studies were submitted to fulfil post-authorisation measures requested in the initial marketing authorisation application assessment report." Opinion adopted on 09.12.2021. Request for Supplementary Information adopted on 28.10.2021.	Positive Opinion adopted by consensus on 09.12.2021.
Edarbi - azilsartan medoxomil - EMEA/H/C/002293/II/0030/G Takeda Pharma A/S, Rapporteur: Johann Lodewijk Hillege, "Group of variations: · Type II C.I.4. - Update of SmPC sections 4.2, 4.8 and 5.1 with paediatric clinical data from study AR14.001 (PIP study 8) following the outcome of procedure EMEA/H/C/002293/P46/012. · Type II C.I.4. - Update of SmPC section 5.2 with paediatric clinical data from study TAK-	

491_109 (PIP study 7) following the outcome of procedure EMEA/H/C/002293/P46/011. · Type II C.I.4. - Update of SmPC section 5.3 with data from juvenile animal toxicity studies. · Type II C.I.4. - Update of SmPC section 4.5 with drug-drug interaction information from clinical pharmacology studies TAK-491-013 and TAK-563-004. Furthermore, the MAH is taking the opportunity to update the PI in line with the latest QRD template version 10.2, update the local representatives for Ireland, Slovenia and United Kingdom in the Package Leaflet (PL) and update minor editorial/typographical to Product information."	
Enhertu - trastuzumab deruxtecan - EMEA/H/C/005124/II/0005/G Daiichi Sankyo Europe GmbH, Rapporteur: Sinan B. Sarac, "Submission of two final study reports recommended at the time of the initial MA: I. study investigating in vitro pharmacological action of MAAA-11181d on receptors, channels, transporters and enzymes (Study No.: TW04-0008917); II. pharmacodynamic study to investigate the in-vitro binding profile of MAAA-1181a in Human, Monkey, and Rat Liver Microsomes (Study No.: AE-8630-G). Submission of the final report of the in vitro CYP3A4, CYP1A2 and CYP2B6 induction study in primary human hepatocytes (Study No.: TCRM-DMPK-2020-19)." Opinion adopted on 18.11.2021. Request for Supplementary Information adopted on 16.09.2021.	Positive Opinion adopted by consensus on 18.11.2021.
Erleada - apalutamide - EMEA/H/C/004452/II/0016 Janssen-Cilag International N.V., Rapporteur: Blanca Garcia-Ochoa, "Update of sections 4.4 and 4.8 of the SmPC in order to add Stevens-Johnson Syndrome (SJS) to the list of adverse drug reactions (ADRs) with frequency not known. Cases of SJS were observed in post-marketing data. The Package Leaflet is updated accordingly. SmPC new text Cases of Stevens-Johnson Syndrome (SJS) were observed in association with Erleada treatment	Positive Opinion adopted by consensus on 18.11.2021.

in post-marketing data and has been added to the list of adverse drug reactions (ADRs) with frequency not known." Opinion adopted on 18.11.2021. Request for Supplementary Information adopted on 14.10.2021, 02.09.2021.	
Evrysdi - risdiplam - EMEA/H/C/005145/II/0003, Orphan Roche Registration GmbH, Rapporteur: Bruno Sepodes, "Update of section 4.8 of the SmPC to add undesirable effects based on post-marketing experience. The Package Leaflet (PL) is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of local representatives in the PL." Opinion adopted on 18.11.2021.	Positive Opinion adopted by consensus on 18.11.2021.
Eylea - aflibercept - EMEA/H/C/002392/II/0073 Bayer AG, Rapporteur: Alexandre Moreau, "C.I.13 Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority. PFS design change." Request for Supplementary Information adopted on 16.09.2021.	
Fasenra - benralizumab - EMEA/H/C/004433/II/0039 AstraZeneca AB, Rapporteur: Fátima Ventura, "C.I.4 Update of section 5.1 in order to include information on the maintenance of long-term safety based on the results from study D3250C00037 (MELTEMI) listed as a category 3 study in the RMP. This is a multicenter, open-label safety extension study to evaluate the safety and tolerability of a fixed 30 mg dose of benralizumab in adults with severe asthma. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to bring the Product information in line with the latest QRD template version 10.2." Opinion adopted on 09.12.2021.	Positive Opinion adopted by consensus on 09.12.2021.
Ganfort - bimatoprost / timolol - EMEA/H/C/000668/II/0038 Allergan Pharmaceuticals Ireland, Rapporteur:	Positive Opinion adopted by consensus on 25.11.2021.

Sinan B. Sarac, "C.I.4 Update of section 4.8 of the SmPC in order to add periorbital and lid changes associated with periorbital fat atrophy and skin tightness to the list of adverse drug reactions (ADRs) with frequency uncommon." Opinion adopted on 25.11.2021.	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0114 Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, "Update of sections 5.1 of the SmPC in order to update efficacy information based on final results from study KEYNOTE-087 listed as an imposed PAES in the Annex II; this is a multicenter, single-arm, multi-cohort, non-randomized Phase 2 study of IV pembrolizumab in participants with relapsed or refractory classical Hodgkin lymphoma (cHL)." Request for Supplementary Information adopted on 18.11.2021.	Request for supplementary information adopted with a specific timetable.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0115 Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, "Update of section 5.1 of the SmPC in order to update efficacy information based on final results from study KEYNOTE-426 listed as imposed PAES in the Annex II; this is a Phase III Randomized, Open-label Study to Evaluate Efficacy and Safety of Pembrolizumab (MK-3475) in combination with Axitinib versus Sunitinib Monotherapy as a First-line Treatment for Locally Advanced or Metastatic Renal Cell Carcinoma (mRCC)." Request for Supplementary Information adopted on 02.12.2021.	Request for supplementary information adopted with a specific timetable.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0116 Merck Sharp & Dohme B.V., Rapporteur: Armando Genazzani, "Update of section 5.1 of the SmPC in order to update efficacy information based on final results from study KEYNOTE-177 listed as PAES in Annex II of the Product Information; this is a 2-arm, multicenter, international, randomized, open-label, Phase 3 study evaluating the efficacy and safety of pembrolizumab monotherapy versus globally-accepted SOC therapies for Colorectal	Positive Opinion adopted by consensus on 09.12.2021.

carcinoma (CRC) in participants with locally confirmed Deficient mismatch repair (dMMR) or Microsatellite instability-high (MSI-H) unresectable or metastatic CRC who have not received prior chemotherapy for their disease." Opinion adopted on 09.12.2021.	
Kovaltry - octocog alfa - EMEA/H/C/003825/II/0038 Bayer AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of the SmPC sections 4.8 and 5.1 to include data from the LEOPOLD Kids Part B (previously submitted as Art 46; an addendum on biomarker data is included in this submission) and Extension study results included as part of this submission. In addition, an editorial revision in section 4.2 and a clarification in section 6.5 of the SmPC are proposed. Section 4 of the Package is updated accordingly. A correction of a typo in the Greek product information is also included. The Risk Management Plan for Kovaltry is updated using Revision 2.0.1 of the template format." Request for Supplementary Information adopted on 02.12.2021.	Request for supplementary information adopted with a specific timetable.
LEDAGA - chlormethine - EMEA/H/C/002826/II/0027, Orphan Helsinn Birex Pharmaceuticals Limited, Rapporteur: Sinan B. Sarac, "Update of section 4.2 of the SmPC in order to allow flexibility in the starting frequency of the treatment based on current clinical practice; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 20.05.2021.	See 9.1
Mavenclad - cladribine - EMEA/H/C/004230/II/0016 Merck Europe B.V., Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to add hypersensitivity to the list of adverse drug reactions (ADRs) with frequency "common" based on a review of cumulative clinical and post-marketing data. The Package Leaflet is updated accordingly." Opinion adopted on 02.12.2021. Request for Supplementary Information adopted on 02.09.2021, 20.05.2021, 14.01.2021.	Positive Opinion adopted by consensus on 02.12.2021.
Methylthioninium chloride Proveblue -	

methylthioninium chloride - EMEA/H/C/002108/II/0052/G Provepharm SAS, Rapporteur: Kristina Dunder, "-Update of sections 4.2 and 5.2 of the SmPC in order to change the posology recommendations in patients with renal and hepatic impairment and update of the pharmacokinetic information respectively, based on results from: an open-label, parallel group, population-matched, single-dose study to investigate the influence of renal impairment on the pharmacokinetics of ProvayBlue (Study Report PVP-2016006). The package leaflet and labelling are updated accordingly. The applicant takes this opportunity to update the Product Information according to the QRD template v10.1 and v10.2. - Update of sections 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information with other medicinal products and update of the pharmacokinetic information respectively, based on results from: an open-label, randomized, two-period, crossover study to assess the effect of a single dose of methylene blue 5 mg/ml on the pharmacokinetics of the probe drugs midazolam, caffeine, warfarin, omeprazole and dextromethorphan in healthy subjects (Study Report PVP-2016004). The package leaflet and labelling are updated accordingly."	
Natpar - parathyroid hormone - EMEA/H/C/003861/II/0030/G, Orphan Takeda Pharmaceuticals International AG, Rapporteur: Karin Janssen van Doorn, "Submission of the clinical study reports of the following two studies: • SHP634-402 - A Phase 4, Open-Label, Single-Center Clinical Study of Extended use of rhPTH(1-84) in Hypoparathyroidism • SHP634-404 - An Open-label Study Investigating the Safety and Efficacy of rhPTH(1-84) in Subjects with Hypoparathyroidism." Request for Supplementary Information adopted on 16.09.2021.	
Noxafil - posaconazole - EMEA/H/C/000610/II/0067 Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau, "Update of sections 4.3, 4.4 and 4.5 of the SmPC in order to add drug-drug interaction information between posaconazole	Positive Opinion adopted by consensus on 25.11.2021.

and venetoclax. The Package leaflet is updated accordingly." Opinion adopted on 25.11.2021. Request for Supplementary Information adopted on 30.09.2021.	
Obizur - susoctocog alfa - EMEA/H/C/002792/II/0042 Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, "Submission of the final report from OBIZUR study 241502. This is a Phase 3, multicenter, single-arm, open-label study of the efficacy and safety of B-Domain deleted recombinant porcine factor VIII (BAX 802) in subjects with congenital hemophilia A with factor VIII inhibitors undergoing surgical or other invasive procedures. No changes to the PI are proposed."	
OCALIVA - obeticholic acid - EMEA/H/C/004093/II/0030, Orphan Intercept Pharma International Limited, Rapporteur: Blanca Garcia-Ochoa, "Update of section 4.3 of the SmPC in order to include contraindication in patients with decompensated cirrhosis (e.g., Child-Pugh Class B or C) or a prior decompensation event based on the MAH's conclusion that it will not be feasible to establish the safety and efficacy of Ocaliva in these patients from either of the ongoing studies 747-302 and 747-401 listed as Specific Obligations in Annex II. Consequently, dosing instructions for patients with CP-B and CP-C cirrhosis are no longer applicable and section 4.2 has been updated accordingly. In addition, section 4.4 of the SmPC to include a new warning on monitoring and management of patients for possible progression of PBC and other hepatic adverse reactions. The MAH also took the opportunity to remove the outdated term "primary biliary cirrhosis" from section 4.1 and to make editorial changes to sections 4.8, 4.9, 5.1 and Annex IIE to improve clarity and correct typographical errors. The Package Leaflet is updated accordingly. Furthermore, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2" Request for Supplementary Information adopted on 16.09.2021.	
Oncaspar - pegaspargase -	Request for supplementary information adopted

EMEA/H/C/003789/II/0038 Les Laboratoires Servier, Rapporteur: Alexandre Moreau, "Update of sections 4.4 and 4.8, of the SmPC in order to add a new warning on the risk of osteonecrosis and to include it as an adverse drug reaction associated with pegaspargase use with an unknown frequency, following review of all available non-clinical, epidemiological and clinical data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2." Request for Supplementary Information adopted on 25.11.2021, 28.05.2021.	with a specific timetable.
Oxlumo - lumasiran - EMEA/H/C/005040/II/0007, Orphan Alnylam Netherlands B.V., Rapporteur: Martina Weise, "Update of section 5.3 of the SmPC in order to update the non-clinical information based on the final results from the 26-week GLP carcinogenicity study of lumasiran by subcutaneous injection in TgRasH2 mice, as agreed as part of protocol assistance (EMEA/H/SA/4014/2/2019/PA/PR/I). In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet." Opinion adopted on 09.12.2021.	Positive Opinion adopted by consensus on 09.12.2021.
Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0128 Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, "C.I.4, Update of section 4.2 of the SmPC in order to update the dosing information for Pradaxa coated granules and to introduce a new format of the dosing tables for all dosage forms of Pradaxa to avoid incorrect interpretation and possible mistakes. In addition, a guidance related to the Schwartz formula is proposed to be included in section 4.2 of the SmPC. The Package Leaflet was updated accordingly. Furthermore, the MAH took the opportunity to request introduction of the link to a training video by scanning the QR code in Annex IIIA and IIIB and to include additional updates to Annex IIIA and mock-ups." Request for Supplementary Information adopted on 11.11.2021, 22.07.2021.	

REKAMBYS - rilpivirine - EMEA/H/C/005060/II/0006

Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC in order to amend an existing warning on section post-injections reactions, based on the availability of new information from ongoing phase 3/3b clinical trials. Section 2 of the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement some minor editorial changes." Request for Supplementary Information adopted on 21.10.2021.

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

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

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

Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, "Update of sections 4.2 and 5.3 of the SmPC in order to reflect the need to monitor open growth plates in adolescent patients based on the results from a non-clinical juvenile toxicity study LOXO-292-TOX-028. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to correct figures in section 5.1 of the SmPC."

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

Upjohn EESV, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8 and 5.1 to include long-term safety data in adults for the approved dose, and evidence of safe and effective use in adults in higher than recommended doses, based on study A1481324; a multinational, multicentre randomized, double-blind, parallel-group study in 385 adults with Pulmonary Arterial

Hypertension (PAH) undertaken to assess the effects of different dose levels of oral sildenafil on mortality. In addition, the MAH took the opportunity to implement editorial changes in the SmPC."	
Rydapt - midostaurin - EMEA/H/C/004095/II/0022, Orphan Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, "Update of section 5.1 of the SmPC in order to update efficacy information in elderly patients, based on final results from study ADE02T listed as PAES in the Annex II; this is a phase II study to investigate the efficacy of midostaurin in combination with intensive induction, consolidation including allogenic SCT and single agent maintenance in patients aged 18-70 with FLT3 ITD mutated AML ."	
Saxenda - liraglutide - EMEA/H/C/003780/II/0030 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, "Update in the SmPC section 5.1 based on results from phase 3a clinical trial NN8022-4179, listed as part of PIP, to evaluate Efficacy/safety of liraglutide in obese children with Prader-Willi Syndrome from 6 up to 18 years." Request for Supplementary Information adopted on 16.09.2021.	
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0042 Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include information on heterologous boosting using a 50 ug dose of Spikevax to boost subjects that have previously completed a primary vaccination series with any authorised COVID-19 vaccine, based on data from the DMID Study 21-0012, a Phase 1/2 heterologous SARS-CoV-2 vaccine dosing (mRNA-1273 booster) study of the various vaccines authorised in the US under Emergency Use Authorisation in participants ≥ 18 years old (NCT04889209). In addition, the MAH took the opportunity to make minor editorial changes/corrections throughout the product information."	See 9.1

TAGRISSO - osimertinib - EMEA/H/C/004124/II/0045 AstraZeneca AB, Rapporteur: Blanca Garcia-Ochoa, "Update of section 5.3 of the SmPC in order to reflect the outcome of the 104 Week Oral (Gavage) Carcinogenicity Study (507363) in the Rat submitted as recommended by the CHMP." Request for Supplementary Information adopted on 11.11.2021.	
TAKHZYRO - lanadelumab - EMEA/H/C/004806/II/0022, Orphan Takeda Pharmaceuticals International AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Kirsti Villikka, "Update to the SmPC sections 4.8 and 5.1 to reflect the result of study DX-2930-04 (HELP Study ExtensionTM: An Open-Label Study to Evaluate the Long-Term Safety and Efficacy of DX-2930 for Prevention Against Acute Attacks of Hereditary Angioedema (HAE)). The Risk Management Plan is also updated following the completion of study DX-2930-04 and according to GVP Module V Rev 2 Integrated RMP template. In addition, the MAH is taking the opportunity to include a refrigeration statement for the multi-pack pre-filled syringe in the SmPC and pre-filled syringe PIL in section 6.4." Request for Supplementary Information adopted on 16.09.2021.	
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0067 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to include the new ADR of rhinorrhoea for atezolizumab in combination therapy, as part of the grouped term of nasopharyngitis identified in the IMpassion031 study and reviewed in the context of a drug safety report. The package leaflet is proposed to be updated accordingly. Additional amendments are proposed to the footnotes of ADRs in the SmPC, the removal of the term 'lung infection', the inclusion of the term 'orthostatic hypertension' and the inclusion of a new footnote listing the preferred terms covered for the ADR of psoriasis. In addition, the MAH took the opportunity of this variation to further clarify the posology in section 4.2 of the SmPC."	Positive Opinion adopted by consensus on 02.12.2021.

Opinion adopted on 02.12.2021.	
Vaborem - meropenem / vaborbactam - EMEA/H/C/004669/II/0010/G Menarini International Operations Luxembourg S.A., Rapporteur: Filip Josephson, "A grouped application including 8 type II variations (C.I.4) and 1 type II variation (C.I.13): Update of section 4.5 of the SmPC based on the results of a series of non-clinical drug-drug interaction studies undertaken with vaborbactam or meropenem. The Package Leaflet has been updated accordingly. In addition, the MAH has submitted non-clinical data on the phototoxicity potential of meropenem from a 3T3 neutral red uptake phototoxicity test." Request for Supplementary Information adopted on 25.11.2021, 11.03.2021.	Request for supplementary information adopted with a specific timetable.
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0090 MCM Vaccine B.V., Rapporteur: Christophe Focke, "Update of section 4.8 of the Summary of Product Characteristics (SmPC) in order to add Convulsions with or without fever with frequency Not known to the list of post-marketing adverse events. The package leaflet (PL) is updated accordingly." Opinion adopted on 02.12.2021.	Positive Opinion adopted by consensus on 02.12.2021.
Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0047 AstraZeneca AB, Rapporteur: Sol Ruiz, "Submission of the final report from MS1222-0004 study "Binding of PF4 to AZD1222 and Purified ChAdOx1" and the Greinacher et al (Greinacher et al 2021) paper, titled "A prothrombotic thrombocytopenic disorder resembling heparin-induced thrombocytopenia following Coronavirus-19 vaccination" listed as a category 3 studies in the RMP."	
Veklury - remdesivir - EMEA/H/C/005622/II/0026/G Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, "Grouped variation updating sections 5.2 and 5.3 of the SmPC in order to add	Request for supplementary information adopted with a specific timetable.

additional pharmacokinetic (PK) data coming from non clinical and clinical studies to fulfil two Post-Authorisation Measures for Veklury: Recommendation (REC) number 4 (non-clinical data to further characterise a previously unidentified metabolite, M27); and REC number 7 (to submit data from additional analysis of the circulating species of remdesivir from the human mass-balance study, GS-US-399-4231). Both were agreed during the initial conditional marketing application (EMEA/H/C/005622)." Request for Supplementary Information adopted on 02.12.2021.	
Veklury - remdesivir - EMEA/H/C/005622/II/0028/G Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, " C.I.4. Grouping variation to update section 5.1 of the SmPC in order to add information related to in vitro testing reports of B.1.1.28 and B.1.617 variants with additional provision of the cell culture resistance report to further understand the antiviral activity of Remdesivir. They are listed as part of the specific obligation (SOB 012) in the Annex II of the renewal procedure EMEA/H/C/005622/R/0015 for Veklury. C.I.13. Grouping variation for the submission of the virology reports for GS-US-540-5773 and GS-US-540-5774 studies and the submission of the ACTT-1 final viral load analysis included as part of the specific obligation (SOB 012) in the Annex II of the renewal procedure EMEA/H/C/005622/R/0015 for Veklury."	
VITRAKVI - larotrectinib - EMEA/H/C/004919/II/0021 Bayer AG, Rapporteur: Filip Josephson, Co-Rapporteur: Alexandre Moreau, "Update of section 5.2 of the SmPC in order to reflect the outcome of an updated analysis of the population pharmacokinetic (PopPk) model based on additional PK sampling in patients aged 1 month to 6 years from study LOXO-TRK-15003 (SCOUT) imposed as a specific obligation (SOB). The MAH is also proposing to delete this SOB from Annex II. The MAH took the opportunity of this variation to introduce corrections to section 4.8 of the SmPC and to Annex II."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 02.12.2021.	
Vocabria - cabotegravir - EMEA/H/C/004976/II/0008 ViiV Healthcare B.V., Rapporteur: Jean-Michel Race, "Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on week 96 results from the clinical study 207966 (ATLAS-2M). This is an open-label, randomized, Phase IIIb trial to demonstrate non-inferior antiviral activity and safety of CAB + RPV Q8W compared with CAB + RPV Q4W. Supporting Cabotegravir (CAB) Long-acting Injectable (LA) + Rilpivirine (RPV) LA every 2 months (Q8W) dosing regimen for the treatment of HIV-1 infection."	
Xagrid - anagrelide - EMEA/H/C/000480/II/0091 Shire Pharmaceuticals Ireland Limited, Rapporteur: Alexandre Moreau, "C.I.4 Update of section 4.4 of the SmPC in order to add a new warning on the risks of fatal thrombotic complications associated with abrupt treatment discontinuation based on New Pharmacovigilance data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to perform a minor editorial change in section 4.2." Request for Supplementary Information adopted on 09.12.2021, 02.09.2021.	Request for supplementary information adopted with a specific timetable.
WS2145 **DuoPlavin-EMEA/H/C/001143/WS2145/0059** **Iscover-EMEA/H/C/000175/WS2145/0145** **Plavix-EMEA/H/C/000174/WS2145/0143** sanofi-aventis groupe, Lead Rapporteur: Bruno Sepodes, "Update of section 4.5 of the SmPC to add the drug-drug interaction between clopidogrel and rosuvastatin based on a review of the available data including literature and the MAH safety database. The package leaflet is updated accordingly." Opinion adopted on 25.11.2021.	Positive Opinion adopted by consensus on 25.11.2021.
WS2154 **CONTROLOC Control-EMEA/H/C/001097/WS2154/0038** **PANTOLOC Control-EMEA/H/C/001100/**	Request for supplementary information adopted with a specific timetable.

WS2154/0043
PANTOZOL Control-EMEA/H/C/001013/ WS2154/0040
SOMAC Control-EMEA/H/C/001098/ WS2154/0039

Takeda GmbH, Lead Rapporteur: Romaldas Mačiulaitis, "C.1.4 - Update section 4.8 of the SmPC to update the existing term "Interstitial nephritis" to "Tubulointerstitial nephritis (TIN)" in line with the updated Company Core Data Sheet.
In addition, section 4.4 of the SmPC for centralised authorised products is updated with the Excipient warning for Sodium as per EMA guideline EMA/CHMP/302620/2017/EN Rev. 1.
The Package Leaflet is updated accordingly.
In addition, the MAH took the opportunity to update the list of local representatives in the PL and to bring the PI in line with the last QRD template (version 10.1).
This procedure also includes NAPs as listed in Annex B."
Request for Supplementary Information adopted on 09.12.2021.

WS2163
Combivir-EMEA/H/C/000190/WS2163/ 0103
Kivexa-EMEA/H/C/000581/WS2163/0093
Trizivir-EMEA/H/C/000338/WS2163/0127

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

B.5.3. CHMP-PRAC assessed procedures

Adenuric - febuxostat - EMEA/H/C/000777/II/0061 Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop, PRAC Rapporteur: Jan Neuhauser, "C.I.4 - Update of sections 4.4, 4.8 and 5.1 of the SmPC based on the final results from study FAST (Febuxostat versus Allopurinol Streamlined Trial) listed as a category 3 study in the RMP; this is an interventional study investigating the cardiovascular safety of febuxostat in comparison with allopurinol in patients with chronic symptomatic hyperuricaemia. The Package Leaflet is updated accordingly. The RMP version 8.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to update the warning relevant to the content of sodium according to the Annex to the European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use'." Request for Supplementary Information adopted on 14.10.2021, 24.06.2021.	
Bosulif - bosutinib - EMEA/H/C/002373/II/0050/G Pfizer Europe MA EEIG, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to reflect results from the studies B1871039 (SOB) and B1871040 (category 3); study B1871039 is A Phase 4 Safety and Efficacy Study of Bosutinib in Patients With Philadelphia Chromosome Positive Chronic Myeloid Leukemia Previously Treated With One or More Tyrosine Kinase Inhibitors and study B1871040 is An Open-Label Bosutinib Treatment Extension Study for Subjects With Chronic Myeloid Leukemia (CML) who Have Previously Participated in Bosutinib Studies B1871006 or B1871008. The Package Leaflet is updated accordingly. The MAH request deletion of the SOB from annex II of the PI and request consideration for switch of the Conditional Marketing Authorisation to a full Marketing Authorisation. The RMP version 6.0 has also been submitted. In addition, the MAH took the	See 9.1

opportunity to update the list of local representatives for Belgium, Luxemburg, Germany and Northern Island in the Package Leaflet. The MAH is also asking the deletion of the product from the additional monitoring list." Request for Supplementary Information adopted on 16.09.2021.	
Bridion - sugammadex - EMEA/H/C/000885/II/0042 Merck Sharp & Dohme B.V., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "C.I.3 type II to update sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to change posology recommendations and update safety, efficacy and pharmacokinetic information in children and adolescents (2-17 years) following EMEA/H/C/0885/P46/025 and based on final results from study P089MK8616. This is a Phase 4 Double-Blinded, Randomized, Active Comparator-Controlled Clinical Trial to Study the Efficacy, Safety and Pharmacokinetics of Sugammadex (MK-8616) for Reversal of Neuromuscular Blockade in Pediatric Participants. In addition, the MAH took the opportunity to implement some minor editorial changes throughout the Product Information (section 4.4 of Annex I and Annex II). The Package Leaflet is updated in accordance and the MAH took the opportunity to update the list of local representatives. Version 7.2 of the RMP has also been submitted to incorporate changes due to the completeness of PN089 and the MAH took the opportunity to update the RMP with information on completed clinical studies PN089, PN146 and PN145 and to implement the RMP GVP Module V Rev 2 template." Request for Supplementary Information adopted on 16.09.2021.	
Caprelsa - vandetanib - EMEA/H/C/002315/II/0043 Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, "C.I.4 Update of section 5.1 of the SmPC in order to update pharmacodynamic information based on interim results from study D4200C00104, listed as a specific obligation in the Annex II. This is an observational study (including a retrospective arm to evaluate the Benefit/Risk of vandetanib (Caprelsa) 300 mg in	See 9.1

RET mutation negative and RET mutation positive patients with symptomatic, aggressive, sporadic, unresectable, locally advanced/ metastatic thyroid cancer (MTC)), to confirm the efficacy and safety of Caprelsa in RET-negative patients with the aim to fulfil SOB001 and convert Caprelsa from conditional to normal Marketing Authorisation. In addition the MAH takes to opportunity to rectify the Dutch translation of the Caprelsa Product Information." Request for Supplementary Information adopted on 24.06.2021, 28.05.2020.	
Cosentyx - secukinumab - EMEA/H/C/003729/II/0076 Novartis Europharm Limited, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Eva A. Segovia, "C.I.4 - Update of sections 4.2 and 5.1 of the SmPC in order to introduce a new posology regimen for adult plaque psoriasis patients and psoriatic arthritis patients with concomitant moderate to severe plaque psoriasis based on the final results from study CAIN457A2324 and exposure-response modelling; this is a randomized, double-blind, multicenter study assessing short (16 weeks) and long-term efficacy (up to 1 year), safety, and tolerability of sub-cutaneous secukinumab in subjects of body weight 90 kg or higher with moderate to severe chronic plaque-type psoriasis; the Package Leaflet is updated accordingly. The RMP version 9.0 has also been submitted." Request for Supplementary Information adopted on 16.09.2021, 24.06.2021.	See 9.1
COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0018 Janssen-Cilag International N.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of an updated RMP version 2.5 in order to include the following: • To include thrombocytopenia (including immune thrombocytopenia) as an important identified risk following the outcome of the signal of Embolic and Thrombotic events (SDA 018.1, EPITT number 19689) and the opinion of procedure EMEA/H/C/005737/II/0006/G • To propose studies aimed at further	Positive Opinion adopted by consensus on 02.12.2021.

characterisation of Thrombosis with Thrombocytopenia syndrome (TTS) and thrombocytopenia, following the outcome of the signal of Embolic and Thrombotic events (SDA 018.1, EPITT number 19689) • To include Guillain-Barré syndrome as an important identified risk and update the RMP accordingly (EMEA/H/C/005737/II/0012) In addition, the MAH took the opportunity to update in the EU-RMP the submission milestone dates for VAC31518COV4001 and VAC31518COV4002 studies." Opinion adopted on 02.12.2021. Request for Supplementary Information adopted on 30.09.2021.	
Dengvaxia - dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171/II/0016/G Sanofi Pasteur, Rapporteur: Christophe Focke, PRAC Rapporteur: Sonja Hrabcik, "Update of section 4.5. of the SmPC to include coadministration data on human papillomavirus (HPV) vaccines and tetanus, diphtheria, and pertussis (Tdap) vaccine from CYD67, CYD71 and CYD66 final study reports respectively (final reports from three MEA studies listed as category 3 studies in the RMP); these studies are focused on immunogenicity and safety of the concomitant administration. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 6.3 is approved with this variation" Opinion adopted on 02.12.2021. Request for Supplementary Information adopted on 10.06.2021, 11.02.2021.	Positive Opinion adopted by consensus on 02.12.2021.
Erleada - apalutamide - EMEA/H/C/004452/II/0017 Janssen-Cilag International N.V., Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Tiphaine Vaillant, "Update of sections 5.3 of the SmPC in order to update non-clinical information based on final results from study TOX11338 listed as PAM (EMEA/H/C/004452/MEA/006); this is a 2-year carcinogenicity study of JNJ-56021927-AAA by oral gavage in rats; The RMP version 4.1 has also been submitted. In addition, the MAH has	Request for supplementary information adopted with a specific timetable.

taken this opportunity to include general information in the RMP regarding study TITAN (PCR3002)." Request for Supplementary Information adopted on 02.12.2021.	
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0068 Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of section 4.4 of the SmPC in order to add baseline monitoring in addition to the current warnings for periodic monitoring of cardiac failure and cardiac arrhythmias in patients receiving ibrutinib. The Package Leaflet is updated accordingly. The RMP version 18.2 has also been submitted." Opinion adopted on 02.12.2021. Request for Supplementary Information adopted on 30.09.2021.	Positive Opinion adopted by consensus on 02.12.2021.
Imraldi - adalimumab - EMEA/H/C/004279/II/0048/G Samsung Bioepis NL B.V., Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Ulla Wändel Liminga"B.II.a.5 (Type II): To introduce an additional concentration of 40 mg/0.4 mL (same 40 mg strength) for the solution for subcutaneous injection in pre-filled syringe (PFS) and pre-filled pen (PFP). B.II.e.5.a.1 (Type IA): To add 2 presentations B.II.e.5.a.1 (Type IA): To add 2 presentations B.II.e.5.a.1 (Type IA): To add 2 presentations B.II.e.5.a.1 (Type IA): To add 2 presentations An updated Risk Management Plan (version 7.0) is provided in relation to this application.	
Lojuxta - lomitapide - EMEA/H/C/002578/II/0046 Amryt Pharmaceuticals DAC, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "To propose an alternative study (LILITH) to the currently agreed protocol for the CAPTURE study. The new study proposes an evaluation of the effect of lomitapide treatment on major adverse cardiovascular events (MACE) in patients with homozygous familial hypercholesterolemia. Consequential submission of an updated RMP (version 6.4) and Annex IID of the Product Information. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template	

version 10.2" Request for Supplementary Information adopted on 22.07.2021, 09.04.2021.	
LUTATHERA - lutetium (177lu) oxodotreotide - EMEA/H/C/004123/II/0030, Orphan Advanced Accelerator Applications, Rapporteur: Janet Koenig, PRAC Rapporteur: Adam Przybylkowski, "Update of the SmPC sections 4.4, 4.8 and 5.1 based on the pivotal Phase III study, NETTER-1. Additionally, updates are proposed in the PI to correct some information based on currently approved data. The PL is updated accordingly. The RMP v. 2.0 has been submitted. The MAH took also the opportunity to update the details of local representatives in the PL."	
Mekinist - trametinib - EMEA/H/C/002643/II/0051 Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: David Olsen, "Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations in hepatic impairment and update pharmacokinetic information based on final results from study MEC116354 listed as a category 3 study in the RMP; this is a Phase I Trial of Single Agent Trametinib (GSK1120212) in Advanced Cancer Patients with Hepatic Dysfunction. The RMP version 18 has also been submitted."	
NINLARO - ixazomib - EMEA/H/C/003844/II/0033, Orphan Takeda Pharma A/S, Rapporteur: Armando Genazzani, PRAC Rapporteur: Annika Folin, "C.I.11 Submission of the final report for the final analysis of OS for study C16010 fulfilling an obligation in the Annex II of the Product Information. This is a phase 3 study to evaluate efficacy and safety of ixazomib in combination with LenDex in adult patients with relapsed and/or refractory multiple myeloma. Section 4.4 is also updated to include a warning about occurrence of Stevens-Johnson syndrome. The Package Leaflet is updated accordingly. An updated RMP (version 7.0) has been submitted. The applicant also took the opportunity to update the list of local representatives." Opinion adopted on 02.12.2021.	Positive Opinion adopted by consensus on 02.12.2021.

Request for Supplementary Information adopted on 28.10.2021, 02.09.2021.

Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0022/G

Alexion Europe SAS, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.4, 4.8 and 5.1 of the SmPC based the final study report from study 14-505 (ANNEXA-4). This is a Prospective, open-label study of andexanet alfa in patients receiving a factor Xa inhibitor who have acute major bleeding to confirm safety and efficacy in patients with acute major bleeds. The provision of this study report fulfils Specific Obligation 001, and as a consequence it has been deleted in the Annex II. The package leaflet was updated accordingly, and the applicant took the opportunity to implement editorial changes in the Annexes. The revised RMP version 2.4 has also been submitted.
Change to the summary of pharmacovigilance system due to change in QPPV."
Request for Supplementary Information adopted on 16.09.2021.

Onpattro - patisiran - EMEA/H/C/004699/II/0022, Orphan

Alnylam Netherlands B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Rhea Fitzgerald, "Type II variation C.I.4 in the Summary of Product Characteristics (SmPC), Labelling or Package Leaflet (PL) due to new quality, preclinical, clinical or pharmacovigilance data: update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC to confirm that the safety profile of pasitiran in liver transplant recipients is comparable to data in patients without liver transplant, based on final results from study ALN-TTR02-008, a global phase 3b, open-label, extension study to evaluate safety, efficacy and pharmacokinetics of patisiran in patients with hereditary transthyretin-mediated amyloidosis (HATTR amyloidosis) with disease progression post-orthotopic liver transplant (OLT). The RMP version 1.1 has also been submitted. In addition, the MAH took the opportunity to make some minor changes to the English PI in SmPC sections 5.1, 6.3 (In line with EMA recommendation from procedure EMEA/H/C/004699/IB/0014), PL sections 2

(minor typographical error changes), 6 (update to contact numbers of local MAH representatives in Cyprus and Malta, and MAH local representative from 'United Kingdom' to 'United Kingdom [Northern Ireland] in line with the QRD template version 10.2) and implement minor linguistic changes and typographical error corrections in the Italian PI translation."	
Praluent - alirocumab - EMEA/H/C/003882/II/0065 sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 5.1 of the SmPC in order to include information on the effect of alirocumab on the neurocognitive function based on final results from the study R727-CL-1532 listed as a category 3 study in the RMP; this is an interventional study to evaluate the neurocognitive function during the treatment, as well as the effect of the medicinal product in comparison with placebo on lipoproteins and to assess the safety and tolerability. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2 and to update the list of local representatives." Opinion adopted on 02.12.2021. Request for Supplementary Information adopted on 02.09.2021.	Positive Opinion adopted by consensus on 02.12.2021.
Pyramax - pyronaridine / artesunate - EMEA/H/W/002319/II/0023/G Shin Poong Pharmaceutical Co., Ltd., Rapporteur: Jean-Michel Race, PRAC Rapporteur: Nathalie Gault, "Grouping of variations providing the final clinical study reports (CSR) of two completed studies: - Study SP-C-021-15: A Phase IIIb/IV cohort event monitoring study conducted in Central Africa to evaluate the safety in patients after the local registration of Pyramax (CANTAM study). This study is a category 3 Required Additional Pharmacovigilance Activity described in the RMP (MEA 013). - SP-C-026-18: A Randomized Open-Label Exploratory Study to Determine The Efficacy of Different Treatment Regimens of Pyramax (Pyronaridine-Artesunate) In Asymptomatic Carriers Of Plasmodium Falciparum	Positive Opinion adopted by consensus on 02.12.2021.

Monoinfections. This non-imposed study was conducted in The Gambia and Zambia and compared asymptomatic subjects with parasitaemia dosed according to the approved label of 3-day dosing with 2-day and 1-day dosing. There have been no new safety findings from the study but the RMP has been updated to reflect its details. As a result of the additional clinical data, corresponding changes to the Product Information (SmPC and PL) are proposed with the Grouping. RMP version 17 has also been submitted, updated to reflect the results of both above-mentioned CSRs, and converted to the new RMP integrated template format (Rev 2.0.1)." Opinion adopted on 02.12.2021. Request for Supplementary Information adopted on 02.09.2021, 06.05.2021, 14.01.2021.	
RAVICTI - glycerol phenylbutyrate - EMEA/H/C/003822/II/0038/G, Orphan Immedica Pharma AB, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Ilaria Baldelli, "Group of variations consisting of: - Submission of the final study report, HPN-100-014 non interventional registry study "Long-Term Registry of Patients with Urea Cycle Disorders (UCDs) conducted in the US". - An update to the RMP (version 7) submitted to remove the important potential risks of carcinogenicity and PAA toxicity. The update to the RMP is based on the review of new and available data including the study report for HPN-100-014 and a new toxicological expert examination of pre-clinical carcinogenicity findings as well as a cumulative review of literature and post marketing data. In accordance with the proposed changes to the RMP, an update of Annex II is requested to waive the imposed condition related to the non-interventional post authorisation safety study (PASS), "European Post-Authorization Registry for RAVICTI (glycerol phenylbutyrate) Oral Liquid in Partnership with the European Registry and Network for Intoxication Type Metabolic Diseases (E-IMD)". The SmPC and Package Leaflet have been updated to delete the information on additional monitoring (including the black triangle)." Request for Supplementary Information adopted	See 9.1

on 22.07.2021.	
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0066 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "C.I.13: Submission of the final report from study WO29635 to fulfil a category 3 study activity (MEA/FSR 007). This is A Phase IB/II study of the safety and pharmacology of Atezolizumab administered with or without Bacille Calmette-Guérin in patients with High Risk Non-Muscle- Invasive Bladder Cancer. The RMP version 22.0 has also been submitted. The RMP has additionally been amended to revise the due date for the submission of the final CSR for study MO39171 (TAIL)." Opinion adopted on 02.12.2021.	Positive Opinion adopted by consensus on 02.12.2021.
Tresiba - insulin degludec - EMEA/H/C/002498/II/0054 Novo Nordisk A/S, Rapporteur: Kristina Dunder, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Annika Folin, "Update of sections 4.6 and 5.1 of the Summary of product characteristics in order to include new clinical data from the pregnancy trial EXPECT conducted for Tresiba. The Package Leaflet is updated in accordance. The RMP version 9.0 is also submitted." Request for Supplementary Information adopted on 02.12.2021.	Request for supplementary information adopted with a specific timetable.
Uptravi - selexipag - EMEA/H/C/003774/II/0034 Janssen-Cilag International N.V., Rapporteur: Martina Weise, PRAC Rapporteur: Nathalie Gault, "Update of section 4.8 of the SmPC to add 'dyspepsia' as a new ADR with frequency 'common', and to include further information on the frequency of 'dyspepsia' and 'anaemia' specific to initial 2-step triple combination therapy, based on the studies AC-065A308 (TRITON) and AC-065A404 (TRACE). AC-065A308 (TRITON) study was a randomized, double-blind, placebo-controlled, parallel-group, Phase 3b, efficacy and safety study comparing triple oral combination therapy (selexipag, macitentan, tadalafil) with double oral combination therapy (placebo, macitentan, tadalafil) in newly diagnosed, treatment-naïve	Request for supplementary information adopted with a specific timetable.

participants with PAH. The AC-065A404 (TRACE) study was a randomized, double-blind, placebo-controlled, parallel-group, exploratory Phase 4 study in participants with PAH to assess the effect of selexipag on daily life physical activity and participant's self-reported symptoms and their impacts. The package leaflet is updated accordingly. A revised RMP version 9.2 was provided as part of the application." Request for Supplementary Information adopted on 02.12.2021.	
WS2098 **Komboglyze-EMEA/H/C/002059/ WS2098/0051** **Onglyza-EMEA/H/C/001039/WS2098/ 0053** AstraZeneca AB, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, "Submission of the final report from study D1680C00016 (MEASURE HF) (listed as a category 3 study in the RMP). This is a 24-week, multicentre, randomised, double-blind, parallel group, placebo-controlled study to investigate the effects of saxagliptin and sitagliptin on cardiac dimensions and function in patients with Type 2 Diabetes Mellitus and Heart Failure. The combined RMP for Komboglyze and Onglyza version 16 has also been submitted." Opinion adopted on 02.12.2021. Request for Supplementary Information adopted on 02.09.2021.	Positive Opinion adopted by consensus on 02.12.2021.

B.5.4. PRAC assessed procedures

PRAC Led **Adasuve - loxapine - EMEA/H/C/002400/II/0033** Ferrer Internacional s.a., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update safety information on Bronchospasm based on final results from study AMDC-204-401 EU PASS (assessed in procedure EMEA/H/C/0002400/II/0032): Post-authorisation Observational Study to Evaluate the Safety of ADASUVE (Staccato loxapine for	Request for supplementary information adopted with a specific timetable.

inhalation) in Agitated Persons in Routine Clinical Care, a category 3 study in the RMP; the Package Leaflet and Labelling 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 02.12.2021.	
PRAC Led **AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0038** sanofi-aventis groupe, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the final PASS OBS12753 study report listed as a category 3 study in the RMP. This is a prospective cohort study of long-term safety of teriflunomide in multiple sclerosis patients in Europe. The updated RMP v 7.1 is proposed." Request for Supplementary Information adopted on 02.12.2021, 30.09.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **COMIRNATY - tozinameran - EMEA/H/C/005735/II/0080** BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of section 4.4 of the SmPC in order to amend an existing warning on anxiety-related reactions to add "numbness" based on the outcome of the Post-Authorisation Measure PAM MEA-002.8 (EMEA/H/C/005735/MEA/002.8, dated 30. September 2021). In addition, the MAH took the opportunity to make minor editorial changes throughout the product information." Request for Supplementary Information adopted on 02.12.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Duavive - estrogens conjugated / bazedoxifene - EMEA/H/C/002314/II/0030** Pfizer Europe MA EEIG, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the final report from study B2311060 listed as a category 3 study in the RMP. This is a non-interventional, post-authorisation safety study of conjugated estrogens/bazedoxifene	Positive Opinion adopted by consensus on 02.12.2021.

(CE/BZA), with the aim to monitor the safety profile of Duavive (CE/BZA) in comparison to estrogen and progestin combination hormone therapy (E+P HT). As a consequence, the warnings on breast cancer and stroke are updated in section 4.4 of the SmPC and section 5.1 of the SmPC was updated to reflect the results of this study. The Package leaflet is updated accordingly." Opinion adopted on 02.12.2021. Request for Supplementary Information adopted on 08.07.2021.	
PRAC Led **Evenity - romosozumab - EMEA/H/C/004465/II/0010** UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 2.0 in order to remove the important identified risk of "immunogenicity", based on the Good Pharmacovigilance Practices (GVP) guidelines, EMA guidance on immunogenicity assessment, and the available non-clinical, clinical and post-marketing data. In addition, following the Pharmacovigilance Risk Assessment Committee (PRAC) recommendation (EMA/PRAC/265359/2021) dated 06 May 2021, the MAH is taking this opportunity to add "cardiac arrythmia" as an important potential risk of romosozumab, update the protocol for the ongoing post authorization safety study (PASS) OP0004 to include cardiac arrhythmias as specific events to monitor, and include a targeted follow-up questionnaire related to cardiac arrhythmias in the RMP Part VII Annex 4. The MAH is also taking this opportunity to introduce minor changes in the PASS protocols of three studies OP0004, OP0005 and OP0006." Request for Supplementary Information adopted on 02.12.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0023** Seqirus Netherlands B.V., Rapporteur: Sol Ruiz, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Update of section 4.6 of the SmPC in order to	Request for supplementary information adopted with a specific timetable.

update information on Pregnancy Registry 130_110B, listed as a category 3 study in the RMP. The PL is updated accordingly. The RMP version 3.1 has also been submitted in order to update information related to the pregnancy study, clinical and post-marketing exposure." Request for Supplementary Information adopted on 02.12.2021.	
PRAC Led **Hemlibra - emicizumab - EMEA/H/C/004406/II/0025** Roche Registration GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Armando Genazzani, "Update of sections 4.4, 4.8 and 5.1 of the Product information concerning immunogenicity and loss of efficacy due to anti-emicizumab antibodies. The RMP (v.3.0) is proposed to be updated accordingly." Request for Supplementary Information adopted on 02.12.2021, 02.09.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Hemlibra - emicizumab - EMEA/H/C/004406/II/0028** Roche Registration GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Armando Genazzani, "Submission of the final study report for BO40853 (Hemlibra Survey to Prescribers and Patients/Carers to Evaluate Awareness, Knowledge, and Compliance to Additional Risk Minimization Measures, listed as a category 3 study in the RMP). An updated RMP (version 4.0) is presented in support of this application," Request for Supplementary Information adopted on 02.12.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Latuda - lurasidone - EMEA/H/C/002713/II/0036** Aziende Chimiche Riunite Angelini Francesco A.C.R.A.F. S.p.A., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "Update of section 4.8 of the SmPC to amend the frequency of ADRs in adults and to add 'syncope' (frequency uncommon) and 'cerebrovascular accident' (frequency rare) following the assessment of the procedure EMEA/H/C/PSUSA/00010114/202010. The	Positive Opinion adopted by consensus on 02.12.2021.

Package Leaflet is updated accordingly. Minor adjustments of the PTs based on the MedDRA definitions were implemented and the ADR 'blood creatine phosphokinase increased' was moved to the SOC Investigations. In addition, the marketing authorisation holder has taken the opportunity to combine all the dosages in a single version of the SmPC, to update the list of local representatives in the PL and to bring the PI in line with the latest QRD template version 10.2 Rev. 1." Opinion adopted on 02.12.2021.	
PRAC Led **Neulasta - pegfilgrastim - EMEA/H/C/000420/II/0116** Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report from study 20170701 listed as a category 3 study in the RMP (MEA-060.5). This is an observational study to assess the effectiveness of the Neulasta patient alert card and to measure medication errors related to the use of the On-Body Injector. Data provided justified additional activity to be included in the Patient Instruction for use in the package leaflet. The MAH took the occasion to amend local representative details for Malta, Germany and to align the PI to the recent QRD template version 10.2. The RMP version 8.0 has also been submitted." Opinion adopted on 02.12.2021. Request for Supplementary Information adopted on 02.09.2021.	Positive Opinion adopted by consensus on 02.12.2021.
PRAC Led **Prolia - denosumab - EMEA/H/C/001120/II/0091/G** Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "- C.I.11.b: Submission of an updated RMP version 28.0 in order to remove osteonecrosis outside the jaw (OOJ) including external auditory canal (OEAC) as an important potential risk. - C.I.11.b: Submission of an updated RMP version 28.0 in order to remove immunogenicity as missing information. - C.I.11.b: Submission of an update RMP version 28.0 in order to introduce changes to	Positive Opinion adopted by consensus on 02.12.2021.

the category 3 PASS-retrospective cohort database study (study 20190038) for the potential increased risk of cardiovascular and cerebrovascular events among women with PMO and men with osteoporosis by adding the study objectives. In addition, the MAH took the opportunity to update the RMP in order to provide the date for the provision of the final study report for study 20190038 and to include the post-marketing exposure data from the last submitted PSUR/PBRER (#13)." Opinion adopted on 02.12.2021.	
PRAC Led **Prolia - denosumab - EMEA/H/C/001120/II/0092** Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report from study 20190038 "Incidence of Cardiovascular and Cerebrovascular Events Among Postmenopausal Women and Men With Osteoporosis Who Initiated Treatment With Denosumab or Zoledronic Acid - a Retrospective Cohort Study". This is an observational PASS listed as category 3 study in the RMP." Opinion adopted on 02.12.2021.	Positive Opinion adopted by consensus on 02.12.2021.
PRAC Led **Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0022** Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Hans Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 2.0 to include clinical safety data from study mRNA-1273 P203 (NCT04649151), a Phase 2/3, randomised, observer-blind, placebo-controlled study evaluating the safety, reactogenicity, and effectiveness of the mRNA-1273 vaccine in healthy adolescents aged ≥ 12 to < 18 years." Request for Supplementary Information adopted on 02.12.2021, 28.10.2021, 02.09.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0028** Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Hans	Request for supplementary information adopted with a specific timetable.

Christian Siersted, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 2.1 to include myocarditis and pericarditis as an important identified risk, as requested by PRAC as an outcome of the myocarditis and pericarditis signal assessment procedure." Request for Supplementary Information adopted on 02.12.2021, 28.10.2021, 02.09.2021.	
PRAC Led **TRISENOX - arsenic trioxide - EMEA/H/C/000388/II/0076** Teva B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "Update of section 4.6 of the SmPC in order to update information on pregnancy and contraception in male patients following the decision and discussion made for EMEA/H/C/PSUSA/00000235/202009. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 02.12.2021.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0040** AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Christophe Focke, "Update of the RMP to version 4.2 in order to: - Add 'Thrombocytopenia, including immune thrombocytopenia' as an important identified risk, as per PRAC outcome of signal assessment procedure on immune thrombocytopenia (EPITT no: 19678); - Add Guillain-Barré Syndrome (GBS) as important identified risk; - Add acute macular neuroretinopathy / acute macular outer retinopathy, paracentral acute middle maculopathy, parasthesia and dysaesthesia in the list of AESIs, as per PRAC outcome of signal assessment procedure on acute macular outer retinopathy (EPITT no: 19703); - Add thrombocytopenia, including immune thrombocytopenia in replacement of 'Thrombocytopenia with associated bleeding' the list of AESIs, as per PRAC outcome of signal assessment procedure on immune thrombocytopenia (EPITT n°: 19678)	Positive Opinion adopted by consensus on 02.12.2021.

- Remove the Enhanced active surveillance (EAS) studies D8111R00003 [EU], D8110R00001 [US], D8111C00004 [UK]); - Add the UK effectiveness study (D8111R00007), as per CHMP conclusion from MEA 010.1; - Add a study D8111R00010 to assess the relationship between the exposure to COVID-19 vaccines and risk of thrombotic thrombocytopenia syndrome. - Update the milestones for study D8111R00006 and correct milestone related to the SAP of Pregnancy registry as well as milestones date related to COV001, COV002, COV003 and COV005." Opinion adopted on 02.12.2021. Request for Supplementary Information adopted on 28.10.2021.	
PRAC Led **VPRIV - velaglucerase alfa - EMEA/H/C/001249/II/0049, Orphan** Takeda Pharmaceuticals International AG, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of final physician data study results for PASS study "Evaluation of the Effectiveness of Risk Minimisation Measures: A Survey among Health Care Professionals and Patient/Caregivers to Assess their Knowledge and Attitudes on Prescribing and Home Administration Conditions of Velaglucerase Alpha (VPRIV) in 6 European Countries" (EUPASS 14255)" Request for Supplementary Information adopted on 02.12.2021, 08.07.2021, 11.02.2021, 26.11.2020.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Vyxeos liposomal - daunorubicin / cytarabine - EMEA/H/C/004282/II/0017, Orphan** Jazz Pharmaceuticals Ireland Limited, Rapporteur: Johanna Lähteenvuo, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, PRAC-CHMP liaison: Bruno Sepodes, "Submission of a final CSR for post-marketing observational study of Vyxeos liposomal to assess the incidence of infusion-related reactions in adult patients. The primary objective of this study is to assess the nature,	Positive Opinion adopted by consensus on 02.12.2021.

incidence, and severity of infusion-related reactions during and for up to one day following the last infusion of a five-day induction course in patients treated with the product. The secondary objective is to assess this information during and for up to one day following the last infusion of a five-day induction course in patients treated with Vyxeos." Opinion adopted on 02.12.2021. Request for Supplementary Information adopted on 08.07.2021, 11.03.2021.	
PRAC Led **Xeljanz - tofacitinib -** **EMEA/H/C/004214/II/0044** Pfizer Europe MA EEIG, Rapporteur: Armando Genazzani, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "C.I.3.b - Update of sections 4.4, 4.8 and 5.1 to add warnings and safety data on serious infections, viral reactivation, non-melanoma skin cancer and fractures. This is based on the final results from study A3921133 listed as a category 3 study in the RMP; this is a post-authorisation safety study conducted to evaluate the safety of tofacitinib 5 mg and 10 mg compared to TNFi in adults' subjects aged ≥50 years with moderately or severely active RA and with at least 1 additional CV risk factor. The Package Leaflet is updated accordingly. The RMP version 21.1 has also been submitted. In addition, the MAH took the opportunity to update the Outer carton (section 4 for oral solution) to include a total volume of 240 mL as requested following the completion of the procedure EMEA/H/C/004214/X/0024/G."	
PRAC Led **WS2064** **Nuwiq-EMEA/H/C/002813/WS2064/0043** **Vihuma-EMEA/H/C/004459/WS2064/0024** Octapharma AB, Lead PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "To provide an updated RMP to remove the completed studies GENA-05 and GENA-15. In addition, the RMP has been updated to GVP Module V Rev.2. No new safety concerns were added." Opinion adopted on 02.12.2021. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 02.12.2021.

on 02.09.2021, 10.06.2021.	
PRAC Led **WS2158** **Exviera-EMEA/H/C/003837/WS2158/0051** **Viekirax-EMEA/H/C/003839/WS2158/0063** AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "To update the Annex IID study milestone due date , for the hepatocellular carcinoma (HCC) recurrence post authorisation safety study (B20-146) following the EMA's recommendation on 6 July 2021. In addition, the MAH is taking the opportunity to introduce few minor linguistic and typographical corrections in the Summary of Product Characteristics (SmPCs) for the Hungarian, Latvian and Romanian translations of the Exviera product information." Opinion adopted on 02.12.2021.	Positive Opinion adopted by consensus on 02.12.2021.

B.5.5. CHMP-CAT assessed procedures

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0005/G, Orphan, ATMP Bristol-Myers Squibb Pharma EEIG, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang	
Libmeldy - atidarsagene autotemcel - EMEA/H/C/005321/II/0004, Orphan, ATMP Orchard Therapeutics (Netherlands) BV, Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege Request for Supplementary Information adopted on 08.10.2021.	
Tecartus - autologous peripheral blood t cells cd4 and cd8 selected and cd3 and cd28 activated transduced with retroviral vector expressing anti-cd19 cd28/cd3-zeta chimeric antigen receptor and cultured - EMEA/H/C/005102/II/0012, Orphan, ATMP Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-	

Berghaus
Request for Supplementary Information adopted on 08.10.2021.

Zolgensma - onasemnogene abeparvovec - EMEA/H/C/004750/II/0020/G, Orphan, ATMP
Novartis Gene Therapies EU Limited, Rapporteur: Carla Herberts, CHMP Coordinator: Johann Lodewijk Hillege

WS2181
Tecartus-EMEA/H/C/005102/WS2181/0014
Yescarta-EMEA/H/C/004480/WS2181/0044
Kite Pharma EU B.V., Lead Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

B.5.6. CHMP-PRAC-CAT assessed procedures

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0009, Orphan, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang, PRAC Rapporteur: Annika Folin, "Update of sections 4.2 and 4.4 of the SmPC, Annex IID and PIL in order to add statements for the use of Abecma exceptionally during shortage of tocilizumab following the "CAT recommendation for the use of CAR-T cell-based therapies in EU during shortages of tocilizumab""

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0047, Orphan, ATMP
Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.2 and 4.4 of the SmPC, Annex IID and PIL (information intended for healthcare professionals) in order to add statements for the use of Kymriah exceptionally during shortage of tocilizumab following the "CAT recommendation for the use of CAR-T cell-based therapies in EU during shortages of tocilizumab"."

WS2206 **Tecartus-EMEA/H/C/005102/WS2206/0015** **Yescarta-EMEA/H/C/004480/WS2206/0045** Kite Pharma EU B.V., Lead Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus, Lead PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2 and 4.4 of the SmPC and Annex IID in order to add statements for the use of Tecartus and Yescarta exceptionally during shortage of tocilizumab following the "CAT recommendation for the use of CAR-T cell-based therapies in EU during shortages of tocilizumab". The RMPs for both products are updated accordingly (version 1.2 for Tecartus and version 5.2 for Yescarta)."	

B.5.7. PRAC assessed ATMP procedures

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

WS2088/G **Brimica Genuair-EMEA/H/C/003969/WS2088/0033/G** **Duaklir Genuair-EMEA/H/C/003745/WS2088/0033/G** AstraZeneca AB, Lead Rapporteur: Ewa Balkowiec Iskra Opinion adopted on 25.11.2021. Request for Supplementary Information adopted on 23.09.2021.	Positive Opinion adopted by consensus on 25.11.2021.
WS2089/G **Bretaris Genuair-EMEA/H/C/002706/WS2089/0047/G** **Eklira Genuair-EMEA/H/C/002211/WS2089/0047/G** AstraZeneca AB, Lead Rapporteur: Ewa Balkowiec Iskra Opinion adopted on 18.11.2021. Request for Supplementary Information adopted on 16.09.2021.	Positive Opinion adopted by consensus on 18.11.2021.
WS2105/G **Corbilta-EMEA/H/C/002785/WS2105/0025/G** **Levodopa/Carbidopa/Entacapone Orion-EMEA/H/C/002441/WS2105/0033/G** **Stalevo-EMEA/H/C/000511/WS2105/0095/G**	Positive Opinion adopted by consensus on 25.11.2021.

Orion Corporation, Lead Rapporteur: Outi Mäki-Ikola Opinion adopted on 25.11.2021. Request for Supplementary Information adopted on 30.09.2021.	
WS2128/G **Eucreas-EMEA/H/C/000807/WS2128/0090/G** **Icandra-EMEA/H/C/001050/WS2128/0093/G** **Zomarist-EMEA/H/C/001049/WS2128/0092/G** Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 11.11.2021.	
WS2131 **Herceptin-EMEA/H/C/000278/WS2131/0176** **Kadcyla-EMEA/H/C/002389/WS2131/0060** **Phesgo-EMEA/H/C/005386/WS2131/0009** Roche Registration GmbH, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 25.11.2021.	Positive Opinion adopted by consensus on 25.11.2021.
WS2139 **Hexacima-EMEA/H/C/002702/WS2139/0121** **Hexyon-EMEA/H/C/002796/WS2139/0125** Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 02.12.2021.	Positive Opinion adopted by consensus on 02.12.2021.
WS2147 **Infanrix hexa-EMEA/H/C/000296/WS2147/0306** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke Opinion adopted on 25.11.2021.	Positive Opinion adopted by consensus on 25.11.2021.
WS2148/G **Hexacima-EMEA/H/C/002702/WS2148/0122/G** **Hexyon-EMEA/H/C/002796/WS2148/0126/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 09.12.2021.	
WS2152 **Aflunov-EMEA/H/C/002094/WS2152/0072** **Foclivia-EMEA/H/C/001208/WS2152/0069** Seqirus S.r.l, Lead Rapporteur: Armando Genazzani Opinion adopted on 18.11.2021. Request for Supplementary Information adopted on 14.10.2021.	Positive Opinion adopted by consensus on 18.11.2021.
WS2161 **Mircera-EMEA/H/C/000739/WS2161/0085** **NeoRecormon-EMEA/H/C/000116/WS2161/0114** Roche Registration GmbH, Lead Rapporteur: Martina Weise Opinion adopted on 02.12.2021.	Positive Opinion adopted by consensus on 02.12.2021.
WS2169 **Mirapexin-EMEA/H/C/000134/WS2169/0101** **Sifrol-EMEA/H/C/000133/WS2169/0092** Boehringer Ingelheim International GmbH, Lead Rapporteur: Sinan B. Sarac, "To update the annexes to bring them in line with QRD version 10.1. In addition, a thorough review of the annexes has been performed and inconsistencies have been corrected."	
WS2171 **Glyxambi-EMEA/H/C/003833/WS2171/0040** **Synjardy-EMEA/H/C/003770/WS2171/0058** Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, "To update section 4.8 of the SmPC and section 4 of the PL to include the side effect 'constipation' in order to align with the Jardiance PI following approval of EMEA/H/C/002677/II/0055." Request for Supplementary Information adopted on 02.12.2021.	Request for supplementary information adopted with a specific timetable.
WS2172 **Aprovel-EMEA/H/C/000141/WS2172/0186** **CoAprovel-EMEA/H/C/000222/WS2172/0205** **Karvea-EMEA/H/C/000142/WS2172/0188** **Karvezide-EMEA/H/C/000221/WS2172/**	Positive Opinion adopted by consensus on 25.11.2021.

0205 sanofi-aventis groupe, Lead Rapporteur: Maria Concepcion Prieto Yerro, Opinion adopted on 25.11.2021.	
WS2178/G **Aflunov-EMEA/H/C/002094/WS2178/0074/G** **Foclivia-EMEA/H/C/001208/WS2178/0071/G** Seqirus S.r.l, Lead Rapporteur: Armando Genazzani Opinion adopted on 09.12.2021.	Positive Opinion adopted by consensus on 09.12.2021.
WS2179/G **Prezista-EMEA/H/C/000707/WS2179/0114/G** **Rezolsta-EMEA/H/C/002819/WS2179/0045/G** **Symtuza-EMEA/H/C/004391/WS2179/0039/G** Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 09.12.2021.	Positive Opinion adopted by consensus on 09.12.2021.
WS2180 **Aprovel-EMEA/H/C/000141/WS2180/0187** **CoAprovel-EMEA/H/C/000222/WS2180/0206** **Karvea-EMEA/H/C/000142/WS2180/0189** **Karvezide-EMEA/H/C/000221/WS2180/0206** sanofi-aventis groupe, Lead Rapporteur: Maria Concepcion Prieto Yerro Opinion adopted on 02.12.2021.	Positive Opinion adopted by consensus on 02.12.2021.

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

PRAC Led **Truvada - emtricitabine / tenofovir disoproxil - EMEA/H/C/000594/II/0173** Gilead Sciences Ireland UC, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, "Removal of the additional risk minimisation measures (aRMMs) for the PrEP indication risks, from the Truvada EU RMP and Annex II of the Truvada PI. With this variation, version 17.2 of the RMP	The MAH withdrew the procedure on 22.11.2021.

(dated 1st July 2021) is submitted." Request for Supplementary Information adopted on 30.09.2021.	

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

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

dimethyl fumarate - EMEA/H/C/006039 treatment of multiple sclerosis	
dimethyl fumarate - EMEA/H/C/006042 treatment of multiple sclerosis,	
tabelecleucel - EMEA/H/C/004577, Orphan, ATMP Atara Biotherapeutics Ireland Limited, treatment of Epstein-Barr virus positive post-transplant lymphoproliferative disease (EBV^+ PTLD)	**Accelerated review**
abaloparatide - EMEA/H/C/005928 treatment of osteoporosis	
spironolactone ph. eur. - EMEA/H/C/005535 Management of refractory oedema	
molnupiravir - EMEA/H/C/005789 Treatment of coronavirus disease 2019 (COVID-19)	
fosdenopterin - EMEA/H/C/005378, Orphan Comharsa Life Sciences Ltd, treatment of molybdenum cofactor deficiency type A	**Accelerated review**
nvx-cov2373 - EMEA/H/C/005808 prevention of coronavirus disease-2019 (COVID-19)	
miglustat - EMEA/H/C/005695, Orphan Amicus Therapeutics Europe Limited, treatment of adults aged 18 years and older with a confirmed diagnosis of Pompe disease	
pirfenidone - EMEA/H/C/005862 treatment of Idiopathic Pulmonary Fibrosis (IPF)	
cipaglucosidase alfa - EMEA/H/C/005703, Orphan	

Amicus Therapeutics Europe Limited, treatment of adults aged 18 years and older with a confirmed diagnosis of Pompe disease	
sugammadex - EMEA/H/C/005935 reversal of neuromuscular blockade induced by rocuronium or vecuronium	
infigratinib - EMEA/H/C/005361, Orphan Helsinn Birex Pharmaceuticals Limited, treatment of cholangiocarcinoma	
vadadustat - EMEA/H/C/005131 Treatment of anaemia	
olipudase alfa - EMEA/H/C/004850, Orphan Genzyme Europe BV, indicated as a disease-modifying enzyme replacement therapy for long-term treatment of non-Central Nervous System (CNS) manifestations of Acid Sphingomyelinase Deficiency (ASMD) in paediatric and adult patients,	**Accelerated review**
sotrovimab - EMEA/H/C/005676 Treatment of coronavirus disease 2019 (COVID-19)	

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

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

amifampridine - EMEA/H/C/005839 treatment of Lambert-Eaton Myasthenic Syndrome List of Questions adopted on 16.09.2021.
dimethyl fumarate - EMEA/H/C/005956 treatment of multiple sclerosis List of Questions adopted on 14.10.2021.
dimethyl fumarate - EMEA/H/C/005955 treatment of multiple sclerosis List of Questions adopted on 14.10.2021.
Sogroya - somapacitan - EMEA/H/C/005030/X/0001/G, Orphan Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber"Extension application to add a new

strength of 5 mg/1.5 mL (3.3 mg/mL) grouped with a Type II Quality variation RMP was updated (version 2.0) accordingly.
Type II variation (B.II.b.1.c)
Type IA variation (B.II.d.1.a)
List of Questions adopted on 14.10.2021.

capmatinib - EMEA/H/C/004845
treatment of non-small cell lung cancer (NSCLC)
List of Questions adopted on 16.09.2021.

insulin aspart - EMEA/H/C/005635
treatment of diabetes mellitus
List of Questions adopted on 16.09.2021.

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

Defitelio - defibrotide - EMEA/H/C/002393/S/0057, Orphan
Gentium S.r.l., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Obizur - susoctocog alfa - EMEA/H/C/002792/S/0044
Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski

Vedrop - tocofersolan - EMEA/H/C/000920/S/0041
Recordati Rare Diseases, Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Melinda Palfi

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

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

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

Fampyra - fampridine - EMEA/H/C/002097/R/0050

Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Liana Gross-Martirosyan

Imraldi - adalimumab - EMEA/H/C/004279/R/0050

Samsung Bioepis NL B.V., Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Daniela Philadelphy, PRAC Rapporteur: Ulla Wändel Liminga

Lorviqua - lorlatinib - EMEA/H/C/004646/R/0019

Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Armando Genazzani, PRAC Rapporteur: Nikica Mirošević Skvrce

Mavenclad - cladribine - EMEA/H/C/004230/R/0022

Merck Europe B.V., Rapporteur: Sinan B. Sarac, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Ondexxya - andexanet alfa - EMEA/H/C/004108/R/0025

Alexion Europe SAS, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (h5n1) (live attenuated, nasal) - EMEA/H/C/003963/R/0047

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

Rubraca - rucaparib - EMEA/H/C/004272/R/0030

Clovis Oncology Ireland Limited, Rapporteur: Blanca Garcia-Ochoa, PRAC Rapporteur: Annika Folin

Rydapt - midostaurin - EMEA/H/C/004095/R/0023, Orphan

Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Ingrid Wang, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Tecentriq - atezolizumab - EMEA/H/C/004143/R/0069

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

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

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

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

B.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

Buvidal - buprenorphine - EMEA/H/C/004651/II/0017
Camurus AB, Rapporteur: Peter Kiely, PRAC Rapporteur: Tiphaine Vaillant, "To add the new therapeutic indication of treatment of moderate to severe chronic pain in patients with opioid dependence. As a consequence, sections 4.1, 4.2, 4.5, 5.1 and 6.6 of the SmPC and sections 1, 3 and Instruction for use of the PL are updated accordingly. The updated RMP version 2.1 has also been submitted."

Eylea - aflibercept - EMEA/H/C/002392/II/0077/G
Bayer AG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Nathalie Gault"C.I.6 (Extension of indication) Extension of indication to include the paediatric indication retinopathy of prematurity (ROP) for Eylea; as a consequence, sections 2, 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Separate Package Leaflet is proposed for the guardians of preterm babies. Version 32.1 of the RMP has also been submitted. B.IV.1.a.3

LIBTAYO - cemiplimab - EMEA/H/C/004844/II/0026

Regeneron Ireland Designated Activity Company (DAC), Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Menno van der Elst, "Extension of indication to include monotherapy treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy for Libtayo; sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3 of the RMP has also been submitted."

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

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

RETSEVMO - selpercatinib - EMEA/H/C/005375/II/0011

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

Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) -

EMEA/H/C/005791/II/0041
Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, "Extension of indication to include use in children 6-11 years of age for Spikevax, based on data from study mRNA-1273-P204, an ongoing Phase 2/3, 2-part, open-label, dose-escalation, age de-escalation and subsequent randomized, observer-blind, placebo-controlled expansion study to evaluate the safety, tolerability, reactogenicity, and effectiveness of mRNA-1273 in healthy children; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance."

Yescarta - axicabtagene ciloleucel - EMEA/H/C/004480/II/0046, Orphan, ATMP
Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Claire Beuneu, CHMP Coordinators: Jan Mueller-Berghaus and Karin Janssen van Doorn, PRAC Rapporteur: Anette Kirstine Stark, "Extension of indication to include treatment of adult patients with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) for Yescarta; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 5.3 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the product information with minor editorial changes."
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0027
Baxalta Innovations GmbH, Rapporteur: Andrea Laslop

Alymsys - bevacizumab - EMEA/H/C/005286/II/0005
Mabxience Research SL, Rapporteur: Christian

Gartner	
Apidra - insulin glulisine - EMEA/H/C/000557/II/0088/G Sanofi-Aventis Deutschland GmbH, Rapporteur: Sinan B. Sarac	
Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0157/G Amgen Europe B.V., Rapporteur: Martina Weise	
Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0158 Amgen Europe B.V., Rapporteur: Martina Weise	
Bexsero - meningococcal group b vaccine (recombinant, component, adsorbed) - EMEA/H/C/002333/II/0106 GSK Vaccines S.r.l, Rapporteur: Kristina Dunder	
Bimzelx - bimekizumab - EMEA/H/C/005316/II/0003/G UCB Pharma S.A., Rapporteur: Peter Kiely	
Bimzelx - bimekizumab - EMEA/H/C/005316/II/0004 UCB Pharma S.A., Rapporteur: Peter Kiely	
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0086 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	See B.5.1
COMIRNATY - tozinameran - EMEA/H/C/005735/II/0089 BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson	See B.5.1
COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0037 Janssen-Cilag International N.V., Rapporteur: Christophe Focke	
Darzalex - daratumumab - EMEA/H/C/004077/II/0056/G, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac	
Erbitux - cetuximab - EMEA/H/C/000558/II/0092 Merck Europe B.V., Rapporteur: Filip Josephson	
Febuxostat Mylan - febuxostat - EMEA/H/C/004374/II/0012 Mylan Pharmaceuticals Limited, Generic,	

Generic of Adenuric, Rapporteur: Elita Poplavska

Fluad Tetra - influenza vaccine (surface antigen, inactivated, adjuvanted) - EMEA/H/C/004993/II/0021
Seqirus Netherlands B.V., Rapporteur: Sol Ruiz

Hepcludex - bulevirtide - EMEA/H/C/004854/II/0009/G, Orphan
Gilead Sciences Ireland Unlimited Company, Rapporteur: Filip Josephson

Hepsera - adefovir dipivoxil - EMEA/H/C/000485/II/0087
Gilead Sciences Ireland UC, Rapporteur: Jean-Michel Race

ILARIS - canakinumab - EMEA/H/C/001109/II/0078
Novartis Europharm Limited, Rapporteur: Jan Mueller-Berghaus

Infanrix hexa - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and haemophilus type B conjugate vaccine (adsorbed) - EMEA/H/C/000296/II/0309/G
GlaxoSmithkline Biologicals SA, Rapporteur: Christophe Focke

Insulin lispro Sanofi - insulin lispro - EMEA/H/C/004303/II/0014/G
sanofi-aventis groupe, Rapporteur: Outi Mäki-Ikola

Invokana - canagliflozin - EMEA/H/C/002649/II/0058
Janssen-Cilag International NV, Rapporteur: Martina Weise

Lamzede - velmanase alfa - EMEA/H/C/003922/II/0023/G, Orphan
Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege

Leqvio - inclisiran - EMEA/H/C/005333/II/0008
Novartis Europharm Limited, Rapporteur: Martina Weise

Memantine Mylan - memantine / memantine hydrochloride - EMEA/H/C/002660/II/0018
Mylan Pharmaceuticals Limited, Generic,

Generic of Ebixa, Rapporteur: Maria Concepcion Prieto Yerro

Menveo - meningococcal group a, c, w135 and y conjugate vaccine - EMEA/H/C/001095/II/0106/G
GSK Vaccines S.r.l, Rapporteur: Johann Lodewijk Hillege

Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0023/G, Orphan
Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac

Natpar - parathyroid hormone - EMEA/H/C/003861/II/0035, Orphan
Takeda Pharmaceuticals International AG, Rapporteur: Karin Janssen van Doorn

Nordimet - methotrexate - EMEA/H/C/003983/II/0021/G
Nordic Group B.V., Rapporteur: Bruno Sepodes

Nplate - romiplostim - EMEA/H/C/000942/II/0081/G
Amgen Europe B.V., Rapporteur: Maria Concepcion Prieto Yerro

Onivyde pegylated liposomal - irinotecan hydrochloride trihydrate - EMEA/H/C/004125/II/0029/G, Orphan
Les Laboratoires Servier, Rapporteur: Filip Josephson

Oyavas - bevacizumab - EMEA/H/C/005556/II/0004
STADA Arzneimittel AG, Duplicate, Duplicate of Alymsys, Rapporteur: Christian Gartner

Polivy - polatuzumab vedotin - EMEA/H/C/004870/II/0013/G, Orphan
Roche Registration GmbH, Rapporteur: Alexandre Moreau

Polivy - polatuzumab vedotin - EMEA/H/C/004870/II/0013/G, Orphan
Roche Registration GmbH, Rapporteur: Alexandre Moreau

POTELIGEO - mogamulizumab - EMEA/H/C/004232/II/0013/G, Orphan
Kyowa Kirin Holdings B.V., Rapporteur: Paula Boudewina van Hennik

Qarziba - dinutuximab beta - EMEA/H/C/003918/II/0035/G, Orphan

EUSA Pharma (Netherlands) B.V., Rapporteur: Paula Boudewina van Hennik	
Rekovelle - follitropin delta - EMEA/H/C/003994/II/0030 Ferring Pharmaceuticals A/S, Rapporteur: Jean-Michel Race	
Retacrit - epoetin zeta - EMEA/H/C/000872/II/0108 Pfizer Europe MA EEIG, Rapporteur: Martina Weise	
RoActemra - tocilizumab - EMEA/H/C/000955/II/0106/G Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus	
Rybelsus - semaglutide - EMEA/H/C/004953/II/0020 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege	
SIBNAYAL - potassium citrate / potassium hydrogen carbonate - EMEA/H/C/005407/II/0002/G Advicenne, Rapporteur: Johann Lodewijk Hillege	
Skyrizi - risankizumab - EMEA/H/C/004759/II/0019/G AbbVie Deutschland GmbH & Co. KG, Rapporteur: Peter Kiely	
Soliris - eculizumab - EMEA/H/C/000791/II/0118/G, Orphan Alexion Europe SAS, Rapporteur: Blanca Garcia-Ochoa	
Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0043/G Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus	See B.5.1
Tigecycline Accord - tigecycline - EMEA/H/C/005114/II/0002/G Accord Healthcare S.L.U., Generic, Generic of Tygacil, Rapporteur: Daniela Philadelphy	
Toviaz - fesoterodine - EMEA/H/C/000723/II/0065/G Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro	
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA),	

poliomyelitis (inact.) and haemophilus type B conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0093/G
MCM Vaccine B.V., Rapporteur: Christophe Focke

Xolair - omalizumab - EMEA/H/C/000606/II/0114
Novartis Europharm Limited, Rapporteur: Kristina Dunder

Zercepac - trastuzumab - EMEA/H/C/005209/II/0015/G
Accord Healthcare S.L.U., Rapporteur: Sol Ruiz

Zercepac - trastuzumab - EMEA/H/C/005209/II/0016
Accord Healthcare S.L.U., Rapporteur: Sol Ruiz

Zutectra - human hepatitis b immunoglobulin - EMEA/H/C/001089/II/0051
Biotest Pharma GmbH, Rapporteur: Jan Mueller-Berghaus

WS2177/G
Nilemdo-EMEA/H/C/004958/WS2177/0018/G
Nustendi-EMEA/H/C/004959/WS2177/0020/G
Daiichi Sankyo Europe GmbH, Lead Rapporteur: Johann Lodewijk Hillege

WS2188/G
Hexacima-EMEA/H/C/002702/WS2188/0124/G
Hexyon-EMEA/H/C/002796/WS2188/0128/G
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

WS2189
Advate-EMEA/H/C/000520/WS2189/0113
ADYNOVI-EMEA/H/C/004195/WS2189/0026
Takeda Manufacturing Austria AG, Lead Rapporteur: Jan Mueller-Berghaus

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

ADYNOVI - rurioctocog alfa pegol - EMEA/H/C/004195/II/0028

Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, "Update of section 4.8 of the SmPC in order to add ''Urticaria'' to the list of adverse drug reactions (ADRs) with frequency ''common''. The Package Leaflet is updated accordingly."

Alecensa - alectinib - EMEA/H/C/004164/II/0037/G

Roche Registration GmbH, Rapporteur: Filip Josephson, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add a new warning, dose modification advice and description of the known ADR haemolytic anaemia based on an updated Drug Safety Report; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce editorial updates in the Maltese and Romanian product information. Moreover, the ATC code for alectinib is being updated from L01XE36 to L01ED03."

AYVAKYT - avapritinib - EMEA/H/C/005208/II/0014, Orphan

Blueprint Medicines (Netherlands) B.V., Rapporteur: Blanca Garcia-Ochoa, "Submission of the final report from study BLU-285-1101 listed as a Specific Obligation in the Annex II of the Product Information. This is an interventional Phase 1 study, designed to evaluate the safety, tolerability, PK, pharmacodynamics, and preliminary antineoplastic activity of avapritinib administered orally in patients with unresectable GIST or other relapsed or refractory solid tumours. The Annex II is updated accordingly."

Blenrep - belantamab mafodotin - EMEA/H/C/004935/II/0006/G, Orphan

GlaxoSmithKline (Ireland) Limited, Rapporteur: Johanna Lähteenvuo, "C.I.4 Update of section 4.4 of the SmPC in order to add a new warning on pneumonitis based on reports from the GSK safety database and clinical trials.
C.I.4 Update of section 4.8 of the SmPC in order to add albuminuria to the list of adverse drug reactions (ADRs) with frequency common based on a safety review by the MAH.
The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to perform minor editorial changes."

Cometriq - cabozantinib - EMEA/H/C/002640/II/0049, Orphan Ipsen Pharma, Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning on hypertension and add hypertensive crisis to the list of adverse drug reactions (ADRs) with frequency not known based on literature review and post-marketing and clinical data. The Package Leaflet is updated accordingly."	
COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0033 Janssen-Cilag International N.V., Rapporteur: Christophe Focke, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to introduce an homologous booster dose (second dose) of COVID-19 vaccine Janssen based on interim efficacy, immunogenicity and safety results from different clinical studies including the two randomised, double blind, placebo-controlled Phase 3 studies COV3001 and COV3009. In addition, an update to introduce a heterologous booster dose of COVID-19 vaccine Janssen following completion of a primary vaccination with an approved mRNA COVID-19 vaccine is introduced based on immunogenicity and safety interim results from the phase 1/2 study DMID 21-0012. In addition, the MAH took the opportunity to update the efficacy data for the primary vaccination schedule based on final analysis from study COV3001. The Package Leaflet is updated accordingly."	See B.5.2 and 9.1
Dapivirine Vaginal Ring 25 mg - dapivirine - EMEA/H/W/002168/II/0014/G International Partnership for Microbicides Belgium AISBL, Rapporteur: Paula Boudewina van Hennik, "C.I.13: Submission of the study report from study MTN-020 (Version 2.0). This is a multicenter, randomized, double-blind, placebo-controlled Phase III safety and effectiveness trial of a vaginal matrix ring containing dapivirine for the prevention of HIV-1 infection in women. C.I.13: Submission of the Clinical Virology Report (Version 4.0). This report describes virologic characterisation of virus from HIV-1 seroconversion events during double-blind, placebo-controlled, randomized, multicenter	

Phase III clinical trials evaluating the safety and efficacy of Dapivirine Vaginal Ring."

Dovprela - pretomanid - EMEA/H/C/005167/II/0008, Orphan

Mylan IRE Healthcare Limited, Rapporteur: Filip Josephson, "Submission of the final report from study Nix-TB-(B-L-Pa) listed as a Specific Obligation the Annex II of the Product Information. This is a phase 3 open-label trial assessing the safety and efficacy of bedaquiline plus pretomanid plus linezolid in subjects with pulmonary infection of either extensively drug-resistant tuberculosis (XDR-TB) or treatment intolerant/non-responsive multi-drug resistant tuberculosis (MDR-TB). The Annex II is updated accordingly."

Eylea - aflibercept - EMEA/H/C/002392/II/0076

Bayer AG, Rapporteur: Alexandre Moreau, "Submission of the final report from study AZURE, a randomised PAES in patients with neovascular (wet) AMD with the primary objective of comparing the standard regime of injections every 8 weeks with a reactive regimen based on visual and anatomic outcomes, based on a CHMP approved protocol."

Eylea - aflibercept - EMEA/H/C/002392/II/0078

Bayer AG, Rapporteur: Alexandre Moreau, "C.I.4
Update of section 6.6 of the SmPC in order to add a cautionary statement for the Eylea pre-filled syringe.; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2, for a text reduction, and to correct a typo."

Fasenra - benralizumab - EMEA/H/C/004433/II/0041

AstraZeneca AB, Rapporteur: Fátima Ventura, "Update of section 5.1 of the SmPC in order to update efficacy information based on the final results from study D3250C00065 (PONENTE); this is a multicenter, open-label, Phase IIIb efficacy and safety study of benralizumab 30 mg administered subcutaneously to reduce oral corticosteroid use in adult patients with severe

eosinophilic asthma on high-dose inhaled corticosteroid plus long-acting β2 agonist and chronic oral corticosteroid therapy. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet."

IMCIVREE - setmelanotide - EMEA/H/C/005089/II/0003, Orphan

Rhythm Pharmaceuticals Netherlands B.V., Rapporteur: Karin Janssen van Doorn, "Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations in patients with renal impairment, based on final results from study RM-493-029, a Phase I, open-label, single-dose study to evaluate the pharmacokinetics of setmelanotide in subjects with varying degrees of renal impairment; with secondary objectives to evaluate the safety and tolerability of a single dose of setmelanotide administered subcutaneously in subjects with varying degrees of renal impairment. The Package Leaflet is updated accordingly."

JEMPERLI - dostarlimab - EMEA/H/C/005204/II/0007

GlaxoSmithKline (Ireland) Limited, Rapporteur: Blanca Garcia-Ochoa, "Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update dose modifications recommendations in immune related adverse reactions, amend existing warnings, and add further immune-related ADRs to the list of adverse drug reactions (ADRs), with different frequencies, based on data from company sponsored trials and literature. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to remove information on Polysorbate 80 and update the list of local representatives in the Package Leaflet."

Myozyme - alglucosidase alfa - EMEA/H/C/000636/II/0087

Genzyme Europe BV, Rapporteur: Alexandre Moreau, "Update of section 4.8 of the SmPC in order to add palpitations, asthenia, malaise, feeling cold and blood pressure decreased to the list of adverse drug reactions (ADRs) with frequency "not-known" following the Final Assessment Report for the Post-Authorisation Measure MEAs 024.13 and 0.25.13 (the 2019 Pompe Disease Registry Annual Report) dated 15 October 2020; the Package Leaflet is

updated accordingly. In addition, the MAH took the opportunity to update section 5.1 of the SmPC to update the internet website address of the Pompe Registry."

Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0133

Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, "- to remove rice cereal from the food compatibility list in the "Instructions for use"- "A) Administration of Pradaxa coated granules with soft foods" of the Package Leaflet for Pradaxa coated granules in sachets based on long term stability results and in-use food compatibility study."

REKAMBYS - rilpivirine - EMEA/H/C/005060/II/0010

Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, "Update of section 4.8 (Table 6) of the SmPC in order to update the adverse reactions section, adding information regarding the majority of pyrexia events having a close temporal association with injections (reported within one week of injections). Based on the data analysis from clinical trials study 201585 FLAIR, 201585 ATLAS and 207966 ATLAS-2M. The Package Leaflet (Section 4) is updated accordingly."

RINVOQ - upadacitinib - EMEA/H/C/004760/II/0014

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, "C.I.4 - Update of section 5.1 of the SmPC in order to update efficacy information based on interim results (Week 156) from studies M14-465 and M13-545; these are randomized phase 3, double blind studies to evaluate the long-term safety, tolerability and efficacy of upadacitinib in subjects with Rheumatoid Arthritis. In addition, the MAH took the opportunity to introduce editorial changes in section 5.1 of the SmPC."

Siklos - hydroxycarbamide - EMEA/H/C/000689/II/0051

Addmedica S.A.S., Rapporteur: Karin Janssen van Doorn, "C.I.3.b
Update of section 5.1 of the SmPC with the available paediatric data from the studies NOHARM and Escort HU according to the PAM-Leg 34."

Spikevax - COVID-19 mRNA vaccine (nucleoside-modified) - EMEA/H/C/005791/II/0042 Moderna Biotech Spain, S.L., Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include information on heterologous boosting using a 50 ug dose of Spikevax to boost subjects that have previously completed a primary vaccination series with any authorised COVID-19 vaccine, based on data from the DMID Study 21-0012, a Phase 1/2 heterologous SARS-CoV-2 vaccine dosing (mRNA-1273 booster) study of the various vaccines authorized in the US under Emergency Use Authorisation in participants ≥ 18 years old (NCT04889209). In addition, the MAH took the opportunity to make minor editorial changes/corrections throughout the product information."	See B.5.2 and 9.1
Tysabri - natalizumab - EMEA/H/C/000603/II/0131 Biogen Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, "C.I.4 Type II Update of sections 5.1 and 5.2 of the SmPC in order to update efficacy and pharmacokinetic information based on final results from study 101MS329 (NOVA) part 1. This is a randomized, controlled phase 3b study of efficacy, safety and tolerability of 6-Week Extended Interval Dosing (EID) of Natalizumab in subjects with Relapsing-Remitting Multiple Sclerosis Switching From Treatment With 4-Week Natalizumab Standard Interval Dosing (SID) in Relation to Continued SID Treatment."	
Tyverb - lapatinib - EMEA/H/C/000795/II/0072/G Novartis Europharm Limited, Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC in order to add skin fissures to the list of adverse drug reactions (ADRs) with frequency common, following recently analysed safety data regarding skin fissures. The Package Leaflet is updated accordingly. The ATC code is also updated."	
Verzenios - abemaciclib - EMEA/H/C/004302/II/0021 Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to include second OS interim results	

from study MONARCH 3; this is a randomised, double blind, placebo-controlled phase 3 study of Nonsteroidal Aromatase Inhibitors (Anastrozole or Letrozole) plus LY2835219, a CDK4/6 Inhibitor, or Placebo in Postmenopausal Women with Hormone Receptor-Positive, HER2-Negative Locoregionally Recurrent or Metastatic Breast Cancer with No Prior Systemic Therapy in this Disease Setting"	
WS2170 **OPDIVO-EMEA/H/C/003985/WS2170/0114** **Yervoy-EMEA/H/C/002213/WS2170/0094** Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy information based on 5 years follow-up OS data from study CA209214; this is a phase 3, randomised, open-label study in previously untreated, intermediate/poor risk advanced RCC."	
WS2174 **Hexacima-EMEA/H/C/002702/WS2174/0123** **Hexyon-EMEA/H/C/002796/WS2174/0127** Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus, "Update of section 4.5 of the SmPC in order to add drug-drug interaction information regarding the co-administration of Hexyon / Hexacima with varicella vaccines based on a re-analysis of the A3L15 clinical trial varicella serological data, submitted in the initial CTD dossier. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to correct some typo errors in the SmPC and PL."	
WS2183 **Infanrix hexa-EMEA/H/C/000296/WS2183/0310** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Christophe Focke, "Update of sections 2 and 4.3 of the SmPC for Infanrix Hexa in order to remove the residue formaldehyde. The PL is updated accordingly. Moreover, these sections are also been updated for the removal of some residues currently mentioned in the Product Information (PI) of	

some of GSK's DTPa/dTpa combined vaccines (NAPs). In addition, the MAH took the opportunity to align the PI to the Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal product for human use" (sections 2, 4.4 and 6.1 of the SmPC). The MAH also took the opportunity to introduce some additional minor changes to the PI and to update the list of local representatives in the Package Leaflet."

B.6.10. CHMP-PRAC assessed procedures

Cablivi - caplacizumab - EMEA/H/C/004426/II/0035, Orphan Ablynx NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Jan Neuhauser, "Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning on increased risk of bleeding and add blood and lymphatic system disorders to the list of adverse drug reactions (ADRs) with frequency not known based on a safety evaluation report; the Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted."
Deltyba - delamanid - EMEA/H/C/002552/II/0053, Orphan Otsuka Novel Products GmbH, Rapporteur: Christophe Focke, PRAC Rapporteur: Laurence de Fays, "Update of section 4.8 of the SmPC in order to update the list of adverse drug reactions (ADRs table) following the development of an improved methodology to identify relevant ADRs likely attributable to delamanid. The section 4 of the Package Leaflet is updated accordingly. The RMP version 3.6 has also been submitted."
ELZONRIS - tagraxofusp - EMEA/H/C/005031/II/0009, Orphan Stemline Therapeutics B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Menno van der Elst, "Submission of the final report from study 20255431 (CRL-263114) 'Characterization of fixed choroid plexus samples from primate study MPI-2231-007 by Immunohistochemistry with DT, CD123, IL-3 and IgG' (MEA002) listed as a category 3 study in the RMP. This is a non-interventional, post-

authorisation study on blood brain barrier (BBB) models in order to determine a potential toxicity biomarker to further investigate the risk of choroid plexus lesions. The RMP version 2.0 has also been submitted."

Enbrel - etanercept - EMEA/H/C/000262/II/0246

Pfizer Europe MA EEIG, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "Update of section 5.1 of the SmPC in order to update clinical information based on final results obtained from the clinical paediatric study B1801023 (CLIPPER 2). The RMP version 7.5 has also been submitted."

Halaven - eribulin - EMEA/H/C/002084/II/0060

Eisai GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "Update of sections 4.2, 5.1 and 5.2 of the SmPC in order to update efficacy and pharmacokinetic information based on results from clinical studies E7389-A001-113, E7389-G000-223 and E7389-G000-213 in the paediatric population (6 months to <18 years); the Package Leaflet is updated accordingly. The RMP version 6.0 has also been submitted."

IBRANCE - palbociclib - EMEA/H/C/003853/II/0037

Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark, "Submission of an updated RMP version 1.8 in order to remove the Important Potential Risk Hyperglycaemia based on the study results from A5481027, a PAM adopted at the initial MA; this is a multicentre, randomized, double-blind, phase 3 study of palbociclib plus letrozole versus placebo plus letrozole for the treatment of previously untreated Asian postmenopausal women with ER-positive, HER2-negative advanced breast cancer to evaluate the effect of palbociclib on hyperglycaemia - category 3 Study."

Imbruvica - ibrutinib - EMEA/H/C/003791/II/0069

Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of the SmPC section 4.4 to include information on fatal and serious

cardiac arrythmias and cardiac failure, relevant warnings and periodical monitoring of patients- following a safety assessment for increased risk of sudden death/cardiac death with the use of ibrutinib. Section 2 of the PL has been updated accordingly. Typographical errors have been corrected throughout the PI. The revised RMP version 11 has been submitted."

Lemtrada - alemtuzumab - EMEA/H/C/003718/II/0038

Sanofi Belgium, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, "Update of sections 4.4 and 4.8 of the SmPC to add Adult Onset Still's Disease (AOSD) to the list of adverse drug reactions (ADRs) with frequency not known, based on a signal validated during a routine pharmacovigilance surveillance; the Package Leaflet is updated accordingly. The MAH took the opportunity to update the list of local representatives in the Package Leaflet. The RMP v.9.0 submitted to include AOSD; and to remove the PASS study OBS13436 (Pregnancy Registry)."

Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0024, Orphan

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

Nerlynx - neratinib - EMEA/H/C/004030/II/0027

Pierre Fabre Medicament, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Menno van der Elst, "Update of section 5.1 of the SmPC in order to update the pharmacokinetic information with descriptive diarrhoea characteristics based on final results from study PUMA-NER-6201 (CONTROL), listed as a category 3 study in the

RMP; this is an Open-Label Study to Characterize the Incidence and Severity of Diarrhea in Patients with Early Stage HER2+ Breast Cancer Treated with Neratinib and Loperamide. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to introduce editorial updates in section 4.2 of the SmPC."

Zejula - niraparib - EMEA/H/C/004249/II/0033, Orphan

GlaxoSmithKline (Ireland) Limited, Rapporteur: Ingrid Wang, PRAC Rapporteur: Jan Neuhauser, "Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning and add MDS/AML to the list of adverse drug reactions (ADRs) with frequency common, and update of section 5.1 based on final results from NOVA study (213356); this is a Phase 3 Randomized Double-Blind Trial of Maintenance with Niraparib Versus Placebo in Patients with Platinum Sensitive Ovarian Cancer. In addition, the MAH 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."

WS2141
Ozempic-EMEA/H/C/004174/WS2141/0024
Rybelsus-EMEA/H/C/004953/WS2141/0018

Novo Nordisk A/S, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Annika Folin, "Submission of the final report from study NN9535-4386 (SUSTAIN-11), listed as a category 3 study in the RMP. This is a 52-week, multi-centre, multinational, open-label, active controlled, two armed, parallel, randomised trial undertaken to investigate the effect on glycaemic control, body weight, safety and health-related quality of life of once-weekly semaglutide s.c. vs insulin aspart three times daily, both as add-on to metformin and optimised insulin glargine U100 treatment in subjects with inadequately controlled T2DM. The RMP version 7.0 has also been submitted."

B.6.11. PRAC assessed procedures

PRAC Led

Calquence - acalabrutinib - EMEA/H/C/005299/II/0011

AstraZeneca AB, Rapporteur: Filip Josephson, PRAC Rapporteur: Željana Margan Koletić, PRAC-CHMP liaison: Selma Arapovic Dzakula, "Submission of an updated RMP version 3 in order to add hepatotoxicity as an important potential risk to the safety concerns."

PRAC Led

Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0114

GlaxoSmithkline Biologicals SA, Rapporteur: Christophe Focke, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Karin Janssen van Doorn, "Submission of the final report from study EPI-HPV-048 listed as a category 3 study in the RMP. This surveillance study is part of two-phase national HPV surveillance programme that was initiated in the UK by the Health Protection Agency in order to evaluate the impact of HPV vaccination on HPV type replacement. The study aimed to assess the prevalence of type-specific HPV deoxyribonucleic acid (DNA) in young women in England since HPV immunisation using Cervarix was introduced. In addition, the MAH has included for information the protocol of study EPI-HPV-099 to address the safety concern "Impact and effectiveness against anal lesions and cancer. The RMP version 25 has also been submitted."

PRAC Led

COMIRNATY - tozinameran - EMEA/H/C/005735/II/0087

BioNTech Manufacturing GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 2.6 to include data from the booster/third dose, including data in patients who have undergone a solid organ transplantation, following the outcomes of procedures EMEA/H/C/005735/II/0062 (third dose in immunocompromise as part of the primary vaccination) and EMEA/H/C/005735/II/0067 (booster dose).

The MAH takes the opportunity to update the RMP regarding the discontinuation of enrolment in study C4591015 (phase 2/3 study to evaluate the safety, tolerability, and immunogenicity in healthy pregnant women 18 years of age and older) and the CSR milestones."	
PRAC Led **COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0029** Janssen-Cilag International N.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 2.4 in order to upgrade the important potential risk of venous thromboembolism (VTE) to an important identified risk as an outcome of the procedure MEA-32, addition of the clinical trial VAC31518COV3003 and update of study VAC18193RSV2008 as additional pharmacovigilance activities to further characterize the important identified risks of Thrombosis with thrombocytopenia syndrome (TTS), Immune thrombocytopenia (ITP), and VTE, and the important potential risk Thrombocytopenia (excluding ITP and TTS) as an outcome of MEA 14.4. In addition, the MAH took the opportunity to include other minor updates in the RMP."	
PRAC Led **COVID-19 Vaccine Janssen - adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein - EMEA/H/C/005737/II/0035** Janssen-Cilag International N.V., Rapporteur: Christophe Focke, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, " Update of section 4.8 of the SmPC in order to add transverse myelitis to the list of adverse drug reactions (ADRs) with frequency not known based on the PRAC request from the post-authorisation measures MEA 14.5 and MEA 14.6 (6th and 7th Monthly Summary Safety Report covering the months of August 2021 and September 2021, respectively) and update of section 4.4 of the SmPC in order to amend the wording on Thrombosis and thrombocytopenia syndrome (TTS) following the PRAC request from the post-authorisation measure MEA 14.5.	

The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement an editorial Quality review document (QRD) comment in the labelling following procedure EMEA/H/C/005737/II/014."

PRAC Led

Cystadrops - mercaptamine - EMEA/H/C/003769/II/0023, Orphan

Recordati Rare Diseases, Rapporteur: Kristina Dunder, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Maria Concepcion Prieto Yerro, "C.I.11 for RMP: Submission of an updated RMP version 1.4 in order to align with the new RMP format according to GVP Rev.2 and to remove a missing information from the list of safety concerns."

PRAC Led

Evoltra - clofarabine - EMEA/H/C/000613/II/0075

Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Tiphaine Vaillant, PRAC-CHMP liaison: Alexandre Moreau, "Update of section 4.6 of the SmPC following a request during EMEA/H/C/PSUSA/00000805/202012 to revise section 4.6 of the SmPC and corresponding sections in the PIL considering the recommendations of the Safety Working Party as reflected in the 'SWP recommendations on the duration of contraception following the end of treatment with a genotoxic drug' and available data. The proposed update of the product information should be based on a detailed scientific rationale from all available 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 bring the PI in line with the latest QRD template version 10.2"

PRAC Led

Obizur - susoctocog alfa - EMEA/H/C/002792/II/0043

Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of the final report from US PASS 241302 study, EUPAS register Number EUPAS36659, listed as a category 3 study in the RMP. This is a post-marketing non-

interventional safety evaluation of Obizur in the treatment of bleeding episodes for patients with acquired hemophilia A (AHA).The primary objective is to determine the incidence of therapy-related serious adverse events (SAEs) in patients with AHA who are prescribed and treated with OBIZUR in routine clinical practice. The RMP version 5.0 has also been submitted."

PRAC Led

OFEV - nintedanib -

EMEA/H/C/003821/II/0046

Boehringer Ingelheim International GmbH, Rapporteur: Peter Kiely, PRAC Rapporteur: Nikica Mirošević Skvrce, PRAC-CHMP liaison: Selma Arapovic Dzakula, "C.I.11 for RMP: Submission of an updated RMP version 11.0 in order to fulfil a request made in the renewal (EMEA/H/C/003821/R/0025) to remove the following safety concerns (Modules SIV, SVII, SVIII; Parts III, V, VI; Appendices 4, 8) :
1-Important identified risks : Diarrhoea, Liver enzyme and bilirubin elevations including DIL, Bleeding, Myocardial infarction);
2-Important potential risks: Venous thromboembolism, Arterial thromboembolism excluding myocardial infarction, Perforation, Hepatic failure, Treatment of pregnant women and teratogenicity, Cardiac failure;
3- Missing information: Treatment of patients with moderate or severe hepatic impairment (Child Pugh B/C), Treatment of Black patients, Treatment of patients with healing wounds, Treatment of patients with severe renal impairment or end-stage renal disease, Treatment of patients receiving full-dose therapeutic anticoagulation, Treatment of breastfeeding women.
Moreover, it is updated ATC code (Part I) and post-marketing exposure (Module SV)."

PRAC Led

Olumiant - baricitinib -

EMEA/H/C/004085/II/0031

Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Adam Przybylkowski, PRAC-CHMP liaison: Ewa Balkowiec Iskra, "C.I.4 - Update of section 4.4 of the SmPC in order to add new warnings on Major Adverse Cardiac Events (MACE) and amend existing warning on Malignancy and

Venous thromboembolism (VTE) following the request made in PSUSA (EMEA/H/C/PSUSA/00010578/202102) and based on interim results from study I4V-MC-B023; this is a retrospective observational study to compare baricitinib relative to the standard of care. The Package Leaflet is updated accordingly. The RMP version 13.1 has also been submitted. In addition, the MAH has submitted a proposal for a DHPC and communication plan."

PRAC Led

Remicade - infliximab - EMEA/H/C/000240/II/0231

Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report of the Remicade AntiRheumatic Therapy in Sweden (ARTIS) registry study. The ARTIS registry study was performed to fulfil a post-authorisation measure in the RMP for Remicade. The updated RMP v20.1. has also been submitted, including revisions agreed in previous procedures."

PRAC Led

Tegsedi - inotersen - EMEA/H/C/004782/II/0026, Orphan

Akcea Therapeutics Ireland Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Submission of an updated RMP version 3.0 to remove carcinogenicity in rats as missing information, add a targeted questionnaire as routine pharmacovigilance measure and a patient alert card as additional risk minimisation for liver transplant rejection. To add 'injection site reactions' and 'immunogenicity' as risks not considered important for inclusion in the summary of safety concerns, and to update the patient alert card with additional warnings on hepatic monitoring and ocular toxicity. Further sections of the RMP are updated."

PRAC Led

Temodal - temozolomide - EMEA/H/C/000229/II/0095

Merck Sharp & Dohme B.V., Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Update of the RMP to version 6.1. to remove all the safety concerns

(important identified risks, important potential risks and missing information). The deletion of the safety concerns is based on the guidance EU GVP Module V (Revision 2)."

PRAC Led

Vaxzevria - COVID 19 Vaccine (ChAdOx1 S [recombinant]) - EMEA/H/C/005675/II/0055

AstraZeneca AB, Rapporteur: Sol Ruiz, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Christophe Focke, "Update of section 4.4 of the SmPC in order to update the warning on thrombosis with thrombocytopenia syndrome to indicate that the frequency after the second dose is lower than after the first dose based on the post-marketing data."

PRAC Led

Zessly - infliximab - EMEA/H/C/004647/II/0020

Sandoz GmbH, Rapporteur: Ingrid Wang, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the updated RMP version 3.0 to remove the RABBIT registry as an additional pharmacovigilance activity in alignment with the updated version of the reference product Remicade RMP (v19) and to remove the BADBIR registry as an additional pharmacovigilance activity."

PRAC Led

WS2185

Entresto-EMEA/H/C/004062/WS2185/0041

Neparvis-EMEA/H/C/004343/WS2185/0039

Novartis Europharm Limited, Lead PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "To provide an updated RMP in response to the assessment report for procedure EMEA/H/C/WS1830. In addition, the following changes have been introduced:
- change to the agreed milestone for study CLCZ696B2320 (EU PASS category 3), to update the date for the submission of the final report ;
- update of section 8.3.1 (Presentation of important identified risks and important potential risks);
- updated exposure and post-marketing data have been provided for the data lock point of

PSUR 9 (31-Jul-21)."

PRAC Led
WS2191
Incresync-
EMEA/H/C/002178/WS2191/0040
Vipdomet- EMEA/H/C/002654/WS2191/0036
Vipidia-EMEA/H/C/002182/WS2191/0029
Takeda Pharma A/S, Lead PRAC Rapporteur: Menno van der Elst, "Submission of a consolidated RMP version 11 for Vipidia, Vipdomet and Incresync in order to:
- Update the RMPs for Alogliptin, Alogliptin/Pioglitazone fixed dose combination (FDC) and Alogliptin/Metformin fixed dose combination (FDC) to consolidate within a single RMP as committed within the PSUR procedure (PSUSA/00010061/202104).
- Following review of cumulative safety data, removal of a number of safety concerns is done based on GVP Module V, Risk Management Systems (revision 2) guidelines.
- Remove the target follow-up Questionnaires of Severe Hypersensitivity and skin reactions, Pancreatitis, Hepatic events and follow up gastrointestinal events and infections from Alogliptin and Alo/Met RMPs.
- Reflect the removal of the inverted black triangle as agreed as part of the alogliptin renewal procedure (EMEA/H/C/002178/R/0023) for Alogliptin and the FDC Alogliptin/Metformin. The black triangle was already removed from the FDC Alogliptin/Pioglitazone RMP as part of the Type II variation (EMEA/H/C/002178/II/0029)."

PRAC Led
WS2192
Dovato-EMEA/H/C/004909/WS2192/0026
Juluca-EMEA/H/C/004427/WS2192/0040
Tivicay-EMEA/H/C/002753/WS2192/0075
Triumeq-EMEA/H/C/002754/WS2192/0099
ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Ingrid Wang, "Update of section 4.8 of the SmPC to add "completed suicide" to the list of adverse drug reactions (ADRs) with frequency "rare" in the dolutegravir

(Tivicay), dolutegravir/ abacavir/lamivudine (Triumeq) and dolutegravir/lamivudine (Dovato) following the finalisation of PSUSA procedure EMEA/H/C/PSUSA/00010075/202101 (reporting period 17 Jan 2020 to 16 Jan 2021) based on reports of completed suicide from participants exposed to Doletugravir containing regimen in ViiV Healthcare-sponsored clinical trials. As the changes impact all Doletugravir containing products, the MAH did a worksharing procedure to include Juluca (Dolutegravir/Rilpivirine) product in accordance with Article 20 (worksharing procedure) of Commission Regulation (EC) 1234/2008. The Package Leaflet are updated accordingly."
PRAC Led **WS2196** **Glyxambi-EMEA/H/C/003833/WS2196/0042** **Jardiance-EMEA/H/C/002677/WS2196/0063** **Synjardy-EMEA/H/C/003770/WS2196/0060** Boehringer Ingelheim International GmbH, Lead PRAC Rapporteur: Eva A. Segovia, "Update of section 4.4 of the SmPC to delete the warning on 'lower limb amputations' as a consequence of the results from the final meta-analysis report of PASS 1245.171 'A meta-analysis of amputation risk in empagliflozin studies (1245.25, 1245.110, 1245.121)' (included as a category 3 study in the RMP). The Package Leaflet has been updated accordingly. Updated RMP versions have also been submitted; version 17 for Jardinace, version 11 for Synjardy and version 6 for Glyxambi."

B.6.12. CHMP-CAT assessed procedures

Luxturna - voretigene neparvovec - EMEA/H/C/004451/II/0026/G, Orphan, ATMP Novartis Europharm Limited, Rapporteur: Sol Ruiz, CHMP Coordinator: Maria Concepcion Prieto Yerro
Tecartus - autologous peripheral blood t cells CD4 and CD8 selected and CD3 and CD28 activated transduced with retroviral

vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - EMEA/H/C/005102/II/0016, Orphan, ATMP
Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus

B.6.13. CHMP-PRAC-CAT assessed procedures

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0009, Orphan, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang, PRAC Rapporteur: Annika Folin, "Update of sections 4.2 and 4.4 of the SmPC, Annex IID and PIL in order to add statements for the use of Abecma exceptionally during shortage of tocilizumab following the "CAT recommendation for the use of CAR-T cell-based therapies in EU during shortages of tocilizumab""

Abecma - idecabtagene vicleucel - EMEA/H/C/004662/II/0010, Orphan, ATMP
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang, PRAC Rapporteur: Annika Folin, "Update of section 5.1 of the SmPC in order to update efficacy information based on 24 month follow up data from the pivotal study submitted during initial (BB2121-MM-001: A Phase 2, Multicenter Study to determine the Efficacy and Safety of bb2121 in Subjects with Relapsed and Refractory Multiple Myeloma) listed as a specific obligation in the Annex II and in the RMP; The annex II is updated with the proposed deletion of the relevant SOB. The RMP version 1.1 has also been submitted."

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0047, Orphan, ATMP
Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.2 and 4.4 of the SmPC, Annex IID and PIL (information intended for healthcare professionals) in order to add

statements for the use of Kymriah exceptionally during shortage of tocilizumab following the "CAT recommendation for the use of CAR-T cell-based therapies in EU during shortages of tocilizumab".”	
WS2206 **Tecartus-EMEA/H/C/005102/WS2206/0015** **Yescarta-EMEA/H/C/004480/WS2206/0045** Kite Pharma EU B.V., Lead Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus, Lead PRAC Rapporteur: Menno van der Elst, “Update of sections 4.2 and 4.4 of the SmPC and Annex IID in order to add statements for the use of Tecartus and Yescarta exceptionally during shortage of tocilizumab following the "CAT recommendation for the use of CAR-T cell-based therapies in EU during shortages of tocilizumab". The RMPs for both products are updated accordingly (version 1.2 for Tecartus and version 5.2 for Yescarta).”	

B.6.14. PRAC assessed ATMP procedures

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

WS2111/G **Eucreas-EMEA/H/C/000807/WS2111/0089/G** **Icandra-EMEA/H/C/001050/WS2111/0092/G** **Zomarist-EMEA/H/C/001049/WS2111/0091/G** Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder	
WS2136 **Esperoct-EMEA/H/C/004883/WS2136/0009** **NovoEight-EMEA/H/C/002719/WS2136/0039** Novo Nordisk A/S, Lead Rapporteur: Jan Mueller-Berghaus	
WS2140 **Infanrix hexa-EMEA/H/C/000296/WS2140/0307** GlaxoSmithkline Biologicals SA, Lead	

Rapporteur: Christophe Focke	
WS2162 **Prezista-EMEA/H/C/000707/WS2162/0113** **Rezolsta-EMEA/H/C/002819/WS2162/0044** **Symtuza-EMEA/H/C/004391/WS2162/0038** Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege, "To update for the 3 Darunavir products (PREZISTA, REZOLSTA and Symtuza), section 4.3, section 4.4 (PREZISTA 100 mg/ml, 400 mg and 800 mg) and section 4.5 of each SmPC to emphasise that the lists of medications in the Contraindications and in the Interactions sections are not comprehensive and are to be considered as examples. The Package Leaflets are updated accordingly. The MAH also has taken the opportunity to include several minor changes as follows: - an update in section 4.5 of the SmPC and section 2 of the Patient leaflet of Symtuza to include information about elbasvir and grazoprevir, in order to align with the info provided in the PREZISTA and REZOLSTA labels (as approved in Feb 2017 in procedure WS1107/G); - correcting the capitalization of 'wort' in St. John's Wort; - adding the prefix for Belgian postcodes to the addresses in the respective Package Leaflets."	
WS2173 **HBVAXPRO-EMEA/H/C/000373/WS2173/0073** **Vaxelis-EMEA/H/C/003982/WS2173/0091** MCM Vaccine B.V., Lead Rapporteur: Christophe Focke	
WS2175 **Corbilta-EMEA/H/C/002785/WS2175/0026** **Levodopa/Carbidopa/Entacapone Orion-EMEA/H/C/002441/WS2175/0034** **Stalevo-EMEA/H/C/000511/WS2175/0096** Orion Corporation, Lead Rapporteur: Outi Mäki-Ikola, "To add Sodium warning to sections 2, 4.4 of the SmPC; section 3 of Labelling and section 2 of Package leaflet to Stalevo and its duplicates Corbilta and	

Levodopa/Carbidopa/Entacapone Orion. QRD template v10.2 update is implemented for Stalevo and Levodopa/Carbidopa/Entacapone Orion. Contact details of local representatives are updated as follows: - Stalevo in France and United Kingdom (Northern Ireland); - Corbilta in France; - Levodopa/Carbidopa/Entacapone Orion in Lithuania, Estonia, Ireland, Latvia and United Kingdom (Northern Ireland). Additionally, missing non-breaking spaces added, wherever applicable according to EMA guidance 'Compilation of QRD decisions on stylistic matters in product information'. Minor linguistic and typographical corrections have been performed in several languages as follows: Stalevo: CS, DE, EL, EN, ES, ET, FR, HR, HU, IS, LT, LV, MT, NL, NO, PL, PT, RO, SK and SL. Corbilta: CS, DA, DE, EL, EN, ES, ET, FR, HR, HU, IS, LT, LV, MT, NL, NO, PL, PT, RO, SK, SL and SV. Levodopa/Carbidopa/Entacapone Orion: CS, DA, DE, EL, EN, ES, ET, FR, HR, HU, IS, LT, LV, MT, NL, PL, PT, RO, SK and SL.”	
WS2208 **Blitzima-EMEA/H/C/004723/WS2208/0051** **Truxima-EMEA/H/C/004112/WS2208/0054** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz	
WS2209 **Blitzima-EMEA/H/C/004723/WS2209/0052** **Truxima-EMEA/H/C/004112/WS2209/0055** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz	

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

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

B.7.2. Monthly Line listing for Type I variations

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

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

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

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

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

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

E. Annex E - EMA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. Timetables – starting & ongoing procedures: For information

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

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

G. ANNEX G

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

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

List of procedures concluding at 13-16 December 2021 CHMP plenary

G.1.1. List of procedures starting in December 2021 for January 2022 CHMP adoption of outcomes

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