22 July 2019
EMA/CHMP/410783/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Agenda for the meeting on 22-25 July 2019

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

22 July 2019, 13:00 – 19:30, room 1C

23 July 2019, 08:30 – 19:30, room 1C

24 July 2019, 08:30 – 19:30, room 1C

25 July 2019, 09:00 – 16:00, room 1C

Health and safety information

In accordance with the Agency's health and safety policy, delegates are to be briefed on health, safety and emergency information and procedures prior to the start of the meeting.

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 7

1.1. Welcome and declarations of interest of members, alternates and experts 7

1.2. Adoption of agenda 7

1.3. Adoption of the minutes 7

2. Oral Explanations 7

2.1. Pre-authorisation procedure oral explanations 7

2.1.1. dapivirine - Article 58 - EMEA/H/W/002168 7

2.1.2. polatuzumab vedotin - Orphan - EMEA/H/C/004870 7

2.2. Re-examination procedure oral explanations 7

2.3. Post-authorisation procedure oral explanations 8

2.3.1. Kyprolis - carfilzomib - EMEA/H/C/003790/II/0031, Orphan 8

2.4. Referral procedure oral explanations 8

3. Initial applications 8

3.1. Initial applications; Opinions 8

3.1.1. deferasirox - EMEA/H/C/005014 8

3.1.2. cannabidiol - Orphan - EMEA/H/C/004675 8

3.1.3. levodopa - EMEA/H/C/004786 8

3.1.4. polatuzumab vedotin - Orphan - EMEA/H/C/004870 9

3.1.5. lidocaine / prilocaine - EMEA/H/C/005298 9

3.1.6. ibalizumab - EMEA/H/C/004961 9

3.1.7. larotrectinib - Orphan - EMEA/H/C/004919 9

3.2. Initial applications; List of outstanding issues (Day 180; Day 120 for procedures with accelerated assessment timetable) 9

3.2.1. arsenic trioxide - EMEA/H/C/005175 9

3.2.2. glucagon - EMEA/H/C/003848 10

3.2.3. dapivirine - Article 58 - EMEA/H/W/002168 10

3.2.4. clofarabine - EMEA/H/C/005039 10

3.2.5. etanercept - EMEA/H/C/004711 10

3.2.6. osilodrostat - Orphan - EMEA/H/C/004821 10

3.2.7. esketamine - EMEA/H/C/004535 11

3.2.8. solriamfetol - EMEA/H/C/004893 11

3.2.9. gilteritinib - Orphan - EMEA/H/C/004752 11

3.2.10. plazomicin - EMEA/H/C/004457 11

3.3. Initial applications; List of questions (Day 120; Day 90 for procedures with accelerated assessment timetable) 11

3.3.1. aripiprazole - EMEA/H/C/005062 11

3.3.2. arsenic trioxide - EMEA/H/C/005235 11

3.3.3. azacitidine - EMEA/H/C/004984 12
3.3.4. influenza vaccine (surface antigen, inactivated) - Article 28 - EMEA/H/C/004993 12
3.3.5. hepatitis B surface antigen - EMEA/H/C/005063 12
3.3.6. insulin lispro - EMEA/H/C/005037 12
3.3.7. melphalan - EMEA/H/C/005173 12
3.3.8. darolutamide - EMEA/H/C/004790 12
3.3.9. pretomanid - Orphan - EMEA/H/C/005167 13
3.3.10. teriparatide - EMEA/H/C/005233 13
3.3.11. pexidartinib - Orphan - EMEA/H/C/004832 13
3.3.12. ozanimod - EMEA/H/C/004835 13
3.3.13. bupivacaine / meloxicam - EMEA/H/C/005205 13
3.4. Update on on-going initial applications for Centralised procedure 13
3.4.1. rituximab - EMEA/H/C/004807 13
3.4.2. rituximab EMEA/H/C/5387 14
3.4.3. imlifidase - Orphan - EMEA/H/C/004849 14
3.5. Re-examination of initial application procedures under Article 9(2) of Regulation no 726/2004 14
3.5.1. Evenity - romosozumab - EMEA/H/C/004465 14
3.6. Initial applications in the decision-making phase 14
3.6.1. Nuceiva - botulinum toxin type a - EMEA/H/C/004587 14
3.7. Withdrawals of initial marketing authorisation application 15
4. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008 15
4.1. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Opinion 15
4.1.1. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/X/0075/G 15
4.2. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 180 list of outstanding issues 15
4.2.1. Remsima - infliximab - EMEA/H/C/002576/X/0062 15
4.3. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 120 List of question 15
4.3.1. Entyvio - vedolizumab - EMEA/H/C/002782/X/0040 15
4.3.2. Ibrance - palbociclib - EMEA/H/C/003853/X/0018 16
4.3.3. Suboxone - buprenorphine / naloxone - EMEA/H/C/000697/X/0042 16
4.4. Update on on-going extension application according to Annex I of Commission Regulation (EC) No 1234/2008 16
4.5. Re-examination procedure of extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008 16

5. Type II variations - variation of therapeutic indication procedure according to Annex I of Commission Regulation (EC) No 1234/2008 16

5.1. Type II variations - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008; Opinions or Requests for supplementary information 16

5.1.1. Axumin - fluciclovine (18F) - EMEA/H/C/004197/II/0011 16

5.1.2. Darzalex - daratumumab - Orphan - EMEA/H/C/004077/II/0029 17

5.1.3. Darzalex - daratumumab - Orphan - EMEA/H/C/004077/II/0030 17

5.1.4. Empliciti - elotuzumab - EMEA/H/C/003967/II/0012 17

5.1.5. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0069 18

5.1.6. Lonsurf - trifluridine / tipiracil - EMEA/H/C/003897/II/0012 18

5.1.7. Lucentis - ranibizumab - EMEA/H/C/000715/II/0074/G 19

5.1.8. Soliris - eculizumab - Orphan - EMEA/H/C/000791/II/0105 19

5.1.9. Stelara - ustekinumab - EMEA/H/C/000958/II/0071 19

5.1.10. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0018 19

5.1.11. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0019 20

5.1.12. Trulicity - dulaglutide - EMEA/H/C/002825/II/0040 20

5.1.13. Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0013 21

5.1.14. Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/II/0015 21

5.1.15. Zerbaxa - ceftolozane / tazobactam - EMEA/H/C/003772/II/0020 21

5.2. Update on on-going Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008 22

5.2.1. OFEV - nintedanib - Orphan - EMEA/H/C/003821/II/0026 22

5.3. Re-examination of Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008 22

5.3.1. Translarna - ataluren - Orphan - EMEA/H/C/002720/II/0047 22

5.3.2. Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0049 23

6. Ancillary medicinal substances in medical devices 23

6.1. Ancillary medicinal substances in medical devices; Opinions/ Day 180 list of outstanding issues / Day 120 list of questions 23

6.1.1. human fibrinogen / human thrombin - EMEA/H/D/004308 23

6.2. Update of Ancillary medicinal substances in medical devices 23

7. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use) 23

7.1. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use) 23

8. Pre-submission issues 24

8.1. Pre-submission issue 24

8.1.1. satralizumab (p-inn) - Orphan - H0004788 24

8.2. Priority Medicines (PRIME) 24
8.2.1. List of applications received 24
8.2.2. Recommendation for PRIME eligibility 24
9. Post-authorisation issues 24
9.1. Post-authorisation issues 24
9.1.1. Eliquis - apixaban - EMEA/H/C/002148 24
9.1.2. NINLARO - ixazomib - EMEA/H/C/003844/R/0017, Orphan 24
9.1.3. NINLARO - ixazomib - EMEA/H/C/003844/II/0014/G, Orphan 25
9.1.4. Venclyxto (EMEA/H/C/004106) LEG/REV 009 25
9.1.5. Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0054/G 25
9.1.6. Zalmoxis - nalotimagene carmaleucel – Orphan, ATMP - EMEA/H/C/002801/R/0015 25
10. Referral procedures 26
10.1. Procedure for Centrally Authorised products under Article 20 of Regulation (EC) No 726/2004 26
10.2. Requests for CHMP Opinion under Article 5(3) of Regulation (EC) No 726/2004 . 26
10.3. Procedure under Articles 5(2) and 10 of Regulation (EC) No 726/2004 26
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 26
10.5. Harmonisation - Referral procedure under Article 30 of Directive 2001/83/EC.... 26
10.6. Community Interests - Referral under Article 31 of Directive 2001/83/EC 26
10.6.1. Methotrexate - JYLAMVO (CAP), NORDIMET (CAP); NAP - EMEA/H/A-31/1463 26
10.7. Re-examination Procedure under Article 32(4) of Directive 2001/83/EC 26
10.8. Procedure under Article 107(2) of Directive 2001/83/EC 27
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 27
10.10. Procedure under Article 29 of Regulation (EC) 1901/2006 27
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 27
11. Pharmacovigilance issue 27
11.1. Early Notification System 27
12. Inspections 27
12.1. GMP inspections 27
12.2. GCP inspections 27
12.3. Pharmacovigilance inspections 27
12.4. GLP inspections 27
13. Innovation Task Force 28
13.1. Minutes of Innovation Task Force 28

13.2. Innovation Task Force briefing meetings 28
13.3. Requests for CHMP Opinion under Article 57(1)J and (1)P of Regulation (EC) No 726/2004 28
13.4. Nanomedicines activities 28
14. Organisational, regulatory and methodological matters 28
14.1. Mandate and organisation of the CHMP 28
14.1.1. Election of CHMP Co-opted Member 28
14.1.2. Seating plan for CHMP under Finish EU Presidency, 1 July – 31 December 2019 28
14.1.3. Timetable for August 2019 Written Procedure 28
14.1.4. Training for CHMP members and assessors in oncology 28
14.1.5. Strategic Review and Learning Meetings (SRLM) 29
14.2. Coordination with EMA Scientific Committees 29
14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC) 29
14.2.2. Committee for Advanced Therapies (CAT) 29
14.2.3. Committee for Herbal Medicinal Products (HMPC) 29
14.2.4. Paediatric Committee (PDCO) 29
14.2.5. Committee for Orphan Medicinal Products (COMP) 29
14.2.6. Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) 29
14.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups 30
14.3.1. Scientific Advice Working Party (SAWP) 30
14.3.2. Name Review Group (NRG) 30
14.3.3. Biologics Working Party (BWP) 30
14.3.4. Oncology Working Party (ONCWP) 30
14.4. Cooperation within the EU regulatory network 30
14.5. Cooperation with International Regulators 30
14.5.1. International Council on Harmonisation (ICH) 30
14.6. Contacts of the CHMP with external parties and interaction with the Interested Parties to the Committee 31
14.6.1. Update on recent interactions with down-stream decision makers 31
14.7. CHMP work plan 31
14.8. Planning and reporting 31
14.9. Others 31
15. Any other business 31
15.1. AOB topic 31
15.1.1. Preparedness of the system and capacity increase 31
15.1.2. Update on Ebola outbreak 31
16. Explanatory notes 32

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 22-25 July 2019. See July 2019 CHMP minutes (to be published post September 2019 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 22-25 July 2019

1.3. Adoption of the minutes

CHMP minutes for 24-27 June 2019

CHMP ORGAM minutes for 15 July 2019

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. dapivirine - Article 58 - EMEA/H/W/002168

Reducing the risk of HIV-1 infection via vaginal intercourse in sexually active HIV-uninfected women

Scope: Possible oral explanation/List of outstanding issues

Action: Possible oral explanation to be held on Tuesday, 23 July 2019 at time 11:00

List of Outstanding Issues adopted on 26.04.2019, 18.10.2018. List of Questions adopted on 09.11.2017.

See 3.2

2.1.2. polatuzumab vedotin - Orphan - EMEA/H/C/004870

Accelerated assessment

Roche Registration GmbH; treatment of mature B cell lymphomas

Scope: Possible oral explanation/Opinion

Action: Oral explanation to be held on Tuesday, 23 July 2019 at time 09:00

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 24.04.2019.

See 3.1

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

2.3.1. Kyprolis - carfilzomib - EMEA/H/C/003790/II/0031, Orphan

Amgen Europe B.V.

Rapporteur: Jorge Camarero Jiménez

Scope: "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 to add a once-weekly dose regimen for carfilzomib (Kyprolis) at 20/70 mg/m^2 in combination with dexamethasone (Kd) for the treatment of the currently indicated patient population. The MAH took the opportunity to implement editorial changes to the SmPC and Patient Information Leaflet (PIL) due to the revised excipients guideline (EMA/CHMP/302620/2017). The PIL is updated accordingly."

Oral explanation

Action: Oral explanation to be held on Tuesday, 23 July 2019 at time 16:00

Request for Supplementary Information adopted on 27.06.2019, 28.02.2019, 15.11.2018.

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. deferasirox - EMEA/H/C/005014

treatment of chronic iron overload

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 29.05.2019. List of Questions adopted on 15.11.2018.

3.1.2. cannabidiol - Orphan - EMEA/H/C/004675

GW Pharma (International) B.V.; Adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.04.2019, 31.01.2019, 15.11.2018. List of Questions adopted on 31.05.2018.

3.1.3. levodopa - EMEA/H/C/004786

treatment of symptoms of OFF periods in Parkinson's disease

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 29.05.2019. List of Questions adopted on 20.09.2018.

3.1.4. polatuzumab vedotin - Orphan - EMEA/H/C/004870

Accelerated assessment

Roche Registration GmbH; treatment of mature B cell lymphomas

Scope: Possible oral explanation/Opinion

Action: Possible oral explanation to be held on Tuesday, 23 July 2019 at time 09:00

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 24.04.2019.

See 2.1

3.1.5. lidocaine / prilocaine - EMEA/H/C/005298

treatment of primary premature ejaculation

Scope: Opinion

Action: For adoption

3.1.6. ibalizumab - EMEA/H/C/004961

treatment of adults infected with HIV-1 resistant to at least 1 agent in 3 different classes

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 29.05.2019, 28.02.2019. List of Questions adopted on 11.12.2018.

3.1.7. larotrectinib - Orphan - EMEA/H/C/004919

Bayer AG; treatment of adult and paediatric patients with locally advanced or metastatic solid tumours

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 29.05.2019, 28.03.2019. List of Questions adopted on 11.12.2018.

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

3.2.1. arsenic trioxide - EMEA/H/C/005175

treatment of relapsed acute promyelocytic leukaemia (APL)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 26.04.2019.

3.2.2. glucagon - EMEA/H/C/003848

treatment of severe hypoglycaemia

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 26.04.2019. List of Questions adopted on 13.12.2018.

3.2.3. dapivirine - Article 58 - EMEA/H/W/002168

Reducing the risk of HIV-1 infection via vaginal intercourse in sexually active HIV-uninfected women

Scope: Possible oral explanation/List of outstanding issues, request by the applicant for an extension to the clock stop to respond to the expected list of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 26.04.2019, 18.10.2018. List of Questions adopted on 09.11.2017.

See 2.1

3.2.4. clofarabine - EMEA/H/C/005039

treatment of acute lymphoblastic leukaemia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 31.01.2019.

3.2.5. etanercept - EMEA/H/C/004711

Rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, axial spondyloarthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, plaque psoriasis, paediatric plaque psoriasis

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 29.05.2019. List of Questions adopted on 20.09.2018.

3.2.6. osilodrostat - Orphan - EMEA/H/C/004821

Novartis Europharm Limited; treatment of cushing's syndrome

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.03.2019.

3.2.7. esketamine - EMEA/H/C/004535

treatment-resistant depression

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.02.2019.

3.2.8. solriamfetol - EMEA/H/C/004893

indicated to improve wakefulness in patients with narcolepsy or obstructive sleep apnoea

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.03.2019.

3.2.9. gilteritinib - Orphan - EMEA/H/C/004752

Accelerated assessment

Astellas Pharma Europe B.V.; treatment of patients who have relapsed or refractory acute myeloid leukemia (AML) with a FLT3 mutation

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 27.05.2019.

3.2.10. plazomicin - EMEA/H/C/004457

treatment of complicated urinary tract infection (cUTI), including pyelonephritis; treatment of bloodstream infection (BSI); treatment of infections due to Enterobacteriaceae

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 28.02.2019.

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

3.3.1. aripiprazole - EMEA/H/C/005062

treatment of schizophrenia, or of moderate to severe manic episodes in bipolar I disorder with sensor to measure medication adherence

Scope: List of questions

Action: For adoption

3.3.2. arsenic trioxide - EMEA/H/C/005235

treatment of relapsed acute promyelocytic leukaemia (APL)

Scope: List of questions

Action: For adoption

3.3.3. azacitidine - EMEA/H/C/004984

treatment of adult patients who are not eligible for haematopoietic stem cell transplantation (HSCT)

Scope: List of questions

Action: For adoption

3.3.4. influenza vaccine (surface antigen, inactivated) - Article 28 - EMEA/H/C/004993

Active immunisation against influenza in the elderly (65 years of age and older) and in children 6 months to less than 6 years of age

Scope: List of questions

Action: For adoption

3.3.5. hepatitis B surface antigen - EMEA/H/C/005063

Prevention of hepatitis B virus infection

Scope: List of questions, request by the applicant for an extension to the clock stop to respond to the list of questions

Action: For adoption

3.3.6. insulin lispro - EMEA/H/C/005037

Treatment of diabetes mellitus in adults

Scope: List of questions

Action: For adoption

3.3.7. melphalan - EMEA/H/C/005173

used alone or in combination with other cytotoxic drugs and/or total body irradiation is indicated in the treatment of: multiple myeloma, malignant lymphoma (Hodgkin, non-Hodgkin lymphoma), acute lymphoblastic and myeloblastic leukemia, childhood neuroblastoma, ovarian adenocarcinoma, mammary adenocarcinoma.
in combination with other cytotoxic drugs and/or total body irradiation, in adult and paediatric population, is indicated as conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (HSCT) in haematological diseases.

Scope: List of questions

Action: For adoption

3.3.8. darolutamide - EMEA/H/C/004790

treatment of non-metastatic castration resistant prostate cancer (nmCRPC)

Scope: List of questions

Action: For adoption

3.3.9. pretomanid - Orphan - EMEA/H/C/005167

FGK Representative Service GmbH; treatment of tuberculosis

Scope: List of questions

Action: For adoption

3.3.10. teriparatide - EMEA/H/C/005233

treatment of osteoporosis

Scope: List of questions

Action: For adoption

3.3.11. pexidartinib - Orphan - EMEA/H/C/004832

Daiichi Sankyo Europe GmbH; treatment of adult patients with symptomatic tenosynovial giant cell tumour (TGCT), also referred to as giant cell tumour of the tendon sheath (GCT-TS) or pigmented villonodular synovitis (PVNS)

Scope: List of questions

Action: For adoption

3.3.12. ozanimod - EMEA/H/C/004835

Treatment of multiple sclerosis

Scope: List of questions

Action: For adoption

3.3.13. bupivacaine / meloxicam - EMEA/H/C/005205

for application into the surgical site to reduce postoperative pain for application into the surgical site to reduce postoperative pain

Scope: List of questions

Action: For adoption

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

3.4.1. rituximab - EMEA/H/C/004807

treatment of Non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukaemia (CLL) and rheumatoid arthritis

Scope: letter by the applicant requesting an extension of the clock stop to respond to the list of outstanding issues adopted on 27.06.2019

Action: For adoption

List of Outstanding Issues adopted on 27.06.2019. List of Questions adopted on 18.10.2018.

3.4.2. rituximab EMEA/H/C/5387

treatment of Non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukaemia (CLL)

Scope: letter by the applicant requesting an extension of the clock stop to respond to the list of outstanding issues adopted on 27.06.2019

Action: For adoption

List of Outstanding Issues adopted on 27.06.2019

3.4.3. imlifidase - Orphan - EMEA/H/C/004849

Hansa Biopharma AB; indicated for desensitization treatment of highly sensitized adult kidney transplant patients with positive crossmatch against an available deceased donor.

Scope: letter by the applicant requesting an extension of the clock stop to respond to the list of questions adopted on 27.06.2019

Action: For adoption

List of Questions adopted on 27.06.2019.

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

3.5.1. Evenity - romosozumab - EMEA/H/C/004465

UCB Pharma S.A.; Treatment of osteoporosis

Scope: Appointment of re-examination Rapporteurs, draft timetable

Action: For adoption

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

Opinion adopted on 27.06.2019, List of Outstanding Issues adopted on 29.05.2019, 28.02.2019, 15.11.2018, 20.09.2018. List of Questions adopted on 26.04.2018.

3.6. Initial applications in the decision-making phase

3.6.1. Nuceiva - botulinum toxin type a - EMEA/H/C/004587

Evolus Pharma Limited; temporary improvement in the appearance of moderate to severe vertical lines between the eyebrows

Scope: Response to the request from the European Commission for clarification on the opinion adopted in April 2019

Action: For adoption

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

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

4.1.1. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/X/0075/G

Vertex Pharmaceuticals (Ireland) Limited

Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon

Scope: "Extension application to add a new strength of 25 mg granules in sachet in the treatment of cystic fibrosis in children aged 6 to less than 12 months old.
C.I.4 - To update sections 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC, and sections 2 and 3 of the PL for the 150 mg film-coated tablet presentations to bring it in line with the new dosage form (25 mg granules), which supports the extension of indication for children aged 6 to 12 months old. The RMP (version 8.3) is updated in accordance.
In addition, the MAH took the opportunity to implement minor updates in the Product Information."

Action: For adoption

List of Questions adopted on 26.04.2019.

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. Remsima - infliximab - EMEA/H/C/002576/X/0062

Celltrion Healthcare Hungary Kft.

Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension application to introduce a new pharmaceutical form (solution for injection), a new strength (120 mg) and a new route of administration (subcutaneous use).
The RMP (version 9.1) is updated in accordance."

Action: For adoption

List of Questions adopted on 28.03.2019.

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

4.3.1. Entyvio - vedolizumab - EMEA/H/C/002782/X/0040

Takeda Pharma A/S

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension application to introduce a new pharmaceutical form (solution for injection), associated with a new strength (108 mg) and a new route of administration (subcutaneous use)."

Action: For adoption

4.3.2. Ibrance - palbociclib - EMEA/H/C/003853/X/0018

Pfizer Europe MA EEIG

Rapporteur: Filip Josephson

Scope: "Extension application to introduce a new pharmaceutical form (film-coated tablets) associated with new strengths."

Action: For adoption

4.3.3. Suboxone - buprenorphine / naloxone - EMEA/H/C/000697/X/0042

Indivior Europe Limited

Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber

Scope: "Extension application to introduce a new pharmaceutical form (sublingual film) associated with four new strengths (2/0.5, 4/1, 8/2, and 16/4 mg) and a new route of administration (either sublingual or buccal administration)"

Action: For adoption

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

No items

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

No items

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

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

5.1.1. Axumin - fluciclovine (18F) - EMEA/H/C/004197/II/0011

Blue Earth Diagnostics Ireland Limited

Rapporteur: Janet Koenig, PRAC Rapporteur: Rugile Pilviniene

Scope: “Extension of indication to include diagnosis and continuing assessment of Glioma in adult patients as a new indication for Axumin; as a consequence, sections 4.1, 4.2, 4.4, 4.6, 5.1, 5.2 and 11 of the SmPC and the Annex II are updated. The Package Leaflet is updated in accordance.”

Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 28.03.2019.

5.1.2. Darzalex - daratumumab - Orphan - EMEA/H/C/004077/II/0029

Janssen-Cilag International NV

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: “Extension of indication to extend the existing therapeutic indication for Darzalex (daratumumab) in combination with lenalidomide and dexamethasone (Rd) for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant (ASCT); 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. The RMP (Version 6, Succession 1) has also been submitted.”

Action: For adoption

5.1.3. Darzalex - daratumumab - Orphan - EMEA/H/C/004077/II/0030

Janssen-Cilag International NV

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: “Extension of indication to extend the existing therapeutic indication for Darzalex (daratumumab) in combination with bortezomib, thalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant (ASCT); as a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP (Version 6, Succession 1) has also been submitted.”

Action: For adoption

5.1.4. Empliciti - elotuzumab - EMEA/H/C/003967/II/0012

Bristol-Myers Squibb Pharma EEIG

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

Scope: “Extension of indication to include treatment in combination with pomalidomide and dexamethasone of adult patients with multiple myeloma. As a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 4.9, 5.1 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list

of local representatives in the Package Leaflet.
The RMP (version 2.0) is updated to reflect the new indication."

Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 26.04.2019, 13.12.2018.

5.1.5. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0069

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication to include first line treatment of advanced or metastatic renal cell carcinoma (RCC) as combination therapy of pembrolizumab together with axitinib based on the results of the first Interim Analysis (IA1) from the pivotal study, KN426, an ongoing, Phase 3, randomized, open-label, multicenter, global study, to evaluate the efficacy and safety of pembrolizumab in combination with axitinib versus sunitinib in previously untreated subjects with advanced/metastatic RCC. It also includes supportive data from KEYNOTE-427 Cohort A (pembrolizumab monotherapy) and a Sponsored Study A4061051 (axitinib monotherapy). 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.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The risk management plan (RMP) Version 24.1 is submitted."

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019, 26.04.2019.

5.1.6. Lonsurf - trifluridine / tipiracil - EMEA/H/C/003897/II/0012

Les Laboratoires Servier

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Annika Folin

Scope: "Extension of indication to include Lonsurf indicated for the treatment of adult patients with metastatic gastric cancer including adenocarcinoma of the gastroesophageal junction, who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, platinum-, and either a taxane- or irinotecan-based chemotherapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. RMP version 6.1 has also been submitted and updated in accordance with Template Rev 2."

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019, 31.01.2019.

5.1.7. Lucentis - ranibizumab - EMEA/H/C/000715/II/0074/G

Novartis Europharm Limited

Rapporteur: Kristina Dunder, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include new indication for Lucentis vial presentation: treatment of retinopathy of prematurity (ROP) in preterm infants; as a consequence, sections 2, 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. In addition, RMP version 18.0 is also submitted. B.IV.1.a.1 – To introduce a low volume high accuracy syringe, as a stand-alone medical device for the administration of the Lucentis 0.2mg paediatric dose (corresponding to 0.02 ml of the Lucentis 10 mg/ml solution for injection in vial presentations)."

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019, 31.01.2019.

5.1.8. Soliris - eculizumab - Orphan - EMEA/H/C/000791/II/0105

Alexion Europe SAS

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Eva A. Segovia

Scope: "Extension of indication for Soliris to include treatment of adult patients with Neuromyelitis Optica Spectrum Disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody (Ab) positive. As a consequence the SmPC sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, Annex II and package leaflet are revised. The updated RMP version 19 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 26.04.2019.

5.1.9. Stelara - ustekinumab - EMEA/H/C/000958/II/0071

Janssen-Cilag International NV

Rapporteur: Jayne Crowe, Co-Rapporteur: Mark Ainsworth, PRAC Rapporteur: Rhea Fitzgerald

Scope: "Extension of indication for Stelara to include treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic or have medical contraindications to such therapies. As a consequence, the SmPC, Package Leaflet and RMP have been updated."

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019, 26.04.2019.

5.1.10. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0018

Roche Registration GmbH

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

Scope: “Extension of indication to include Tecentriq, in combination with carboplatin and etoposide, indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC); 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. RMP version 8.0 has been submitted”

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019, 31.01.2019.

5.1.11. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0019

Roche Registration GmbH

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

Scope: “Extension of indication to include Tecentriq, in combination with nab-paclitaxel and carboplatin, indicated for the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC) who do not have EGFR mutant or ALK-positive NSCLC; 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. RMP version 9.0 has been submitted.”

Action: For adoption

Request for Supplementary Information adopted on 29.05.2019, 31.01.2019.

5.1.12. Trulicity - dulaglutide - EMEA/H/C/002825/II/0040

Eli Lilly Nederland B.V.

Rapporteur: Martina Weise, PRAC Rapporteur: Amelia Cupelli

Scope: “Extension of indication to include a new indication for Trulicity; “to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke), in adults with type 2 diabetes mellitus who have multiple cardiovascular risk factors without established cardiovascular disease, and in adults with type 2 diabetes mellitus with established cardiovascular disease.”
The data supporting this new indication is derived from Study GBDJ (Researching Cardiovascular Events with a Weekly INcretin in Diabetes (REWIND)); a single pivotal Phase 3 long-term cardiovascular outcomes study, which assessed the efficacy and safety of treatment with once-weekly injection of dulaglutide 1.5 mg when added to glucose-lowering regimen of patients with type 2 diabetes (T2D), compared to the addition of a once weekly placebo injection. This study is a post-authorisation measure (PAM) (MEA 004) included in the dulaglutide RMP.
As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are being updated and the Package Leaflet is updated accordingly.
In addition, the MAH is taking the opportunity to update the wording of the existing indication in section 4.1 of the SmPC and to implement a minor change in section 5.1 of the SmPC, in the glycaemic control summary subsection, based on the results from the dulaglutide study as add-on to sodium-glucose co-transporter 2 inhibitor therapy which was assessed as part of II/25. An updated RMP version 3.1 was provided as part of the application.”

Action: For adoption

5.1.13. Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0013

Pfizer Europe MA EEIG

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jean-Michel Dogné

Scope: "Extension of indication for Trumenba to include active immunisation of children 1-9 years old. Sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated in parallel based on the results from the two pivotal studies B1971017 and B1971035. The Package Leaflet is updated in accordance. The RMP version 2.0 has also been submitted.
In addition, the Marketing authorisation holder (MAH) took the opportunity to submit a corrected version of the final report of study B1971016, which was included in the initial marketing authorisation application."

Action: For adoption

Request for Supplementary Information adopted on 28.02.2019.

5.1.14. Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/II/0015

Pfizer Ireland Pharmaceuticals

Rapporteur: Bjorg Bolstad, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Rugile Pilviniene

Scope: "Extension of indication to include paediatric patients aged 3 months to less than 18 years for Zavicefta (for the treatment of cIAI and cUTI), based on data from paediatric studies D4280C00014, C3591004 and C3591005 and the population PK modelling/simulation analyses (CAZ-MS-PED-01 and CAZ-MS-PED-02).
As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2, 6.3 and 6.6 of the SmPC are updated in order to reflect this additional population, the paediatric posology, paediatric safety information, the description of the clinical trials and handling instructions for paediatric dosing. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct the sodium content in SmPC sections 2 and 4.4 and PL section 2 and the volumes of distribution of ceftazidime and avibactam in SmPC section 5.2. Furthermore, the MAH is also introducing a correction in the Czech SmPC to add missing values in the table in SmPC section 5.1. The RMP version 3.0 has also been submitted."

Action: For adoption

5.1.15. Zerbaxa - ceftolozane / tazobactam - EMEA/H/C/003772/II/0020

Merck Sharp & Dohme B.V.

Rapporteur: Bjorg Bolstad, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension of indication to include treatment of Nosocomial pneumonia, including ventilator associated pneumonia for Zerbaxa, based on results from the randomised, double-blind, multicentre clinical trial CXA-NP-11-04 (PN008).
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance (sections 1, 2, 3, 4 and 6).
The applicant also took the opportunity to implement editorial changes in section 5.2 of the SmPC and to bring section 4.4 of the SmPC and section 2 of the PL in line with the latest Annex

to the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'.
Version 2.1 of the RMP was also submitted."

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019, 29.05.2019, 28.03.2019.

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

5.2.1. OFEV - nintedanib - Orphan - EMEA/H/C/003821/II/0026

Boehringer Ingelheim International GmbH

Rapporteur: Peter Kiely, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of indication to include new indication for OFEV for the treatment of Systemic Sclerosis associated Interstitial Lung Disease (SSc-ILD).
As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The MAH takes this opportunity to also introduce minor linguistic corrections to the Annexes for France and Sweden. The RMP version 7.0 has also been submitted."

Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

List of questions to patients

Action: For adoption

Request for Supplementary Information adopted on 27.06.2019

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

5.3.1. Translarna - ataluren - Orphan - EMEA/H/C/002720/II/0047

PTC Therapeutics International Limited

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: "Extension of indication to include non-ambulatory patients with Duchenne muscular dystrophy; this variation additionally presents, as supportive data, the final results of the long term clinical study PTC-124-GD-019-DMD (an Open-Label Study for Previously Treated Ataluren (PTC124) Patients with Nonsense Mutation Dystrophinopathy), submitted in line with the requirements of the Article 46 of the Paediatric Regulation.
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. The RMP version 8.0 has also been submitted."

Appointment of Re-examination rapporteurs, Draft timetable

Action: For adoption

Opinion adopted on 27.06.2019. Oral explanation held on 25.06.2019. Request for Supplementary Information adopted on 28.02.2019, 13.12.2018.

5.3.2. Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0049

Novartis Europharm Limited

Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia

Scope: "Extension of indication to include first line treatment of adult and paediatric patients aged 2 years and older with severe aplastic anaemia for Revolade in combination with standard immunosuppressive therapy; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 50 has also been updated."

Appointment of Re-examination rapporteur(s), draft timetable

Action: For adoption

Opinion adopted on 27.06.2019. Oral explanation held on 24.06.2019. Request for Supplementary Information adopted on 28.02.2019, 15.11.2018, 26.07.2018.

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

6.1.1. human fibrinogen / human thrombin - EMEA/H/D/004308

to support the endogenous clotting process and increase of haemostasis in surgical procedures

Scope: Withdrawal of application for consultation procedure for ancillary medicinal substances in medical devices

Action: For information

List of Outstanding Issues adopted on 28.03.2019. List of Questions adopted on 22.03.2018.

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. satralizumab (p-inn) - Orphan - H0004788

Roche Registration GmbH; satralizumab is indicated in adult and adolescent patients for the treatment of neuromyelitis optica and neuromyelitis optica spectrum disorders

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

Action: For adoption

8.2. Priority Medicines (PRIME)

Disclosure of 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. Eliquis - apixaban - EMEA/H/C/002148

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bart van der Schueren

Scope: DHPC on Eliquis 5 mg tablets package leaflet found in packs of Eliquis 2.5 mg tablets adopted via written procedure on 10 July 2019

Action: For information

9.1.2. NINLARO - ixazomib - EMEA/H/C/003844/R/0017, Orphan

Takeda Pharma A/S

Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Annika Folin

Scope: Renewal of Conditional Marketing Authorisation

Action: For adoption

9.1.3. NINLARO - ixazomib - EMEA/H/C/003844/II/0014/G, Orphan

Takeda Pharma A/S

Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Annika Folin

Scope: "Group of variations consisting of a type 2 variation to include submission of final report of progression free survival (PFS) in fulfilment of SOB004 and a type IB variation to request and extension of the due date of SOB003. Annex II is amended accordingly. Consequently the RMP is updated (version 4.0)."

Action: For adoption

Request for Supplementary Information adopted on 14.03.2019.

9.1.4. Venclyxto (EMEA/H/C/004106) LEG/REV 009

AbbVie Deutschland GmbH & Co. KG

Rapporteuer: Filip Josephson, Co-Rapporteur: Paula Boudewina van Hennik

Scope: PRAC & CHMP Rapporteurs' AR on MAH's responses to address questions regarding clinical trial data in Multiple myeloma and possible impact on Venclyxto's CLL approved indication.

Action: For discussion

9.1.5. Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0054/G

Janssen-Cilag International NV

Rapporteur: Jorge Camarero Jiménez

Scope: "Type II.B.II.e.6.z addition of functional secondary packaging (film-coated tablets in electronic connectivity-enabled blister; electronic wallet) as a new presentation (56 tablets pack sizes) EU/1/11/714/004. Type IA.B.II.e.5.a addition of new presentation (60 tablets) EU/1/11/714/005 (electronic wallet)."

Re-adoption of Request for Supplementary Information

Action: For adoption

Request for Supplementary Information adopted on 26.04.2019, 14.02.2019.

9.1.6. Zalmoxis - nalotimagene carmaleucel – Orphan, ATMP - EMEA/H/C/002801/R/0015

MolMed S.p.A

Rapporteur: Carla Herberts, Co-Rapporteur: Sol Ruiz, CHMP Coordinators: Paula Boudewina van Hennik and Maria Concepcion Prieto Yerro, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: update on annual renewal

Action: for discussion

Opinion adopted on 27.06.2019. Request for Supplementary Information adopted on 24.05.2019.

10. Referral procedures

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

No items

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

No items

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

No items

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

No items

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

No items

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

10.6.1. Methotrexate - JYLAMVO (CAP), NORDIMET (CAP); NAP - EMEA/H/A-31/1463

Applicants: Nordic Group B.V. (Nordimet), Therakind Limited (Jylamvo), various

Referral PRAC Rapporteur: Martin Huber; Referral PRAC Co-rapporteur: Željana Margan Koletić

Jylamvo EMEA/H/C/003756 - Rapporteur: Bruno Sepodes, PRAC Rapporteur: Jan Neuhauser

Nordimet EMEA/H/C/003983 - Rapporteur: Bruno Sepodes, PRAC Rapporteur: Martin Huber

Scope: Opinion following PRAC Recommendation

Action: For discussion

Review of the benefit-risk balance following notification by Spain of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

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

July 2019 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

Action: For information

13.2. Innovation Task Force briefing meetings

Information related to briefing meetings taking place with applicants cannot be released at the present time as it is deemed to contain commercially confidential information

No items

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

No items

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Election of CHMP Co-opted Member

Election of CHMP co-opted member in light of the expiry of the mandate of co-opted member Sol Ruiz on 21.07.2019.

Action: For adoption

Agreed area of expertise: Quality and safety (biological) with expertise in advanced therapies (gene, cell and tissue therapies)

Deadline for nominations 18 July 2019 – end of business. Please send any nominations

14.1.2. Seating plan for CHMP under Finish EU Presidency, 1 July – 31 December 2019

CHMP Seating Plan 1 July – 31 December 2019, under Finnish EU presidency

Action: For information

14.1.3. Timetable for August 2019 Written Procedure

Action: For adoption

14.1.4. Training for CHMP members and assessors in oncology

Action: For discussion

14.1.5. Strategic Review and Learning Meetings (SRLM)

CHMP-PRAC SRLM under the Finish presidency of the European Union (EU) Council – Helsinki, Finland, 21-23 October 2019

Action: For information

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on 08-11 July 2019

Action: For information

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for July 2019

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 17-19 July 2019

Action: For information

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 08-11 July 2019

Action: For information

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at July 2019 PDCO

Action: For information

Report from the PDCO meeting held on 23-26 July 2019

Action: For information

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 16-18 July 2019

Action: For information

14.2.6. Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh)

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 23-25 July 2019

Action: For information

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

14.3.1. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 08-11 July 2019. Table of conclusions

Action: For information

Scientific advice letters: Disclosure of information related to scientific advice letters cannot be released at present time as these contain commercially confidential information.

14.3.2. Name Review Group (NRG)

Naming of doxorubicin liposomal vs non-liposomal formulations

Action: For discussion

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP July 2019 meeting to CHMP for adoption:

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

Action: For adoption

14.3.4. Oncology Working Party (ONCWP)

Chairs: Pierre Demolis/Paolo Foggi

Guideline on MRD as an endpoint in clinical trials in Multiple Myeloma

List of questions to the SAG Oncology

Action: For adoption

Follow up from June ORGAM

14.4. Cooperation within the EU regulatory network

14.5. Cooperation with International Regulators

14.5.1. International Council on Harmonisation (ICH)

ICH E19 – Safety data collection

Action: For discussion

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

14.6.1. Update on recent interactions with down-stream decision makers

Report from the EMA/payer meeting on 18 June 2019, and the EMA/EUnetHTA bilateral on 4 July 2019

Action: For information

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Preparedness of the system and capacity increase

Action: For information

15.1.2. Update on Ebola outbreak

Action: For information

16. 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)*

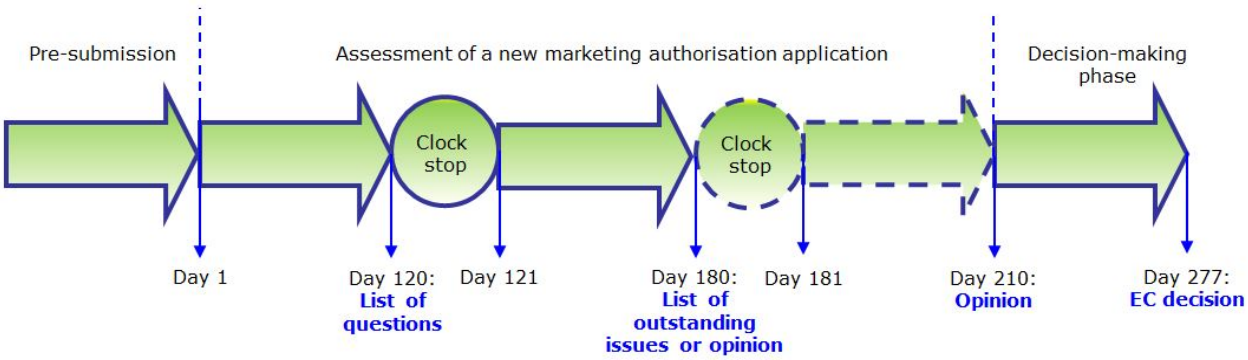
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

22 July 2019
EMA/CHMP/413338/2019

Annex to 22-25 July 2019 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 3
B.2.1. Renewals of Marketing Authorisations requiring 2nd Renewal 3
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 6
B.4. EPARs / WPARs 9
B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES 10
B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects 10
B.5.2. CHMP assessed procedures scope: Non-Clinical and Clinical aspects 15
B.5.3. CHMP-PRAC assessed procedures 28
B.5.4. PRAC assessed procedures 35
B.5.5. CHMP-CAT assessed procedures 40
B.5.6. CHMP-PRAC-CAT assessed procedures 41
B.5.7. PRAC assessed ATMP procedures 41
B.5.8. Unclassified procedures and worksharing procedures of type I variations 41
B.5.9. Information on withdrawn type II variation / WS procedure 46
B.5.10. Information on type II variation / WS procedure with revised timetable 46
B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION 46
B.6.1. Start of procedure for New Applications: timetables for information 46
B.6.2. Start of procedure for Extension application according to Annex I of Reg. 1234/2008): timetables for information 47
B.6.3. Restart of procedure - responses received to Day 120 List of Questions timetables: for information 48

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.6.4. Annual Re-assessments: timetables for adoption 48
B.6.5. Renewals of Marketing Authorisations: timetables for adoption provided only if the validation has been completed 48
B.6.6. VARIATIONS – START OF THE PROCEDURE 49
B.6.7. Type II Variations scope of the Variations: Extension of indication 49
B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects 52
B.6.9. CHMP assessed procedures scope: Non-Clinical and Clinical aspects 55
B.6.10. CHMP-PRAC assessed procedures 63
B.6.11. PRAC assessed procedures 69
B.6.12. CHMP-CAT assessed procedures 72
B.6.13. CHMP-PRAC-CAT assessed procedures 72
B.6.14. PRAC assessed ATMP procedures 72
B.6.15. Unclassified procedures and worksharing procedures of type I variations 72
B.7. DOCUMENTS TABLED IN MMD AFTER THE CHMP PLENARY 74
B.7.1. Yearly Line listing for Type I and II variations 74
B.7.2. Monthly Line listing for Type I variations 74
B.7.3. Opinion on Marketing Authorisation transfer (MMD only) 74
B.7.4. Notifications in accordance with Article 61(3) of Council Directive 2001/83/EC (MMD only) 74
B.7.5. Request for supplementary information relating to Notification of Type I variation (MMD only) 74
B.7.6. Notifications of Type I Variations (MMD only) 74

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) 74

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) 74

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES 74

E.1. PMF Certification Dossiers: 74
E.1.1. Annual Update 74
E.1.2. Variations: 74
E.1.3. Initial PMF Certification: 74
E.2. Time Tables – starting & ongoing procedures: For information 74

F. ANNEX F - Decision of the Granting of a Fee Reduction / Fee Waiver 75

F.1. Parallel Distribution - Pursuant to Article 9 of Council Regulation (EC) No. 2743/98 of 14 December 1998, as amended 75
F.2. Request for scientific opinion on justification of exceptional circumstance and for imperative grounds of public health 75

G. ANNEX G 75

G.1. Final Scientific Advice (Reports and Scientific Advice letters): 75
G.2. Ongoing procedures 75
G.3. PRIME 75
G.3.1. List of procedures concluding at 22-25 July 2019 CHMP plenary: 75
G.3.2. List of procedures starting in July 2019 for September 2019 CHMP adoption of outcomes 75

H. ANNEX H - Product Shared Mailboxes – e-mail address.....75

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for July 2019: **For adoption**

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

Final Outcome of Rapporteurship allocation for July 2019: **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

Chenodeoxycholic acid Leadiant - chenodeoxycholic acid - EMEA/H/C/004061/S/0010, Orphan
Leadiant GmbH, Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: Adam Przybylkowski

Elaprase - idursulfase - EMEA/H/C/000700/S/0080
Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Cerdelga - eliglustat - EMEA/H/C/003724/R/0022, Orphan
Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Eva A. Segovia

Senshio - ospemifene - EMEA/H/C/002780/R/0028

Shionogi B.V., Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Joseph Emmerich, PRAC Rapporteur: Kirsti Villikka

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Cyramza - ramucirumab - EMEA/H/C/002829/R/0031
Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Kolbeinn Gudmundsson (IS) (MNAT with IS for Clinical Efficacy, IS for Clinical Safety, IS for Coordination, FI for Non-Clinical, FI for Quality, LT for Clinical Pharmacology), PRAC Rapporteur: Brigitte Keller-Stanislawski
Request for Supplementary Information adopted on 29.05.2019.

Exviera - dasabuvir - EMEA/H/C/003837/R/0045
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Maria del Pilar Rayon

Lymphoseek - tilmanocept - EMEA/H/C/002085/R/0016
Norgine B.V., Rapporteur: Jayne Crowe, Co-Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Rugile Pilviniene
Request for Supplementary Information adopted on 29.05.2019.

Lynparza - olaparib - EMEA/H/C/003726/R/0029
AstraZeneca AB, Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Amelia Cupelli
Request for Supplementary Information adopted on 27.06.2019.

MULTAQ - dronedarone - EMEA/H/C/001043/R/0042
sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Menno van der Elst
Request for Supplementary Information adopted on 29.05.2019.

Moventig - naloxegol - EMEA/H/C/002810/R/0028
Kyowa Kirin Holdings B.V., Rapporteur: Bart Van der Schueren, Co-Rapporteur: Ewa Balkowiec

Iskra, PRAC Rapporteur: Ronan Grimes
Request for Supplementary Information adopted on 29.05.2019.

OFEV - nintedanib - EMEA/H/C/003821/R/0025, Orphan
Boehringer Ingelheim International GmbH, Rapporteur: Peter Kiely, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica Mirošević Skvrce
Request for Supplementary Information adopted on 29.05.2019.

Rasagiline ratiopharm - rasagiline - EMEA/H/C/003957/R/0014
Teva B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Ana Sofia Diniz Martins
Request for Supplementary Information adopted on 27.06.2019.

SCENESSE - afamelanotide - EMEA/H/C/002548/R/0026, Orphan
Clinuvel Europe Limited, Rapporteur: Janet Koenig, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Martin Huber

Sevelamer carbonate Winthrop - sevelamer carbonate - EMEA/H/C/003971/R/0022
Genzyme Europe BV, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Laurence de Fays

Tyverb - lapatinib - EMEA/H/C/000795/R/0060
Novartis Europharm Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Annika Folin

Vectibix - panitumumab - EMEA/H/C/000741/R/0094
Amgen Europe B.V., Rapporteur: Bjorg Bolstad, Co-Rapporteur: Konstantinos Markopoulos, PRAC Rapporteur: David Olsen

Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/R/0054
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Maria del Pilar Rayon

Xadago - safinamide - EMEA/H/C/002396/R/0032

Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Rhea Fitzgerald

Xydalba - dalbavancin - EMEA/H/C/002840/R/0028
Allergan Pharmaceuticals International Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Rugile Pilviniene

B.2.3. Renewals of Conditional Marketing Authorisations

Adcetris - brentuximab vedotin - EMEA/H/C/002455/R/0067, Orphan
Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst

NINLARO - ixazomib - EMEA/H/C/003844/R/0017, Orphan
Takeda Pharma A/S, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Annika Folin

See agenda 9.1

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 08-11 July 2019 PRAC:

Vascular endothelial growth factor (VEGF) inhibitors
ZALTRAP, INLYTA, AVASTIN, MVASI, ZIRABEV, CABOMETYX, COMETRIQ, KISPLYX, LENVIMA, OFEV, VOTRIENT, ICLUSIG, CYRAMZA, STIVARGA, NEXAVAR, SUTENT, FOTIVDA, CAPRELSA, VARGATEF - Signal of artery dissections and aneurysms – PRAC recommendation on a variation
Action: For adoption

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its July 2019 meeting:

EMEA/H/C/PSUSA/00001172/201811
(doxorubicin)
CAPS:
Caelyx (EMEA/H/C/000089) (doxorubicin), Janssen-Cilag International NV, Rapporteur: Ondřej Slanař
Myocet (EMEA/H/C/000297) (doxorubicin hydrochloride), Teva B.V., Rapporteur: Filip

Josephson
NAPS:
DOXORUBICIN ACTAVIS - ACTAVIS GROUP PTC EHF
DOXORUBICIN EBEWE - SANDOZ PHARMACEUTICALS D.D.
DOXORUBICIN HCL OMNICARE - OMNICARE PHARMA GMBH
PRAC Rapporteur: Eva Jirsová “Period Covered From: 11/11/2015 To: 11/11/2018”

EMEA/H/C/PSUSA/00001892/201812
(liraglutide)
CAPS:
Saxenda (EMEA/H/C/003780) (liraglutide), Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege
Victoza (EMEA/H/C/001026) (liraglutide), Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst “Period Covered From: 01/01/2018 To: 31/12/2018”

EMEA/H/C/PSUSA/00002264/201812
(paclitaxel)
CAPS:
Apealea (EMEA/H/C/004154) (paclitaxel), Oasmia Pharmaceutical AB, Rapporteur: Bart Van der Schueren
NAPS:
PACLITAXEL APTIL PHARMA - APTIL PHARMA LIMITED
“From: 27/12/2015 To: 27/12/2018”

EMEA/H/C/PSUSA/00002798/201811
(sufentanil)
CAPS:
Dzuveo (EMEA/H/C/004335) (sufentanil), FGK Representative Service GmbH, Rapporteur: Kolbeinn Gudmundsson
Zalviso (EMEA/H/C/002784) (sufentanil), Grunenthal GmbH, Rapporteur: Milena Stain
NAPS:
NAPS - EU
PRAC Rapporteur: Adam Przybylkowski “Period Covered From: 01/12/2015 To: 30/11/2018”

EMEA/H/C/PSUSA/00002940/201811
(thyrotropin alfa)
CAPS:
Thyrogen (EMEA/H/C/000220) (thyrotropin alfa), Genzyme Europe BV, Rapporteur: Peter Kiely, PRAC Rapporteur: Rhea Fitzgerald “From:

30/11/2015 To: 30/11/2018”

EMEA/H/C/PSUSA/00003085/201812
(ustekinumab)
CAPS:
Stelara (EMEA/H/C/000958) (ustekinumab), Janssen-Cilag International NV, Rapporteur: Jayne Crowe “Period Covered From: 30/12/2017 To: 30/12/2018”

EMEA/H/C/PSUSA/00010263/201812
(umeclidinium)
CAPS:
Incruse Ellipta (EMEA/H/C/002809) (umeclidinium bromide), GlaxoSmithKline (Ireland) Limited, Rapporteur: Maria Concepcion Prieto Yerro
Rolufta Ellipta (EMEA/H/C/004654) (umeclidinium), GlaxoSmithKline Trading Services Limited, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Amelia Cupelli “Period Covered From: 18/12/2017 To: 17/12/2018”

EMEA/H/C/PSUSA/00010264/201812
(umeclidinium bromide / vilanterol)
CAPS:
Anoro Ellipta (EMEA/H/C/002751) (umeclidinium / vilanterol), GlaxoSmithKline (Ireland) Limited, Rapporteur: Peter Kiely
Laventair Ellipta (EMEA/H/C/003754) (umeclidinium / vilanterol), GlaxoSmithKline (Ireland) Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Amelia Cupelli “Period Covered From: 18/12/2017 To: 17/12/2018”

EMEA/H/C/PSUSA/00010341/201812
(secukinumab)
CAPS:
Cosentyx (EMEA/H/C/003729) (secukinumab), Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, PRAC Rapporteur: Eva A. Segovia “From: 26/12/2017 To: 25/12/2018”

EMEA/H/C/PSUSA/00010379/201901
(nivolumab)
CAPS:
OPDIVO (EMEA/H/C/003985) (nivolumab), Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Period Covered From: 04/07/2018 To: 03/01/2019”

EMEA/H/C/PSUSA/00010391/201812 (lutetium (177Lu) chloride) CAPS: **EndolucinBeta** (EMEA/H/C/003999) (lutetium (177Lu) chloride), ITG Isotope Technologies Garching GmbH, Rapporteur: Peter Kiely **Lumark** (EMEA/H/C/002749) (lutetium lu-177), I.D.B. Holland B.V., Rapporteur: Joseph Emmerich NAPS: **LUTAPOL** - NARODOWE CENTRUM BADAN JADROWYCH PRAC Rapporteur: Ronan Grimes “From: 19/06/2018 To: 19/12/2018”	
EMEA/H/C/PSUSA/00010524/201812 (sofosbuvir / velpatasvir) CAPS: **Epclusa** (EMEA/H/C/004210) (sofosbuvir / velpatasvir), Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins “Period Covered From: 28/06/2017 To: 27/12/2018”	
EMEA/H/C/PSUSA/00010619/201901 (sofosbuvir / velpatasvir / voxilaprevir) CAPS: **Vosevi** (EMEA/H/C/004350) (sofosbuvir / velpatasvir / voxilaprevir), Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins “Period Covered From: 18/07/2018 To: 17/01/2019”	
EMEA/H/C/PSUSA/00010697/201901 (inotersen) CAPS: **Tegsedi** (EMEA/H/C/004782) (inotersen), Akcea Therapeutics Ireland Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Rhea Fitzgerald “Period Covered From: 06/07/2018 To: 05/01/2019”	

B.4. EPARs / WPARs

Azacitidine Celgene - azacitidine - EMEA/H/C/005300 Celgene Europe BV, Treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML) and acute myeloid leukemia (AML), Informed Consent of Vidaza, Informed consent application (Article 10c	For information only. Comments can be sent to the PL in case necessary.

of Directive No 2001/83/EC)	
Evenity - romosozumab - EMEA/H/C/004465 UCB Pharma S.A., Treatment of osteoporosis, 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.
Giapreza - angiotensin ii - EMEA/H/C/004930 La Jolla Pharmaceutical II B.V., treatment of hypotension in adults with distributive or vasodilatory shock who remain hypotensive despite fluid and vasopressor therapy, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Lacosamide UCB - lacosamide - EMEA/H/C/005243 UCB Pharma S.A., treatment of epilepsy, Informed Consent of Vimpat, Informed consent application (Article 10c of Directive No 2001/83/EC)	For information only. Comments can be sent to the PL in case necessary.
Radicava - edaravone - Orphan - EMEA/H/C/004938 Mitsubishi Tanabe Pharma GmbH; treatment of amyotrophic lateral sclerosis (ALS), 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.
WPAR	

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0066, Orphan Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 20.06.2019.
Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0069, Orphan Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik
Advate - octocog alfa -

EMEA/H/C/000520/II/0100 Baxter AG, Rapporteur: Jan Mueller-Berghaus	
Aimovig - erenumab - EMEA/H/C/004447/II/0003/G Novartis Europharm Limited, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 29.05.2019, 28.03.2019.	
AJOVY - fremanezumab - EMEA/H/C/004833/II/0002 TEVA GmbH, Rapporteur: Jan Mueller-Berghaus	
AMGEVITA - adalimumab - EMEA/H/C/004212/II/0017 Amgen Europe B.V., Rapporteur: Kristina Dunder Opinion adopted on 04.07.2019.	Positive Opinion adopted by consensus on 04.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Apealea - paclitaxel - EMEA/H/C/004154/II/0003/G Oasmia Pharmaceutical AB, Rapporteur: Bart Van der Schueren Request for Supplementary Information adopted on 26.04.2019.	
Atazanavir Mylan - atazanavir - EMEA/H/C/004048/II/0012 Mylan S.A.S, Generic, Generic of Reyataz, Rapporteur: Bjorg Bolstad Request for Supplementary Information adopted on 11.07.2019.	Request for supplementary information adopted with a specific timetable.
Atriance - nelarabine - EMEA/H/C/000752/II/0047/G Novartis Europharm Limited, Rapporteur: Sinan B. Sarac	
Benepali - etanercept - EMEA/H/C/004007/II/0042/G Samsung Bioepis NL B.V., Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 02.05.2019.	
Busilvex - busulfan - EMEA/H/C/000472/II/0030/G Pierre Fabre Medicament, Rapporteur: Jorge Camarero Jiménez Opinion adopted on 04.07.2019. Request for Supplementary Information adopted on 02.05.2019.	Positive Opinion adopted by consensus on 04.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0079/G	Request for supplementary information adopted with a specific timetable.

UCB Pharma S.A., Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 11.07.2019.	
Darzalex - daratumumab - EMEA/H/C/004077/II/0018/G, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac Opinion adopted on 11.07.2019. Request for Supplementary Information adopted on 24.01.2019, 08.11.2018.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Docetaxel Kabi - docetaxel - EMEA/H/C/002325/II/0022 Fresenius Kabi Deutschland GmbH, Generic, Generic of Taxotere, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 11.04.2019.	
Dupixent - dupilumab - EMEA/H/C/004390/II/0018/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus	
Erelzi - etanercept - EMEA/H/C/004192/II/0018 Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 11.07.2019.	Request for supplementary information adopted with a specific timetable.
Eylea - aflibercept - EMEA/H/C/002392/II/0053 Bayer AG, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 04.07.2019.	Request for supplementary information adopted with a specific timetable.
Flixabi - infliximab - EMEA/H/C/004020/II/0034 Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus Opinion adopted on 18.07.2019. Request for Supplementary Information adopted on 28.02.2019, 17.01.2019.	Positive Opinion adopted by consensus on 18.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0007 Seqirus Netherlands B.V., Rapporteur: Sol Ruiz	
Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0093	

AstraZeneca AB, Rapporteur: Bart Van der Schueren	
Inhixa - enoxaparin sodium - EMEA/H/C/004264/II/0048/G Techdow Europe AB, Duplicate, Duplicate of Thorinane, Rapporteur: Andrea Laslop	
Jylamvo - methotrexate - EMEA/H/C/003756/II/0005/G Therakind (Europe) Limited, Rapporteur: Bruno Sepodes Request for Supplementary Information adopted on 28.03.2019.	
Lymphoseek - tilmanocept - EMEA/H/C/002085/II/0017 Norgine B.V., Rapporteur: Jayne Crowe Request for Supplementary Information adopted on 26.04.2019.	
Miglustat Gen.Orph - miglustat - EMEA/H/C/004366/II/0003 Gen.Orph, Generic, Generic of Zavesca, Rapporteur: Milena Stain Opinion adopted on 04.07.2019. Request for Supplementary Information adopted on 23.05.2019, 08.11.2018.	Positive Opinion adopted by consensus on 04.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Natpar - parathyroid hormone - EMEA/H/C/003861/II/0013/G, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Bart Van der Schueren Request for Supplementary Information adopted on 29.05.2019, 31.01.2019.	
NovoRapid - insulin aspart - EMEA/H/C/000258/II/0128 Novo Nordisk A/S, Rapporteur: Kristina Dunder	
Ogivri - trastuzumab - EMEA/H/C/004916/II/0003/G Mylan S.A.S, Rapporteur: Koenraad Norga Request for Supplementary Information adopted on 02.05.2019.	
Omnitrope - somatropin - EMEA/H/C/000607/II/0060 Sandoz GmbH, Rapporteur: Johann Lodewijk Hillege	
Onpattro - patisiran - EMEA/H/C/004699/II/0004/G, Orphan Alnylam Netherlands B.V., Rapporteur: Kristina Dunder	

Request for Supplementary Information adopted on 29.05.2019.	
OPDIVO - nivolumab - EMEA/H/C/003985/II/0067/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez	
Prasugrel Mylan - prasugrel - EMEA/H/C/004644/II/0003/G Mylan S.A.S, Generic, Generic of Efient, Rapporteur: Alar Irs Request for Supplementary Information adopted on 11.07.2019, 16.05.2019.	Request for supplementary information adopted with a specific timetable.
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0145 CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 04.07.2019. Request for Supplementary Information adopted on 26.04.2019.	Positive Opinion adopted by consensus on 04.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Rebif - interferon beta-1a - EMEA/H/C/000136/II/0141 Merck Europe B.V., Rapporteur: Filip Josephson	
Skyrizi - risankizumab - EMEA/H/C/004759/II/0002/G AbbVie Deutschland GmbH & Co. KG, Rapporteur: Peter Kiely Request for Supplementary Information adopted on 18.07.2019.	Request for supplementary information adopted with a specific timetable.
Thyrogen - thyrotropin alfa - EMEA/H/C/000220/II/0104/G Genzyme Europe BV, Rapporteur: Peter Kiely Request for Supplementary Information adopted on 14.06.2019.	
Voncento - human coagulation factor viii / human von willebrand factor - EMEA/H/C/002493/II/0041/G CSL Behring GmbH, Rapporteur: Paula Boudewina van Hennik	
Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0056/G Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez Opinion adopted on 18.07.2019. Request for Supplementary Information adopted on 29.05.2019.	Positive Opinion adopted by consensus on 18.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1620 **Humalog-EMEA/H/C/000088/WS1620/0175** **Liprolog-EMEA/H/C/000393/WS1620/0136** Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 14.06.2019.	

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

Amglidia - glibenclamide - EMEA/H/C/004379/II/0004, Orphan Ammtek, Rapporteur: Martina Weise, “Update of sections 4.2 and 5.1 of the SmPC to reconcile posology instructions with the actual use of the product in clinical practice in order to avoid overdosing, to harmonise sections related to “Dosage adjustments and long-term treatment management” and remove reference to the off-label use of crushed tablets. This update is based on recently published literature, the ISPAD consensus guideline, and in line with the NEOGLI CSR. In addition, the applicant took the opportunity to make editorial corrections. The requested variation proposed amendments to the Summary of Product Characteristics and Package Leaflet.” Opinion adopted on 04.07.2019.	Positive Opinion adopted by consensus on 04.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Atriance - nelarabine - EMEA/H/C/000752/II/0046/G Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, “Update to the Annex II to remove the SOB based on final results from the Study NLR506AUS02T (COG AALL0434) 'Intensified methotrexate, nelarabine and augmented BFM therapy for children and young adults with newly diagnosed T-ALL and T-LBL'. As a result sections 4.8 and 5.1 of the SmPC are updated. Additionally the MAH took the opportunity to update section 4.6 of the SmPC to revise information on the male and female contraception taking into consideration available non-clinical and clinical safety data as well as internal MAH's guidelines based on information from literature, health authority and working	

group guidelines. Moreover, the MAH took the opportunity to update details of the local representatives in the PL and introduce minor editorial changes in the PI. The revised RMP version 10 is included in this submission." Request for Supplementary Information adopted on 28.02.2019.	
Bosulif - bosutinib - EMEA/H/C/002373/II/0036 Pfizer Europe MA EEIG, Rapporteur: Janet Koenig, "Submission of a population pharmacokinetic (popPK) analysis PMAR-884 that was conducted to fulfil a post-authorisation measure (PAM) requested by the CHMP as part of the assessment of Bosulif for the first-line treatment of chronic myelogenous leukaemia (CML) indication (variation EMEA/H/C/002373/II/0025/G)." Opinion adopted on 18.07.2019. Request for Supplementary Information adopted on 14.03.2019.	Positive Opinion adopted by consensus on 18.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
CellCept - mycophenolate mofetil - EMEA/H/C/000082/II/0146 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of sections 4.7 and 4.8 of the SmPC to update the safety information based on the reassessment of all available evidence from clinical trials and post-marketing experience, in order to present adverse drug reactions (ADRs) rather than adverse events (AEs). Additionally, section 5.2 of the SmPC is updated based on current literature on the pharmacokinetics in geriatric patients. The Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes throughout the PI and to bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 26.04.2019.	
Cosentyx - secukinumab - EMEA/H/C/003729/II/0051 Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, "Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include additional dosing information for Ankylosing Spondylitis (AS) patients based on final results from study	

CAIN457F2314; this is a randomized, double-blind, double dummy, placebo controlled, parallel-group, Phase 3 multicenter study of secukinumab versus placebo to demonstrate efficacy at 16 weeks and to assess long-term efficacy up to week 156 in patients with active AS; the Package Leaflet is updated accordingly."	
Deltyba - delamanid - EMEA/H/C/002552/II/0037, Orphan Otsuka Novel Products GmbH, Rapporteur: Koenraad Norga, "xC.I.13 MIC report as amendment to CSR 242-09-213" Request for Supplementary Information adopted on 11.07.2019.	Request for supplementary information adopted with a specific timetable.
EXJADE - deferasirox - EMEA/H/C/000670/II/0066 Novartis Europharm Limited, Rapporteur: Alexandre Moreau, "To update the Exjade SmPC (section 5.1) to reflect the results of clinical study CICL670A2302 (TELESTO) with Exjade in patients with myelodysplatic syndrome (MDS)." Request for Supplementary Information adopted on 29.05.2019.	
Gilenya - fingolimod - EMEA/H/C/002202/II/0053 Novartis Europharm Limited, Rapporteur: Alexandre Moreau, "Type II (C.I.4): - to update section 4.4 of the SmPC (subsection 'Return of disease activity (rebound)' and subsection 'Stopping therapy') to add information to prescribers on the timing of reported events and further recommendations on monitoring of patients. - to update section 4.6 of the SmPC to add a warning for women stopping treatment for the purpose of becoming pregnant and for pregnant women, and addition of a cross-reference to section 4.4 subsection 'Return of disease activity (rebound)'. - to update section 4.8 of the SmPC to add a new adverse reaction 'Severe exacerbation of disease after Gilenya discontinuation' with frequency 'Not known'. The package leaflet is updated accordingly." Request for Supplementary Information adopted on 29.05.2019, 07.03.2019.	
IBRANCE - palbociclib - EMEA/H/C/003853/II/0016 Pfizer Europe MA EEIG, Rapporteur: Filip	

Josephson, “Update of section 5.1 of the SmPC in order to update with information following submission of the final results from the pivotal Study A5481023 “A double blind, Phase 3 trial of fulvestrant with or without palbociclib in pre- and postmenopausal women with hormone receptor positive, HER2-negative metastatic breast cancer that progressed on prior endocrine therapy” listed as a recommendation at the time of initial MA.”
Request for Supplementary Information adopted on 02.05.2019, 31.01.2019.

Imbruvica - ibrutinib - EMEA/H/C/003791/II/0048, Orphan
Janssen-Cilag International NV, Rapporteur: Filip Josephson, “Update of section 4.4 of the SmPC Special warnings and precautions for use in order to add a warning under “bleeding-related events’ based on the final clinical study reports results to evaluate the risks of major hemorrhage with the administration of Imbruvica (ibrutinib)). The study is listed in section III.2 additional Pharmacovigilance Activities A non-interventional PASS clinical study report (CSR) for serious haemorrhage in the RMP.
In addition, the Marketing authorisation holder (MAH) took the opportunity to include a minor edit in the list of local representatives in the Package Leaflet.”
Request for Supplementary Information adopted on 29.05.2019, 14.03.2019.

Kanuma - sebelipase alfa - EMEA/H/C/004004/II/0019, Orphan
Alexion Europe SAS, Rapporteur: Bart Van der Schueren, “Submission of the final report from study LAL-CL04, in order to fulfil this recommendation (REC). This is an open label multicentre extension study to evaluate the long-term safety, tolerability and efficacy of sebelipase alfa in adult subjects with liver dysfunction due to lysosomal acid lipase deficiency who previously received treatment in study LAL-CL01.”
Request for Supplementary Information adopted on 29.05.2019, 21.03.2019.

Keytruda - pembrolizumab - EMEA/H/C/003820/II/0074
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, “Submission of the final CSR version

03 for KEYNOTE-013 summarising final data from the rrcHL cohort."
Request for Supplementary Information adopted on 14.06.2019.

Kyntheum - brodalumab -
EMEA/H/C/003959/II/0011
LEO Pharma A/S, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC "Mechanism of action" subsection with information about the cytokine IL-17C."

Kyprolis - carfilzomib -
EMEA/H/C/003790/II/0031, Orphan
Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 to add a once-weekly dose regimen for carfilzomib (Kyprolis) at 20/70 mg/m^2 in combination with dexamethasone (Kd) for the treatment of the currently indicated patient population. The MAH took the opportunity to implement editorial changes to the SmPC and Patient Information Leaflet (PIL) due to the revised excipients guideline (EMA/CHMP/302620/2017). The PIL is updated accordingly."
Request for Supplementary Information adopted on 27.06.2019, 28.02.2019, 15.11.2018.

Kyprolis - carfilzomib -
EMEA/H/C/003790/II/0038, Orphan
Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of section 6.6 of the SmPC with information regarding the handling and preparation of Kyprolis. The PL is updated accordingly."

Lonquex - lipegfilgrastim -
EMEA/H/C/002556/II/0048
Teva B.V., Rapporteur: Outi Mäki-Ikola, "Update of section 5.1 of the SmPC in order to include information based on results from study XM22-ONC-40041 listed as an imposed PASS in the Annex II; this is a multinational, multicentre, randomised, double-blind, placebo- and active-controlled study to further investigate the risks of disease progression and mortality associated with pegfilgrastim."
Request for Supplementary Information adopted on 28.03.2019.

MabThera - rituximab -
EMEA/H/C/000165/II/0165

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, “Change in the posology section as 8 cycles of MabThera should be used in combination with 6-8 (previously 8) cycles of CHOP chemotherapy.”

Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0026
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Joseph Emmerich, “Update of section 5.1 of the SmPC in order to reflect data from two Asian regional Phase 3 studies: study M15-592 (VOYAGE-1 - A Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of ABT-493/ABT-530 in Treatment-Naïve and Treatment-Experienced, Non-Cirrhotic Asian Adults with Chronic Hepatitis C Virus Genotype (GT) 1 to GT6 Infection With or Without Human Immunodeficiency Virus Co-Infection) and study M15-593 (VOYAGE-2 - An Open-Label Study to Evaluate the Efficacy and Safety of ABT-493/ABT-530 in Treatment-Naïve and Treatment-Experienced Asian Adults With Chronic Hepatitis C Virus Genotype (GT) 1 to GT6 Infection With Compensated Cirrhosis and With or Without Human Immunodeficiency Virus Co-Infection).”

Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0007, Orphan
Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, “Update of sections 4.8 and 5.1 of the SmPC based on safety and efficacy data for paediatric patients with relapsed or refractory AML from a systematic literature review.”

Mylotarg - gemtuzumab ozogamicin - EMEA/H/C/004204/II/0008, Orphan
Pfizer Europe MA EEIG, Rapporteur: Sinan B. Sarac, “Update the SmPC section 4.2 to specify the dose and schedule for the second induction. Furthermore, a statement in SmPC section 4.2 was added to increase awareness about the actual recommended (maximum) dose of Mylotarg and information regarding traceability added to section 4.4. In addition, the Marketing authorisation holder (MAH) took the opportunity to include minor editorial changes in sections 4.2, 4.4, 4.8 and 5.2 of the SmPC and to make minor updates to bring the PI in line with the latest QRD template version.”

Natpar - parathyroid hormone - EMEA/H/C/003861/II/0018/G, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Bart Van der Schueren, “Update of sections 4.4 and 4.8 of the SmPC in order to include information related to the potential risk of hypersensitivity reactions based on the review of cumulative postmarketing safety data, as well as the postmarketing cases of hypersensitivity with a frequency of unknown. Update of section 4.4 of the SmPC in order to include information related to the potential risk of seizure due to severe hypocalcemia, to add a warning based on the review of cumulative postmarketing safety data. The Package Leaflet has been revised accordingly.” Request for Supplementary Information adopted on 23.05.2019.	
OPDIVO - nivolumab - EMEA/H/C/003985/II/0069 Bristol-Myers Squibb Pharma EEIG, Co-Rapporteur: Paula Boudewina van Hennik, “Update of sections 4.2, 5.1 and 6.6 of the SmPC in order to introduce a new dosing regimen and schedule for adjuvant treatment of melanoma based on population PK data and Exposure-Response (E-R) Efficacy analysis. The Package leaflet has been updated accordingly.”	
Repatha - evolocumab - EMEA/H/C/003766/II/0035/G Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, “Update of section 5.1 of the SmPC following completion of studies 20110110 (OSLER) and 20120138 (OSLER-2) listed as a category 3 studies in the RMP; Study 20110110 (OSLER) was a multicenter, randomized, controlled, open-label, 5-year extension study to assess the long-term safety and efficacy of Repatha in patients with hyperlipidaemia; Study 20120138 (OSLER-2) was a multicenter, randomized, controlled, open-label, 3-year extension study designed to assess the long-term safety and efficacy of Repatha in patients with hypercholesterolemia. This variation is submitted to meet the requirement of MEA 002 (OSLER) and MEA 005 (OSLER-2).”	
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) -	

EMEA/H/C/004336/II/0016 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, “Update of section 4.5 of the SmPC in order to update the information related to coadministration based on the final results from studies ZOSTER-035 and ZOSTER-042; these are immunogenicity and safety studies in which Shingrix was co-administered either with Merck's 23-valent pneumococcal polysaccharide vaccine (Pneumovax 23; ZOSTER-035) or with GSK's reduced-antigen-content diphtheria and tetanus toxoids and acellular pertussis (dTpa) vaccine (Boostrix; ZOSTER-042); the Package Leaflet is updated accordingly.”	
Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0017 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, “Update of section 4.5 of the SmPC in order to update the information on concomitant administration based on final results from study ZOSTER-048 (REC005); this is an immunogenicity and safety study of Shingrix in subjects previously vaccinated with Zostavax; the Package Leaflet is updated accordingly.”	
Strensiq - asfotase alfa - EMEA/H/C/003794/II/0035/G, Orphan Alexion Europe SAS, Rapporteur: Daniela Melchiorri, “Update of sections 4.4, 4.6, 4.8 and 5.2 of the SmPC with the results of the integrated safety analysis of pooled asfotase alfa clinical studies, and section 5.1 of the SmPC with the final results of study ENB-002-08/ENB-003-08 (an open-label, non-randomised, non-controlled study) and study ENB-010-10 (a controlled, open label study to evaluate the efficacy, safety, and PK of asfotase alfa in infants and children ≤ 5 years of age with hypophosphatasia (HPP)). The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the SmPC and Package Leaflet.” Request for Supplementary Information adopted on 26.04.2019, 28.02.2019.	
Taltz - ixekizumab - EMEA/H/C/003943/II/0026/G Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, “Type II- C.I.4 -Update of section 5.1 of the SmPC based on results of study RHCF - a	Positive Opinion adopted by consensus on 18.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

52-Week Multicenter, Randomized, Open-Label, Parallel-Group Study Evaluating the Efficacy and Safety of Ixekizumab versus Adalimumab in Patients with Psoriatic Arthritis Who Are Biologic Disease-Modifying Anti-Rheumatic Drug Naïve. Type II- C.I.4 -Update of section 4.5 of the SmPC based on results of study RHBU – a study evaluating of the effect of ixekizumab on the pharmacokinetics of cytochrome P450 substrates in patients with moderate-to-severe plaque psoriasis." Opinion adopted on 18.07.2019. Request for Supplementary Information adopted on 14.06.2019.	
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0028 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC with new ADRs identified in IMpower132 study. This change is supported by safety data as presented in a drug safety report referring to the IMpower132 safety report (report 1089805) previously submitted to the Agency. The package leaflet is updated accordingly." Opinion adopted on 11.07.2019.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0059 Biogen Netherlands B.V., Rapporteur: Martina Weise, "Update of sections 4.8 and 5.1 of the SmPC in order to add the efficacy and safety information based on final results from study 109MS311, a multicentre extension study to determine the long-term safety and efficacy in paediatric subjects with RRMS (final study report already submitted under P46- 020). The Package Leaflet is updated accordingly."	
Translarna - ataluren - EMEA/H/C/002720/II/0053/G, Orphan PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "C.I.4: Update of section 5.3 of the SmPC in order to update the safety information based on final results Charles River 9001126 Three-month juvenile toxicology and toxicokinetic study planned in neonatal dogs listed as category 3 study in the RMP (MEA-005). C.I.13 Submission of the final report from study WIL-523008 listed as category 3 study in the RMP (MEA/003). This is a Seven-day tolerability and	Request for supplementary information adopted with a specific timetable.

pharmacokinetic study in neonatal dogs. C.I.13 Submission of the final report from study WIL-523009 listed as category 3 study in the RMP (MEA/004). This is a one-month juvenile dose range-finding toxicology and toxicokinetic study planned in neonatal dogs age correlating with dosing in newborn paediatric patients to 2 years of age. C.I.13 Submission of the final report from study (Charles River 5700755 listed as category 3 study in the RMP (MEA/0024). This is a 28-day investigational toxicology and toxicokinetic study of ataluren in juvenile beagle dogs with an 8-week recovery period – Category 3." Request for Supplementary Information adopted on 18.07.2019.	
Tremfya - guselkumab - EMEA/H/C/004271/II/0014 Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, "update of sections 4.8 and 5.1 of the SmPC in order to update the safety information based on final results from the phase 3 Eclipse study CNTO1959PSO3009, comparing guselkumab (Tremfya) and secukinumab (Cosentyx) for the treatment of moderate to severe plaque psoriasis." Request for Supplementary Information adopted on 11.07.2019.	Request for supplementary information adopted with a specific timetable.
Verzenios - abemaciclib - EMEA/H/C/004302/II/0003 Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC in order to add a criterion for discontinuing abemaciclib in the event of specific hepatic changes based on available safety data. In addition, the Marketing authorisation holder (MAH) took the opportunity to make editorial changes to section 5.1 of the SmPC." Request for Supplementary Information adopted on 29.05.2019.	
Xarelto - rivaroxaban - EMEA/H/C/000944/II/0064 Bayer AG, Rapporteur: Kristina Dunder, "Submission of the final report from an interventional phase III study (COMMANDER HF, 2.5 mg rivaroxaban compared to placebo)." Request for Supplementary Information adopted on 16.05.2019.	
Xermelo - telotristat ethyl -	Request for supplementary information adopted

EMEA/H/C/003937/II/0014, Orphan Ipsen Pharma, Rapporteur: Martina Weise, "To update sections 4.2 and 5.2 of the SmPC following final results from study LX1606-111; this is a Phase 1, open-label, parallel-group study to evaluate the single-dose pharmacokinetics of Telotristat Ethyl in Male and Female Subjects with Severe Hepatic Impairment and Matched Subjects with Normal Function; the Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 11.07.2019.	with a specific timetable.
WS1506/G **Nuwiq-EMEA/H/C/002813/WS1506/0026/G** **Vihuma-EMEA/H/C/004459/WS1506/0009/G** Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.2, 4.8 and 5.1 of the SmPC based on clinical data from studies GENA-21 and GENA-13. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 26.04.2019, 13.12.2018.	
WS1523 **Epclusa-EMEA/H/C/004210/WS1523/0031** **Harvoni-EMEA/H/C/003850/WS1523/0072** **Sovaldi-EMEA/H/C/002798/WS1523/0054** **Vosevi-EMEA/H/C/004350/WS1523/0022** Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, "Update of sections 4.4 and 4.5 of the SmPC in order to implement new information on the use of sofosbuvir-based therapy with concomitant drugs, based on final results from study GS-US-334-2130. This was a phase I study to evaluate the effects of cytochrome P450 and drug transporter inducers on sofosbuvir and probe drug pharmacokinetics in healthy subjects. Furthermore, section 4.3 of the Sovaldi SmPC was updated in order to remove the use of rifabutin as a contraindication. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor editorial changes throughout the Product Information." Opinion adopted on 04.07.2019. Request for Supplementary Information adopted	Positive Opinion adopted by consensus on 04.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

on 26.04.2019, 14.02.2019.	
WS1527/G **Cymbalta-EMEA/H/C/000572/WS1527/0078/G** **Duloxetine Lilly-EMEA/H/C/004000/WS1527/0014/G** **Xeristar-EMEA/H/C/000573/WS1527/0081/G** **Yentreve-EMEA/H/C/000545/WS1527/0063/G** Eli Lilly Nederland B.V., Duplicate, Duplicate of Ariclaim, Yentreve, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Maria del Pilar Rayon, “C.I.4 (Type II) - Update of sections 4.4 and 4.6 of the SmPC in order to add a warning on the risk of postpartum haemorrhage based on final results from study F1J-MC-B057 listed as a category 3 in the RMP; this is an observational study to assess maternal and foetal outcomes following exposure to duloxetine. The Package Leaflet is updated accordingly. C.I.11.z (Type IB) - to stop enrolment of study F1J-MC-B034 (study B034), another study included in the current EU-RMP Version 12.4 as an additional pharmacovigilance activities to address missing information regarding duloxetine exposure due to pregnancy. The RMP version 13 has also been submitted. In addition, the Worksharing applicant (WSA) took the opportunity to correct the term “sucrase-isomaltase” in section 4.4 of the SmPC in line with the Annex to the EC guideline on ‘Excipients in the labelling and package leaflet of medicinal products for human use’ (EMA/CHMP/302620/2017 corr. 1*) and to bring the PI in line with the latest QRD template version 10. The Xeristar 30 mg SmPC & Xeristar 60 mg SmPC and the Yentreve 20 mg SmPC & Yentreve 40 mg SmPC have been combined in a single SmPC, respectively, following the Policy on combined SmPCs (EMA/333423/2015).” Request for Supplementary Information adopted on 11.04.2019.	
PRAC Led **WS1601** **Glyxambi-EMEA/H/C/003833/WS1601/0022** **Jentadueto-EMEA/H/C/002279/WS1601/0051**	Request for supplementary information adopted with a specific timetable.

Trajenta-EMEA/H/C/002110/WS1601/0038

Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of sections 4.2 and 5.1 of the Trajenta SmPC, update of sections 4.2, 4.4 and 5.1 of the Jentadueto SmPC and section 5.1 of the Glyxambi SmPC, based on the final results from study 1218.74 (CAROLINA study) listed as a category 3 study in the RMP of Jentadueto and Trajenta, in order to fulfil Trajenta MEA 008.1 and Jentadueto MEA 001.1; this is a phase III randomized, parallel group, double blind study to evaluate Cardiovascular safety of linagliptin versus glimepiride in patients with type 2 diabetes mellitus at high cardiovascular risk. The Package Leaflet for Trajenta is updated accordingly. The RMP version 13.0 for Jentadueto and Trajenta and version 5.0 for Glyxambi have also been submitted. In addition, the Worksharing applicant (WSA) took the opportunity to make corrections throughout the product information for Glyxambi and Jentadueto and to make corrections to the Bulgarian, French, Swedish translations for Glyxambi."
Request for Supplementary Information adopted on 11.07.2019.

WS1613

Epclusa-EMEA/H/C/004210/WS1613/0039

Vosevi-EMEA/H/C/004350/WS1613/0029

Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, "Update of section 4.5 of the SmPC in order to add new information regarding co-administration with atorvastatin, based on final results from study GS-US-342-4034. Study GS-US-342-4034 was a phase 1 study to evaluate the effect of sofosbuvir/velpatasvir fixed dose combination on the pharmacokinetics of atorvastatin.
The Package Leaflet is updated accordingly.
In addition, the Worksharing Applicant took the opportunity to amend Annex II of the Product Information with regards to the due date for submission of study DAA-PASS. This study is designed to evaluate the recurrence of hepatocellular carcinoma and the date has been postponed from Q2 2021 to Q2 2023, as

approved in the framework of WS1476. Furthermore, the MAH implemented minor editorial updates throughout the Product Information." Request for Supplementary Information adopted on 20.06.2019.	

B.5.3. CHMP-PRAC assessed procedures

Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0150 Amgen Europe B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Update of the SmPC sections 4.4, 4.8, 5.1 based on the study data from Study 20070782 - a phase 3, randomized, double-blind, placebo-controlled, noninferiority study in subjects with chemotherapy-induced anemia receiving multi-cycle chemotherapy for the treatment of advanced stage nonsmall-cell lung cancer (NSCLC); study of epoetin alfa in metastatic breast cancer (EPO-ANE-3010) and the Company Core Data Sheet. In addition, the section 4.6 has been revised based on the recommendation from last Periodic Safety Update Report Number 33 dated 15 January 2018. Furthermore, the MAH took the opportunity to introduce minor editorial changes, update the information on local representatives and align the PI with the requirements of the QRD template 10.0. The PL is updated accordingly. The revised RMP version 9.3 has been also submitted." Request for Supplementary Information adopted on 28.03.2019.	
BYETTA - exenatide - EMEA/H/C/000698/II/0069 AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Submission of a justification for extrapolating exenatide once weekly clinical data (previously assessed for Bydureon) to exenatide twice daily (Byetta) in order to include the latest agreed RMP versions for Bydureon (v30, v31s2 and v32s2) also in the dossier for Byetta. As a consequence, the removal of the important potential risk 'Cardiac Events' is proposed also for Byetta." Opinion adopted on 11.07.2019.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Ferriprox - deferiprone - EMEA/H/C/000236/II/0128 Apotex B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update section 4.4 of the SmPC and the patient/carer reminder card in order to update and change the recommended frequency of ANC monitoring throughout Ferriprox treatment from a weekly basis to every week for the first six months of Ferriprox therapy, once every two weeks after six months of Ferriprox therapy, and to monthly after one year of therapy. The package leaflet has been updated accordingly. The RMP version 13.2 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update minor linguistic amendments in the HU and MT product information." Opinion adopted on 11.07.2019. Request for Supplementary Information adopted on 16.05.2019, 29.11.2018.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0034, Orphan Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final CSR for Study BO21005 comparing the efficacy of obinutuzumab in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone/prednisolone (CHOP; G-CHOP) versus rituximab and CHOP (R CHOP) in previously untreated patients with CD20-positive diffuse large B-cell lymphoma (DLBCL); this is an RMP category 3 study." Opinion adopted on 11.07.2019. Request for Supplementary Information adopted on 16.05.2019.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Giotrif - afatinib - EMEA/H/C/002280/II/0031 Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "Update of sections 4.4 and 4.8 of the SmPC in order to add gastrointestinal (GI) perforation as an additional side effect based on summarises of clinical trial and post-marketing safety data. The Package Leaflet and the RMP are updated accordingly. The RMP version 8.0 has been submitted including also the update of the RMP due to transition to the revision 2 template as per pharmacovigilance guidance and taking in	

consideration the recommendation received during renewal procedure EMEA/H/C/002280/R/0026. In addition the MAH took the opportunity to correct some typographical errors in the German, Austrian and Spanish PIs, to include a linguistic review comments received from Czech Authority during linguistic review of procedure EMEA/H/C/002280/R/0026 in the SmPC and to update the list of the local representatives for Austria in the package leaflet."	
Insuman - insulin human - EMEA/H/C/000201/II/0130 Sanofi-Aventis Deutschland GmbH, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Jean-Michel Dogné, "Submission of the final report from a completed Phase 3 study, HUBIN-L-05335, listed as a category 3 post-authorisation efficacy / safety study in the RMP. This study covers the evaluation of Insuman Implantable 400 IU/ml in patients with Type 1 diabetes treated with the Medtronic MiniMed Implantable Pump System using Insuplant 400 IU/ml, addressing the Post-Authorisation Measure MEA040. In this application, the RMP v4.0 combines the updates related to HUBIN-L-05335 study final results and the approval of amended protocol V2 of the ongoing Post Authorization Safety Study HUBIN-C-06380 (MEA/047.4 & MEA/047.5, concerning PRAC decision: EMA/PRAC/256519/2018 dated 17-May-2018; updates are limited to Annex 3 of Part VII)." Request for Supplementary Information adopted on 11.07.2019.	Request for supplementary information adopted with a specific timetable.
Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0029/G Orexigen Therapeutics Ireland Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber, "Group of variations consisting of the: 2) C.I.3.b: to update section 4.8 on the list of adverse drug reactions and their corresponding frequencies following the PRAC outcome on PSUR procedure (PSUSA/10366/201709). 2) C.I.4: to update sections 4.2, 4.4 and 5.2 of the SmPC to add results from a phase I open label parallel study to evaluate the pharmacokinetics of a single oral dose of extended-release	

combination of naltrexone and bupropion in subjects with normal hepatic function or varying degrees of impaired hepatic function and remove the recommendation to not use naltrexone/bupropion in patients with mild hepatic impairment. The existing warning has also been updated accordingly. The warning related to contraindications has also been aligned to section 4.3 to add end-stage renal failure patients. Consequentially an updated RMP (version 11) has also been submitted. In addition, the MAH takes the opportunity to update the warning on lactose to be in accordance with EC guideline on Guideline on "Excipients in the labelling and package leaflet of medicinal products for human use".” Request for Supplementary Information adopted on 29.05.2019, 28.02.2019, 15.11.2018.	
NINLARO - ixazomib - EMEA/H/C/003844/II/0014/G, Orphan Takeda Pharma A/S, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Annika Folin, “Group of variations consisting of a type 2 variation to include submission of final report of progression free survival (PFS) in fulfilment of SOB004 and a type IB variation to request and extension of the due date of SOB003. Annex II is amended accordingly. Consequently the RMP is updated (version 4.0).” Request for Supplementary Information adopted on 14.03.2019.	See agenda 9.1
Pelgraz - pegfilgrastim - EMEA/H/C/003961/II/0005 Accord Healthcare S.L.U., Rapporteur: Sol Ruiz, PRAC Rapporteur: Menno van der Elst Request for Supplementary Information adopted on 29.05.2019.	
PREVYMIS - letermovir - EMEA/H/C/004536/II/0011, Orphan Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Kirsti Villikka, “Update of sections 4.4 and 4.5 of the SmPC in order to update the safety information following the final results of a clinical pharmacology trial entitled “A Study to Assess the Effect of Rifampin on the Single-Dose and Steady-State Pharmacokinetics of MK-8228 in Healthy Adult Subjects” (MK-8228-038) listed as a category 3	

study in the RMP; the Package Leaflet is updated accordingly. The RMP version 2.1 has also been submitted." Request for Supplementary Information adopted on 29.05.2019.	
Reagila - cariprazine - EMEA/H/C/002770/II/0010 Gedeon Richter Plc., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ana Sofia Diniz Martins, "Submission of in vitro metabolism study report (R188-A15) and consequential update of the Risk Management Plan" Request for Supplementary Information adopted on 11.07.2019.	Request for supplementary information adopted with a specific timetable.
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0058 Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Submission of CSR of study 109MS310, an open-label study to assess the effects of Tecfidera on lymphocyte subsets in subjects with relapsing remitting multiple sclerosis, listed as category 3 study in the RMP. The RMP (version 10.1) has been updated as a consequence of the completion of this study. The revised RMP also includes updates to reflect safety information available through to the data lock point of 24 January 2019 and to align with the EU RMP Module V (revision 2.01)." Request for Supplementary Information adopted on 11.07.2019.	Request for supplementary information adopted with a specific timetable.
Tyverb - lapatinib - EMEA/H/C/000795/II/0062 Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "Submission of the final report from study EGF117165/LAP016A2206 listed as an obligation in the Annex II of the Product Information. This is an open-label, phase II study to evaluate biomarkers associated with response to subsequent therapies in subjects with HER2-positive metastatic breast cancer receiving treatment with trastuzumab in combination with lapatinib or chemotherapy. The Annex II and the RMP are updated to reflect the completion of this study. The RMP version 36.0 has also been submitted to address the PRAC recommendation from the last PSUR review."	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 11.07.2019.	
Vemlidy - tenofovir alafenamide - EMEA/H/C/004169/II/0020 Gilead Sciences Ireland UC, Rapporteur: Janet Koenig, PRAC Rapporteur: Amelia Cupelli, "Update of sections 4.8 and 5.1 of the SmPC based on safety information from interim results at week 48 of a phase 3, randomized, double blind study (GS-US-320-4018) conducted to evaluate the efficacy and safety of switching from tenofovir disoproxil fumarate (TDF) 300 mg QD to tenofovir alafenamide (TAF) 25 mg QD in subjects with CHB who are virologically suppressed, listed as a category 3 study in the RMP; the Package Leaflet is updated accordingly. The RMP version 4.1 has also been submitted."	
Wakix - pitolisant - EMEA/H/C/002616/II/0017, Orphan BIOPROJET PHARMA, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.4, 4.5, 4.6 of the SmPC in order to reflect available information of co-administration of pitolisant with CYP3A4 substrats based on the results from studies R-B478-2.649, R.BF2.649-SK-005, R-B472-1.11413. The MAH took the opportunity to update the section 5.2 of SMPC to more accurately reflect information previously assessed during procedure EMEA/H/C/2616/II/0004/G (CD 13/10/2017). The RMP version 6.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to clarify the details about finished product manufacturers in the Package Leaflet." Opinion adopted on 11.07.2019. Request for Supplementary Information adopted on 14.03.2019.	Negative Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0015, Orphan Ipsen Pharma, Rapporteur: Martina Weise, PRAC Rapporteur: Adam Przybylkowski, "To update section 5.1 of the SmPC based on final results from study LX1606.1-302.CS (TELEPATH) listed as a category 3 study in the RMP; this is a multicentre, phase III, long-term extension study to further evaluate the safety and tolerability of telotristat etiprate in patients with carcinoid	Request for supplementary information adopted with a specific timetable.

syndrome (CS). The updated RMP version 4.0 has also been submitted, also updating to GVP Module V (Rev 2).” Request for Supplementary Information adopted on 11.07.2019.	
WS1557 **Exelon-EMEA/H/C/000169/WS1557/0120** **Prometax-EMEA/H/C/000255/WS1557/0121** Novartis Europharm Limited, Lead Rapporteur: Alexandre Moreau, Lead PRAC Rapporteur: Ghania Chamouni, “Submission of the final report of the Drug Utilization Study (CENA713D2409) aimed to assess the extent of inappropriate use of Exelon and Prometax. The DUS final report is fulfilling the post-authorisation measures Exelon MEA 034 and Prometax MEA 035.” Opinion adopted on 11.07.2019. Request for Supplementary Information adopted on 14.03.2019.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1582 **Actraphane-EMEA/H/C/000427/WS1582/0076** **Actrapid-EMEA/H/C/000424/WS1582/0070** **Insulatard-EMEA/H/C/000441/WS1582/0073** **Mixtard-EMEA/H/C/000428/WS1582/0077** **Protaphane-EMEA/H/C/000442/WS1582/0072** Novo Nordisk A/S, Lead Rapporteur: Sinan B. Sarac, Lead PRAC Rapporteur: Hans Christian Siersted, “To update the Human Insulin RMP to version 3.1 in order to reclassify the risk of 'Medication errors' (including human error-related medication errors) from an important potential risk to an important identified risk following a Pharmacovigilance Risk Assessment Committee (PRAC) request (EMEA/H/C/PSUSA/00001753/201710) and in accordance with the Good practice guide on risk minimisation and prevention of medication errors, issued by the PRAC in 2015. Furthermore, in accordance with the updated GVP Module V guidance on RMPs, the Work sharing applicant (WSA) proposed to remove this risk as it is fully characterised and managed through routine pharmacovigilance and no additional pharmacovigilance activities or	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

additional risk minimisation measures are planned or being currently undertaken. Information regarding the avoidance of accidental mix-ups/medication errors is included in the PIL for the concerned products. In consequence, section 4.4 of the SmPC was updated in order to add a warning on accidental mix-ups/medication. Additionally, the WSA took the opportunity to include minor updates to Annex IIIA to bring the PI in line with the latest QRD template version." Opinion adopted on 11.07.2019. Request for Supplementary Information adopted on 16.05.2019.	

B.5.4. PRAC assessed procedures

PRAC Led **Bydureon - exenatide - EMEA/H/C/002020/II/0059** AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final CSR for Study H80-MC-B016; a modified Prescription-Event Monitoring Program (Modified PEM) to be conducted in the UK, enrolling patients with Type 2 diabetes mellitus, to quantify the incidence of acute pancreatitis in the first 12 months after initiating treatment with prescription exenatide once weekly. An updated RMP version 33 was provided as part of the application. The provision of the final CSR addresses Post-authorisation Measure MEA 010.5." Opinion adopted on 11.07.2019. Request for Supplementary Information adopted on 16.05.2019.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Cotellic - cobimetinib - EMEA/H/C/003960/II/0016** Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 4.0 in order to align with the current GVP Rev 2; additionally, a change is made in line with the PRAC recommendation from procedure EMEA/H/C/003960/MEA/PRO 003." Opinion adopted on 11.07.2019.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Request for Supplementary Information adopted on 14.06.2019.	
PRAC Led **Flixabi - infliximab - EMEA/H/C/004020/II/0039** Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Update of the RMP to replace the current registries with one company-sponsored initiated registry (PERFUSE) and three IBD registries (CEDUR, CREDIT, and DREAM)" Request for Supplementary Information adopted on 11.07.2019, 11.04.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Keytruda - pembrolizumab - EMEA/H/C/003820/II/0068** Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP (finally agreed version 24.0) in order to discuss the effectiveness of the educational materials put in place for Keytruda at the time of the initial marketing authorisation and to provide a proposal to update these materials as well as to revise the safety specification as requested by PRAC during PSUSA/00010403/2018 procedure." Opinion adopted on 11.07.2019. Request for Supplementary Information adopted on 16.05.2019, 14.03.2019.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Komboglyze - saxagliptin / metformin hydrochloride - EMEA/H/C/002059 /II/0046** AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 15 in order to implement the revised GVP template Rev.2. As a result, the list of safety concerns has been revised and a number of important identified risks, important potential risks and missing information have been reclassified and have been removed from the RMP." Opinion adopted on 11.07.2019.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Noxafil - posaconazole - EMEA/H/C/000610/II/0057**	Request for supplementary information adopted with a specific timetable.

Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP (version 15.1) in order to bring it in line with the guidance included in Good Pharmacovigilance Practices (GVP) Module V (Rev. 2), with the consequent applicable re-evaluation of some safety concerns. In addition to the above updates, the MAH took the opportunity to include data from the completed clinical trial in paediatric subjects PN097 (the CSR for which was submitted to the Agency in February 2019: P46 029), and update the due date for submission of the final report for the ongoing post-marketing efficacy trial PN069 (changed from December 2019 to 4th quarter of 2020)." Request for Supplementary Information adopted on 11.07.2019.	
PRAC Led **Orencia - abatacept - EMEA/H/C/000701/II/0124/G** Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kimmo Jaakkola, PRAC-CHMP liaison: Outi Mäki-Ikola, "Submission of the final reports from studies IM101125, IM101127, IM101211, IM101213 (four C.I.13 variations) and the interim report from study IM101121 listed as category 3 studies in the RMP. These are biologic registries and pharmacoepidemiology studies to assess the risk associated with the use of abatacept during post-marketing in geographically diverse populations and subgroups. The RMP (version 26.2) was updated to reflect the completion of the studies IM101125, IM101127, IM101211, and IM101213. Due to feasibility issues the study IM101121 has been removed from the RMP and "Adverse Pregnancy Outcomes" was removed from the RMP safety specification. Two additional epidemiological studies IM101803 and IM101816 aimed to gather more information on malignancies were added as category 3 studies in the RMP. Based on a cumulative search from Company Safety Database, the RMP was updated to remove the safety concern PML from the safety specifications. The following Missing Information items were also removed in the RMP safety specification: combination therapy, including	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

biologic therapy, and elderly patients. Submission of final study report from study IM101488 “Post-marketing Study Assessing the Long-term Safety of Abatacept” (C.I.13 variation), a retrospective cohort study that was conducted separately among 3 existing administrative health care databases in the US. No changes were made to the PI or the RMP as results of the assessment of those data.” Opinion adopted on 11.07.2019. Request for Supplementary Information adopted on 14.03.2019.	
PRAC Led **Rebetol - ribavirin -** **EMEA/H/C/000246/II/0086** Merck Sharp & Dohme B.V., PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Joseph Emmerich, “Submission of an updated RMP version 5.1 in order to revise safety concerns for ribavirin based on GVP module V (rev. 2) guidance. In addition, the MAH took the opportunity to revise the safety concerns of ribavirin in light of the current era of IFN free regimen, as requested in a previous PSUSA procedure (EMEA/H/C/PSUSA/00010007/201707).” Request for Supplementary Information adopted on 11.07.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Somavert - pegvisomant -** **EMEA/H/C/000409/II/0089** Pfizer Europe MA EEIG, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Joseph Emmerich, “Submission of the final report from ACROSTUDY (Study A6291010), an open-label, global, non-interventional post-authorisation safety study (PASS) performed to monitor the long-term safety and outcomes of pegvisomant treatment in clinical practice. This final CSR relates to the Post Approval Measure MEA 059, listed as a category 3 study in the RMP.” Opinion adopted on 11.07.2019. Request for Supplementary Information adopted on 14.03.2019.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Stayveer - bosentan -** **EMEA/H/C/002644/II/0027** Janssen-Cilag International NV, Rapporteur:	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Alexandre Moreau, “Submission of the final report from study AC-052-516, (a category 1 study). This is a non-interventional observational study of the disease characteristics and outcomes of PAH in children and adolescents in real-world clinical settings. The RMP version 10 has also been submitted. The RMP has been updated in line with GVP module 2.” Opinion adopted on 11.07.2019.	
PRAC Led **Tracleer - bosentan - EMEA/H/C/000401/II/0091** Janssen-Cilag International NV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Alexandre Moreau, “Submission of the final report from study AC-052-516, (a category 1 study). This is a non-interventional observational study of the disease characteristics and outcomes of PAH in children and adolescents in real-world clinical settings. The RMP version 10 has also been submitted. The RMP has been updated in line with GVP module 2.” Opinion adopted on 11.07.2019.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Tysabri - natalizumab - EMEA/H/C/000603/II/0114** Biogen Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, “Update of the RMP (version 25.0) with information related to extended interval dosing that will be added to the educational materials. Annex IID of the PI also reflects the above changes.” Request for Supplementary Information adopted on 11.07.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Vectibix - panitumumab - EMEA/H/C/000741/II/0093** Amgen Europe B.V., Rapporteur: Bjorg Bolstad, PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Bjorg Bolstad, “Submission of RMP version 23 for panitumumab to align the important identified and potential risks and	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

missing information with the EMA guideline on Good Pharmacovigilance Practices Module V (Rev. 2). As a result Annex II has been updated. The MAH is taking the opportunity to update sections 4.2 and 4.4 to include the table on dose modification previously located in the section 4.4. The section 4.4 is also updated to implement the latest excipient guideline recommendation on sodium content. In addition, minor corrections are introduced in the section 4.8 of the SmPC and in the list of the local representatives." Opinion adopted on 11.07.2019. Request for Supplementary Information adopted on 16.05.2019.	
PRAC Led **WS1608** **Filgrastim Hexal-EMEA/H/C/000918/WS1608/0049** **Zarzio-EMEA/H/C/000917/WS1608/0050** Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "The scope of the above mentioned variation application is to align on the due dates and deliverables for the post-authorization measure, MEA007. The due date is extended from Dec 2019 to March 2020, to combine the annual safety report (ASR) with the 5-year interim clinical study report (CSR) in 2020 and the final CSR in 2024 and for the MEA to cover the entire duration of study EP06-501." Request for Supplementary Information adopted on 16.05.2019.	

B.5.5. CHMP-CAT assessed procedures

Kymriah - tisagenlecleucel - EMEA/H/C/004090/II/0011, Orphan, ATMP Novartis Europharm Limited, Rapporteur: Rune Kjeken, CHMP Coordinator: Ingrid Wang Request for Supplementary Information adopted on 19.07.2019.	Request for supplementary information adopted with a specific timetable.
YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0007, Orphan, ATMP Kite Pharma EU B.V., Rapporteur: Jan	

Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus, Request for Supplementary Information adopted on 24.05.2019.	

B.5.6. CHMP-PRAC-CAT assessed procedures

Zalmoxis - nalotimagene carmaleucel - EMEA/H/C/002801/II/0016, Orphan, ATMP MolMed S.p.A, Rapporteur: Carla Herberts, Co-Rapporteur: Sol Ruiz, CHMP Coordinators: Paula Boudewina van Hennik and Maria Concepcion Prieto Yerro, PRAC Rapporteur: Brigitte Keller-Stanislawski, "The MAH is proposing to terminate the study TK008 (specific obligation for the CMA) and replace it with study TK013" Request for Supplementary Information adopted on 24.05.2019. Clockstop extension requested to respond to RSI For adoption.	

B.5.7. PRAC assessed ATMP procedures

PRAC Led **Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0034, ATMP** Amgen Europe B.V., Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "To update the RMP for Imlygic to version 7.0 in order to add 2 category 3 studies (Studies 20180062 and 20180099), as well as an internal evaluation of managed distribution process metrics, to evaluate the effectiveness of additional risk minimization measures (aRMM)."	

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

WS1585 **Infanrix hexa-EMEA/H/C/000296/WS1585/0258** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 11.07.2019.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1593 **Ambirix-EMEA/H/C/000426/WS1593/**	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP

0098 **Twinrix Adult-EMEA/H/C/000112/WS1593/0133** **Twinrix Paediatric-EMEA/H/C/000129/WS1593/0134** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 11.07.2019.	Members were in agreement with the CHMP recommendation.
WS1595 **Kalydeco-EMEA/H/C/002494/WS1595/0078** **Symkevi-EMEA/H/C/004682/WS1595/0009** Vertex Pharmaceuticals (Ireland) Limited, Lead Rapporteur: Maria Concepcion Prieto Yerro, "To provide a final Environmental Risk Assessment report." Request for Supplementary Information adopted on 16.05.2019.	
WS1602/G **Leganto-EMEA/H/C/002380/WS1602/0030/G** **Neupro-EMEA/H/C/000626/WS1602/0084/G** UCB Pharma S.A., Lead Rapporteur: Bruno Sepodes Opinion adopted on 04.07.2019.	Positive Opinion adopted by consensus on 04.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1615 **Actraphane-EMEA/H/C/000427/WS1615/0078** **Actrapid-EMEA/H/C/000424/WS1615/0072** **Insulatard-EMEA/H/C/000441/WS1615/0075** **Levemir-EMEA/H/C/000528/WS1615/0093** **Mixtard-EMEA/H/C/000428/WS1615/0079** **Protaphane-EMEA/H/C/000442/WS1615/0074** **Ryzodeg-EMEA/H/C/002499/WS1615/0032** **Tresiba-EMEA/H/C/002498/WS1615/0038** **Xultophy-EMEA/H/C/002647/WS1615/0030** Novo Nordisk A/S, Lead Rapporteur: Sinan B. Sarac Opinion adopted on 11.07.2019.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1621
Bexsero-EMEA/H/C/002333/WS1621/0077
Menveo-EMEA/H/C/001095/WS1621/0087
GSK Vaccines S.r.l, Lead Rapporteur: Johann Lodewijk HillegeThis WS includes MRP/NAPs."

WS1623
Hexacima-EMEA/H/C/002702/WS1623/0091
Hexaxim-EMEA/H/W/002495/WS1623/0096
Hexyon-EMEA/H/C/002796/WS1623/0095
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

WS1626/G
Glyxambi-EMEA/H/C/003833/WS1626/0023/G
Jardiance-EMEA/H/C/002677/WS1626/0044/G
Synjardy-EMEA/H/C/003770/WS1626/0040/G
Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege

WS1628
Aflunov-EMEA/H/C/002094/WS1628/0051
Foclivia-EMEA/H/C/001208/WS1628/0046
Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri
Request for Supplementary Information adopted on 20.06.2019.

WS1631/G
Mirapexin-EMEA/H/C/000134/WS1631/0090/G
Sifrol-EMEA/H/C/000133/WS1631/0081/G
Boehringer Ingelheim International GmbH, Lead Rapporteur: Mark Ainsworth

WS1635
Ryzodeg-EMEA/H/C/002499/WS1635/0033
Tresiba-EMEA/H/C/002498/WS1635/0039
Xultophy-EMEA/H/C/002647/WS1635/0031
Novo Nordisk A/S, Lead Rapporteur: Kristina

Dunder	
WS1638 **Trevicta-EMEA/H/C/004066/WS1638/0023** **Xeplion-EMEA/H/C/002105/WS1638/0044** Janssen-Cilag International NV, Lead Rapporteur: Kristina Dunder Opinion adopted on 11.07.2019.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1639 **Entresto-EMEA/H/C/004062/WS1639/0025** **Neparvis-EMEA/H/C/004343/WS1639/0024** Novartis Europharm Limited, Lead Rapporteur: Johann Lodewijk Hillege	
WS1640 **PegIntron-EMEA/H/C/000280/WS1640/0138** **ViraferonPeg-EMEA/H/C/000329/WS1640/0131** Merck Sharp & Dohme B.V., Lead Rapporteur: Filip Josephson	
WS1641 **Corlentor-EMEA/H/C/000598/WS1641/0053** **Ivabradine** **Anpharm-EMEA/H/C/004187/WS1641/0013** **Procoralan-EMEA/H/C/000597/WS1641/0052** Les Laboratoires Servier, Duplicate, Duplicate of Procoralan, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 11.07.2019.	Positive Opinion adopted by consensus on 11.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1642/G **Rixathon-EMEA/H/C/003903/WS1642/0024/G** **Riximyo-EMEA/H/C/004729/WS1642/0024/G** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus	
WS1645 **Exelon-EMEA/H/C/000169/WS1645/0123** **Prometax-EMEA/H/C/000255/WS1645/0124** Novartis Europharm Limited, Lead Rapporteur:	

Alexandre Moreau	
WS1646 **Fluenz Tetra-EMEA/H/C/002617/WS1646/0091** **Pandemic influenza vaccine H5N1 AstraZeneca-EMEA/H/C/003963/WS1646/0024** AstraZeneca AB, Lead Rapporteur: Bart Van der Schueren	
WS1650 **Olanzapine Glenmark-EMEA/H/C/001085/WS1650/0031** **Olanzapine Glenmark Europe-EMEA/H/C/001086/WS1650/0028** **Olazax-EMEA/H/C/001087/WS1650/0024** **Olazax Disperzi-EMEA/H/C/001088/WS1650/0025** Glenmark Arzneimittel GmbH, Generic, Generic of Olansek (SRD), Zyprexa, Zyprexa Velotab, Lead Rapporteur: Alexandre Moreau, “To updated section 4.8 of the SmPC to add "stuttering", section 5.2 of the SmPC to include new section with a sub heading 'Hepatic Impairment' and text related to smoking in line with PI text of the reference product. The PL has been updated accordingly. In addition the MAH has taken the opportunity to align the annexes with minor linguistic changes in line with the reference product.” Request for Supplementary Information adopted on 11.07.2019.	Request for supplementary information adopted with a specific timetable.
WS1652/G **Idacio-EMEA/H/C/004475/WS1652/0002/G** **Kromeya-EMEA/H/C/005158/WS1652/0002/G** Fresenius Kabi Deutschland GmbH, Lead Rapporteur: Johann Lodewijk Hillege	
WS1657 **Advate-EMEA/H/C/000520/WS1657/0101** **ADYNOVI-EMEA/H/C/004195/WS1657/0006** Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 04.07.2019.	Positive Opinion adopted by consensus on 04.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1670 **Adjupanrix-EMEA/H/C/001206/WS1670/0065**	

Ambirix-EMEA/H/C/000426/WS1670/0102 **Fendrix-EMEA/H/C/000550/WS1670/0069** **Infanrix hexa-EMEA/H/C/000296/WS1670/0261** **Prepandrix-EMEA/H/C/000822/WS1670/0081** **Rotarix-EMEA/H/C/000639/WS1670/0114** **Synflorix-EMEA/H/C/000973/WS1670/0139** **Twinrix Adult-EMEA/H/C/000112/WS1670/0137** **Twinrix Paediatric-EMEA/H/C/000129/WS1670/0138** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren	
Hexacima-EMEA/H/C/002702/WS1624/0090/G **Hexaxim-EMEA/H/W/002495/WS1624/0095/G** **Hexyon-EMEA/H/C/002796/WS1624/0094/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 04.07.2019.	Positive Opinion adopted by consensus on 04.07.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

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

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

abicipar pegol - EMEA/H/C/005103 treatment of neovascular (wet) age-related macular degeneration (AMD)
amikacin - EMEA/H/C/005264, Orphan Insmed Netherlands B.V., treatment of lung infection as part of combination antibacterial drug regiment in adults
avapritinib - EMEA/H/C/005208 treatment of gastrointestinal stromal tumours
bevacizumab - EMEA/H/C/005106 treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer.

first-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer. first line treatment of patients with advanced and/or metastatic renal cell cancer.	
ioflupane (123i) - EMEA/H/C/005135 is indicated for detecting loss of functional dopaminergic neuron terminals in the striatum	
givosiran - EMEA/H/C/004775, Orphan Alnylam Netherlands B.V., Treatment of acute hepatic porphyria (AHP) in adults and adolescents aged 12 years and older.	**Accelerated review**

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

Halimatoz - adalimumab - EMEA/H/C/004866/X/0013 Sandoz GmbH, Duplicate, Duplicate of Hyrimoz, Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga, “Extension application to add a new strength of 20mg (20mg/0.4ml) for Hyimoz solution for injection in pre-filled syringe. The RMP (version 2.0) is updated in accordance. The MAH took also the opportunity to consolidate the RMP with changes approved in two other procedures (WS1565 and IB/11) and to align the PI with the latest QRD template (v.10.1).”	
Hefiya - adalimumab - EMEA/H/C/004865/X/0013 Sandoz GmbH, Duplicate, Duplicate of Hyrimoz, Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga, “Extension application to add a new strength of 20mg (20mg/0.4ml) for Hyimoz solution for injection in pre-filled syringe. The RMP (version 2.0) is updated in accordance. The MAH took also the opportunity to consolidate the RMP with changes approved in two other procedures (WS1565 and IB/10) and to align the PI with the latest QRD template (v.10.1).”	
Hyrimoz - adalimumab - EMEA/H/C/004320/X/0013 Sandoz GmbH, Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga, “Extension application to add a new strength of 20mg (20mg/0.4ml) for Hyimoz solution for injection in pre-filled syringe. The RMP (version 2.0) is updated in accordance.	

The MAH took also the opportunity to consolidate the RMP with changes approved in two other procedures (WS1565 and IB/11) and to align the PI with the latest QRD template (v.10.1)."

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

Akynzeo - fosnetupitant / netupitant / palonosetron - EMEA/H/C/003728/X/0018
Helsinn Birex Pharmaceuticals Limited, Rapporteur: Peter Kiely, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Amelia Cupelli, "Extension application to introduce the new pharmaceutical form 'powder for concentrate for solution for infusion' and a new strength for the fixed combination of fosnetupitant (pro-drug of netupitant) and palonosetron of 235 mg/0.25 mg, to be administered intravenously (new route of administration)."
List of Questions adopted on 28.03.2019.

Carbaglu - carglumic acid - EMEA/H/C/000461/X/0038, Orphan
Recordati Rare Diseases, Rapporteur: Fátima Ventura, "Extension application to introduce a new pharmaceutical form associated with 2 new strengths (200 mg and 800 mg soluble tablets)."
List of Questions adopted on 28.03.2019.

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

Atriance - nelarabine - EMEA/H/C/000752/S/0048
Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark

Qarziba - dinutuximab beta - EMEA/H/C/003918/S/0016, Orphan
EUSA Pharma (Netherlands) B.V., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski

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

Kengrexal - cangrelor - EMEA/H/C/003773/R/0020
Chiesi Farmaceutici S.p.A., Rapporteur: Johann

Lodewijk Hillege, Co-Rapporteur: Alar Irs, PRAC
Rapporteur: Amelia Cupelli

OCALIVA - obeticholic acid -
EMEA/H/C/004093/R/0018, Orphan
Intercept Pharma International Limited,
Rapporteur: Jorge Camarero Jiménez, PRAC
Rapporteur: Menno van der Elst

Quinsair - levofloxacin -
EMEA/H/C/002789/R/0022
Chiesi Farmaceutici S.p.A., Rapporteur: Ondřej
Slanař, Co-Rapporteur: Bruno Sepodes, PRAC
Rapporteur: Maria del Pilar Rayon

Saxenda - liraglutide -
EMEA/H/C/003780/R/0024
Novo Nordisk A/S, Rapporteur: Johann Lodewijk
Hillege, Co-Rapporteur: Sinan B. Sarac, PRAC
Rapporteur: Menno van der Elst

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

Adcetris - brentuximab vedotin -
EMEA/H/C/002455/II/0070, Orphan
Takeda Pharma A/S, Rapporteur: Paula
Boudewina van Hennik, Co-Rapporteur: Jan
Mueller-Berghaus, PRAC Rapporteur: Menno van
der Elst, “treatment of adults with previously
untreated CD30+ PTCL”

Carmustine Obvius - carmustine -
EMEA/H/C/004326/II/0002
Obvius Investment B.V, Generic, Rapporteur:
Natalja Karpova, PRAC Rapporteur: Jan
Neuhauser, “carmustine with or without total
body irradiation (TBI), as conditioning treatment
prior to allogeneic or autologous haematopoietic
progenitor cell transplantation (HPCT) in
haematological diseases”

Cyramza - ramucirumab -
EMEA/H/C/002829/II/0033
Eli Lilly Nederland B.V., Rapporteur: Paula
Boudewina van Hennik, Co-Rapporteur: Kolbeinn
Gudmundsson (IS) (MNAT with IS for Clinical
Efficacy, IS for Coordination, IS for Clinical
Safety, FI for Quality, FI for Non-Clinical, LT for

Clinical Pharmacology), PRAC Rapporteur: Brigitte Keller-Stanislawski, “Extension of indication for Cyramza, to include in combination with erlotinib, the first-line treatment of adult patients with metastatic non-small cell lung cancer with activating epidermal growth factor receptor (EGFR) mutations.
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 accordingly.
The RMP version 9 has also been submitted.”

Lynparza - olaparib - EMEA/H/C/003726/II/0033

AstraZeneca AB, Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Amelia Cupelli, “Extension of indication to support the use of Lynparza tablets (100mg and 150 mg) for the maintenance treatment of gBRCAm metastatic pancreatic cancer based on the results from the pivotal Phase 3 study, POLO; as a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.8 for lynparza hard capsules (50 mg) to revise list of ADR based on the pooled safety data analysis. The RMP version 18 has also been submitted. Furthermore, the PI is brought in line with the latest guideline regarding the sodium content. The MAH also took the occasion to include some minor editorial changes in the PI.”

Otezla - apremilast - EMEA/H/C/003746/II/0029

Celgene Europe BV, Rapporteur: Peter Kiely, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Eva A. Segovia, “Extension of indication to include treatment of adult patients with oral ulcers associated with Behçet’s disease (BD) who are candidates for systemic therapy. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC and sections 1, 2 and 4 of the PL are updated accordingly. The updated RMP version 12.0 has also been submitted.”
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Rezolsta - darunavir / cobicistat - EMEA/H/C/002819/II/0033

Janssen-Cilag International NV, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, “To extend the approved therapeutic indication of Rezolsta to include the adolescent population (aged 12 years old and older with body weight at least 40 kg). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and sections 1, 2 and 3 of the PL are updated accordingly. The updated RMP version 6.0 has also been submitted. The RMP of the product has been updated to meet the requirements and updated definitions in the European Medicines Agency (EMA) Guideline on good pharmacovigilance practices (GVP) Module V Revision 2 (EMA/838713/2011; Rev 2) and Guidance on the format of the RMP in the European Union (EMA/164014/2018 Rev 2.0.1) including proposed removal of safety concerns. In addition, in order to align the PI with recommendations for other HIV products, the MAH has also taken the opportunity to update section 4.2 of the SmPC with regards to administration Rezolsta in case of vomiting.”	
Stelara - ustekinumab - EMEA/H/C/000958/II/0073 Janssen-Cilag International NV, Rapporteur: Jayne Crowe, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Rhea Fitzgerald, “Extension of indication to include a new population for Stelara solution for injection in children aged 6 to 12 years with moderate to severe psoriasis based on the results of study CNTO1275PSO3013 as a consequence sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated accordingly. The Package Leaflet is updated in accordance. Section 4.8 for Stelara concentrate for solution for infusion is updated accordingly. Minor editorial changes are made to section 4.5 for both formulations. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 15.0 has also been submitted. The MAH took the opportunity to add “follow-up of pregnancy registry” in Part III.1 of the RMP in line with the existing information in Part V.3 of the RMP.”	

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Accofil - filgrastim -
EMEA/H/C/003956/II/0034/G
Accord Healthcare S.L.U., Rapporteur: Outi Mäki-Ikola

Afstyla - lonoctocog alfa -
EMEA/H/C/004075/II/0023/G
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Alprolix - eftrenonacog alfa -
EMEA/H/C/004142/II/0026, Orphan
Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop

Aripiprazole Mylan Pharma - aripiprazole -
EMEA/H/C/003803/II/0012
Mylan S.A.S, Generic, Generic of Abilify, Rapporteur: Bjorg Bolstad

Betaferon - interferon beta-1b -
EMEA/H/C/000081/II/0126/G
Bayer AG, Rapporteur: Martina Weise

Busulfan Fresenius Kabi - busulfan -
EMEA/H/C/002806/II/0014
Fresenius Kabi Deutschland GmbH, Generic, Generic of Busilvex, Rapporteur: John Joseph Borg

Buvidal - buprenorphine -
EMEA/H/C/004651/II/0002
Camurus AB, Rapporteur: Peter Kiely

Cinryze - C1 esterase inhibitor (human) -
EMEA/H/C/001207/II/0071/G
Shire Services BVBA, Rapporteur: Jan Mueller-Berghaus

CRYSVITA - burosumab -
EMEA/H/C/004275/II/0007/G, Orphan
Kyowa Kirin Holdings B.V., Rapporteur: Kristina Dunder

Elaprase - idursulfase -
EMEA/H/C/000700/II/0082
Shire Human Genetic Therapies AB, Rapporteur: Johann Lodewijk Hillege

Extavia - interferon beta-1b -
EMEA/H/C/000933/II/0099/G
Novartis Europharm Limited, Informed Consent of Betaferon, Rapporteur: Martina Weise

HyQvia - human normal immunoglobulin -
EMEA/H/C/002491/II/0051
Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus

Imfinzi - durvalumab -
EMEA/H/C/004771/II/0009
AstraZeneca AB, Rapporteur: Sinan B. Sarac

Lamzede - velmanase alfa -
EMEA/H/C/003922/II/0007, Orphan
Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege

Lonquex - lipegfilgrastim -
EMEA/H/C/002556/II/0053/G
Teva B.V., Rapporteur: Outi Mäki-Ikola

MVASI - bevacizumab -
EMEA/H/C/004728/II/0008
Amgen Europe B.V., Duplicate, Duplicate of KYOMARC, Rapporteur: Bjorg Bolstad

Nimenrix - meningococcal group a, c, w135 and y conjugate vaccine -
EMEA/H/C/002226/II/0092/G
Pfizer Europe MA EEIG, Rapporteur: Bjorg Bolstad

Noxafil - posaconazole -
EMEA/H/C/000610/II/0059
Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau

Nucala - mepolizumab -
EMEA/H/C/003860/II/0025
GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely

Nucala - mepolizumab -
EMEA/H/C/003860/II/0026/G
GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely

OCALIVA - obeticholic acid -
EMEA/H/C/004093/II/0016/G, Orphan
Intercept Pharma International Limited, Rapporteur: Jorge Camarero Jiménez

Ocrevus - ocrelizumab -
EMEA/H/C/004043/II/0014/G
Roche Registration GmbH, Rapporteur: Mark Ainsworth

Pelgraz - pegfilgrastim -
EMEA/H/C/003961/II/0011/G

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

Pemetrexed Hospira - pemetrexed - EMEA/H/C/003970/II/0020/G
Pfizer Europe MA EEIG, Generic, Generic of Alimta, Rapporteur: Alar Irs

Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0180/G
Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder

Repatha - evolocumab - EMEA/H/C/003766/II/0036
Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege

RoActemra - tocilizumab - EMEA/H/C/000955/II/0084/G
Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus

RotaTeq - rotavirus vaccine (live, oral) - EMEA/H/C/000669/II/0079/G
MSD Vaccins, Rapporteur: Kristina Dunder

SomaKit TOC - edotreotide - EMEA/H/C/004140/II/0011, Orphan
Advanced Accelerator Applications, Rapporteur: Maria Concepcion Prieto Yerro

Tremfya - guselkumab - EMEA/H/C/004271/II/0015
Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics

Verzenios - abemaciclib - EMEA/H/C/004302/II/0005
Eli Lilly Nederland B.V., Rapporteur: Filip Josephson

WS1612/G
Herceptin-EMEA/H/C/000278/WS1612/0155/G
Kadcyla-EMEA/H/C/002389/WS1612/0047/G
Roche Registration GmbH, Lead Rapporteur: Jan Mueller-Berghaus

WS1630
Bretaris Genuair-EMEA/H/C/002706/WS1630/0041
Eklira Genuair-EMEA/H/C/002211/WS1630/0041

AstraZeneca AB, Lead Rapporteur: Ewa Balkowiec Iskra

WS1632/G
Brimica Genuair-EMEA/H/C/003969/WS1632/0027/G
Duaklir Genuair-EMEA/H/C/003745/WS1632/0027/G
AstraZeneca AB, Lead Rapporteur: Ewa Balkowiec Iskra

WS1644/G
Insulatard-EMEA/H/C/000441/WS1644/0076/G
Protaphane-EMEA/H/C/000442/WS1644/0075/G
Novo Nordisk A/S, Duplicate, Duplicate of Monotard (SRD), Ultratard (SRD), Lead Rapporteur: Sinan B. Sarac

WS1662
Nuwiq-EMEA/H/C/002813/WS1662/0031
Vihuma-EMEA/H/C/004459/WS1662/0013
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus

WS1674
Actraphane-EMEA/H/C/000427/WS1674/0079
Actrapid-EMEA/H/C/000424/WS1674/0073
Insulatard-EMEA/H/C/000441/WS1674/0077
Mixtard-EMEA/H/C/000428/WS1674/0080
Protaphane-EMEA/H/C/000442/WS1674/0076
Novo Nordisk A/S, Lead Rapporteur: Sinan B. Sarac

WS1678
Rixathon-EMEA/H/C/003903/WS1678/0027
Riximyo-EMEA/H/C/004729/WS1678/0028
Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus

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

Edurant - rilpivirine -

EMEA/H/C/002264/II/0035

Janssen-Cilag International NV, Rapporteur: Paula Boudewina van Hennik, "Update of section 5.1 of the SmPC to reflect the week 240 results from the TMC278-TiDP38-C213(C213) study a phase II, open-label, single-arm trial to evaluate the pharmacokinetics, safety, tolerability, and antiviral activity of rilpivirine in antiretroviral-naïve HIV-1 infected adolescents and children aged ≥6 to <18 years, upon request by CHMP following the assessment of the paediatric study C213 submitted according to Art. 46 procedure (no. EMEA/H/C/2264/P46/028). In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.8 of the SmPC to indicate that no safety concerns were identified in the Week 240 analysis of the C213 trial in adolescents aged ≥12 to <18 years."

Edurant - rilpivirine - EMEA/H/C/002264/II/0036

Janssen-Cilag International NV, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.6 of the SmPC based on the most recent data described in the ARV Pregnancy Registry (APR). In addition, the Marketing authorisation holder (MAH) took the opportunity to update the Package Leaflet to include information on the sodium excipient, as per the revised Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' and the list of local representatives, as well as to make minor editorial changes in the SmPC and in the Package Leaflet."

Eliquis - apixaban - EMEA/H/C/002148/II/0064

Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, "Update of sections 4.2, 4.4, 4.5 and 5.1 of the SmPC in order to update the safety information based on the final results from study CV185316 (AUGUSTUS) , an open-label, randomised, controlled clinical trial to evaluate the safety of apixaban in patients with atrial fibrillation and acute coronary syndrome and/or percutaneous coronary intervention."

Eviplera - emtricitabine / rilpivirine / tenofovir disoproxil -

EMEA/H/C/002312/II/0100
Gilead Sciences Ireland UC, Rapporteur: Johann Lodewijk Hillege, "Submission of the final study report for the drug utilisation study EDMS-ERI-139775027, an observational cohort study to assess rilpivirine utilisation according to the European SmPC, implemented using data from the EuroSIDA study cohort. The study is listed as a Category 3 study in the Eviplera RMP and submission of the final study report fulfils PAM MEA 011.5."

Feraccru - ferric maltol -
EMEA/H/C/002733/II/0022
Norgine B.V., Rapporteur: Maria Concepcion Prieto Yerro, "Update of sections 4.2, 4.4 and 5.2 of the SmPC to include information on patients with chronic kidney disease, following the submission of the final study report of study ST10-01-303."

Fiasp - insulin aspart -
EMEA/H/C/004046/II/0016
Novo Nordisk A/S, Rapporteur: Kristina Dunder, "Update of the SmPC section 4.8 with data from an updated safety pool, further to assessment of the last PSUR assessment for insulin aspart (EMEA/H/C/PSUSA/00001749/201809).
This update is based on 3 efficacy and safety studies: NN1218-3852 (52 week) – a study of Fiasp compared to insulin aspart both in combination with insulin detemir in adults with Type 1 Diabetes; NN1218-3854 a study of Continuous Subcutaneous Insulin Infusion of Fiasp compared to NovoRapid in adults with Type 1 Diabetes; NN1218-4131 a study of Fiasp compared to NovoRapid both in combination with insulin degludec in adults with Type 1 Diabetes.
The patient leaflet has been updated accordingly.
In addition, correction to the labelling for the FlexTouch and vial presentations; resulting in removal of information included in section 17 and 18 from the inner cartons for the multipack for both FlexTouch and vial presentation."

IBRANCE - palbociclib -
EMEA/H/C/003853/II/0024
Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, "Submission of the final report from a non-clinical study (PD-0332991) evaluating the correlation of palbociclib response to RB1 status."

Imnovid - pomalidomide -

EMEA/H/C/002682/II/0036/G, Orphan
Celgene Europe BV, Rapporteur: Jorge Camarero Jiménez, “Group of two type II variations to update sections 4.2, 4.4 and 4.8 of the SmPC and section 4 of the PL with information on anaphylaxis and section 4.8 of SmPC with hypothyroidism ADR following a safety review. This group also includes a Type IB Variation to update section 6.6 of the SmPC in order to include recommendations to minimize the risk of unintended occupational exposures in healthcare professionals. The MAH has also proposed minor updates to section 4.4 of the SmPC and Annex IID regarding the educational materials, prescribing and dispensing restrictions in order to provide more clarity about the recommended maximum duration of treatment.”

Kuvan - sapropterin -
EMEA/H/C/000943/II/0068, Orphan
BioMarin International Limited, Rapporteur: Peter Kiely, “Update of section 5.1 of the Summary Product Characteristics (SmPC) in order to reflect new paediatric information based on study PKU-015 evaluating the effect of Kuvan on neurocognitive function, maintenance of blood phenylalanine concentrations, safety, and population Pharmacokinetics in young Children with Phenylketonuria.
The study is listed as MEA-C-Clinical, category 3 in the RMP for Kuvan and submitted in accordance to article 46 of the paediatric regulation.”

Noxafil - posaconazole -
EMEA/H/C/000610/II/0058
Merck Sharp & Dohme B.V., Rapporteur: Alexandre Moreau, “Update of section 4.8 of the SmPC in order to include 'pseudoaldosteronism' as an adverse event in post-marketing experience, following a review of six case reports in the scientific literature of concurrent hypertension and hypokalemia in patients treated with posaconazole.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.”

Pradaxa - dabigatran etexilate -
EMEA/H/C/000829/II/0118/G
Boehringer Ingelheim International GmbH, Rapporteur: Mark Ainsworth, “Update of section

4.5 of the SmPC in order to add a warning regarding the interaction between Pradaxa and the fixed-dose combination of the P-gp inhibitors glecaprevir and pibrentasvir based on the phase I drug-drug interaction study results. The Package Leaflet was updated accordingly. Update of section 4.8 of the SmPC with new safety information regarding adverse reaction alopecia following the confirmation of signal "alopecia associated with dabigatran" by the EMA and the cumulative review of cases of alopecia and related terms that was provided in PSUR submitted by 27 May 2019. In addition small editorial corrections under "Adverse reaction" Table 2 were made additionally to highlight that information on some side effects was obtained from post-marketing data. The Package Leaflet was updated accordingly."	
Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0181 Pfizer Europe MA EEIG, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to update efficacy information based on results from a public health analysis and publication of data from the CAPiTA (Community-Acquired Pneumonia Immunization Trial in Adults), a double-blind, randomized, placebo-controlled efficacy trial of 13-valent pneumococcal conjugate vaccine (PCV13)."	
Remicade - infliximab - EMEA/H/C/000240/II/0223 Janssen Biologics B.V., Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC and relevant section of the PL to include cerebrovascular accidents as rare undesirable effect."	
Revlimid - lenalidomide - EMEA/H/C/000717/II/0112/G, Orphan Celgene Europe BV, Rapporteur: Alexandre Moreau, "Group of variations including one type II to update sections 4.2, 4.4 and 4.8 of the SmPC and section 4 of the PL with anaphylaxis following a safety review a and a Type IB v to update section 6.6 of the SmPC in order to include recommendations to minimize the risk of unintended occupational exposures in healthcare professionals. The MAH has also proposed minor updates to section 4.4 of the SmPC and Annex	

IID regarding the educational materials, prescribing and dispensing restrictions in order to provide more clarity about the recommended maximum duration of treatment. Finally the MAH took the opportunity to make editorial changes throughout the product information."

RXULTI - brexpiprazole - EMEA/H/C/003841/II/0003

Otsuka Pharmaceutical Netherlands B.V., Rapporteur: Daniela Melchiorri, "To update section 4.4 of the SmPC (paragraph "Impulse-control disorders") based on the Company Core Data Sheet of brexpiprazole. In addition, the applicant has taken the opportunity to update the section 4.2 of the SmPC requested by EMA (see annex to cover letter) and to perform additional changes, i.e. editorial changes in the SmPC and Package Leaflet."

SIMBRINZA - brinzolamide / brimonidine - EMEA/H/C/003698/II/0018/G

Novartis Europharm Limited, Rapporteur: Maria Concepcion Prieto Yerro, "Update of section 5.1 of the SmPC in order to update the safety information with adjunctive use of BID Simbrinza with a PGA therapy based on final results from study CQVJ499A2401; this is a phase 4, multicenter, randomized, double-masked, parallel-group study.
Update of section 5.1 of the SmPC in order to update the safety information with adjunctive use of BID Simbrinza with a PGA/beta-blocker combination therapy based on final results from study CQVJ499A2402; this is a phase 4, multicenter, randomized, double-masked, parallel-group study."

Symkevi - tezacaftor / ivacaftor - EMEA/H/C/004682/II/0012/G, Orphan

Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.5 and 5.2 of the SmPC in order to provide information on drug-drug interactions and pharmacogenetic data based on final results from two post-authorisation measures (PAMs) studies: VX18-661-011 (an open-label phase 1 study to examine the effects of combination of tezacaftor and ivacaftor on the pharmacokinetics and safety of pitavastatin in healthy subjects) and pharmacokinetics study P088

(pharmacogenetic study of TEZ and IVA exposure with respect to CYP3A4*22 genotype)."

TAGRISSO - osimertinib - EMEA/H/C/004124/II/0031
AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, "Update of section 4.8 of the SmPC to include onychalgia in the list of associated clustered terms for paronychia further to a MAH internal safety information review."

TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0061/G
Biogen Netherlands B.V., Rapporteur: Martina Weise, "7xC.I.13: Submission of non-clinical studies:
1) Study Rsch-2013-023: A receptor binding study of Dimethyl Fumarate and Monomethyl Fumarate
2) Study P00012-14-04: Dimethyl Fumarate: A cardiovascular and respiratory assessment following oral administration to conscious, radiotelemetry-instrumented beagle dogs
3-4) Study P00012-05-03 and Study P00012-04-11: Amendments to two-year carcinogenicity study reports in mice and rats with DMF
5) Study P00012-12-02: A toxicity study of Dimethyl Fumarate when administered orally in juvenile male rats
6) Study P00012-13-07: Dimethyl Fumarate: Self-administration assessment in the male Sprague dawley rat
7) Study P00012-14-01: Dimethyl Fumarate: Drug discrimination assessment in the male Sprague dawley rat"

Thalidomide Celgene - thalidomide - EMEA/H/C/000823/II/0061/G, Orphan
Celgene Europe BV, Rapporteur: Alexandre Moreau, "Group of variations including one type II to update sections 4.2, 4.4 and 4.8 of the SmPC and section 4 of the PL with anaphylaxis following a safety review a and a Type IB v to update section 6.6 of the SmPC in order to include recommendations to minimize the risk of unintended occupational exposures in healthcare professionals. The MAH has also proposed minor updates to section 4.4 of the SmPC and Annex IID regarding the educational materials, prescribing and dispensing restrictions in order to provide more clarity."

Truvada - emtricitabine / tenofovir disoproxil - EMEA/H/C/000594/II/0161
Gilead Sciences Ireland UC, Rapporteur: Bruno Sepodes, “Submission of the final clinical study report for the non-interventional study GS-US-276-0103, ‘A Prospective, Observational Study of Individuals Who Seroconvert While Taking Truvada for Pre-Exposure Prophylaxis (PrEP)’, listed as a Category 3 study in the Truvada RMP.”

Vimpat - lacosamide - EMEA/H/C/000863/II/0082
UCB Pharma S.A., Rapporteur: Filip Josephson, “Update of section 4.2 of the SmPC in order to warn that Vimpat tablets must not be divided based on the results of safety Evaluation Report on ‘chopped tablets’.
The Package Leaflet is updated accordingly.”

Xaluprine - mercaptopurine - EMEA/H/C/002022/II/0022, Orphan
Nova Laboratories Ireland Limited, Rapporteur: Filip Josephson, “Update of sections 4.4, 4.8 and 4.9 of the SmPC to add further information on hepatic toxicity. The MAH took the opportunity to implement minor editorial changes to the SmPC and PIL.”

Zoely - nomegestrol acetate / estradiol - EMEA/H/C/001213/II/0050
Theramex Ireland Limited, Rapporteur: Joseph Emmerich, “Update of sections 4.3 and 4.4 of the SmPC in order to add a new contraindication and a new warning regarding meningioma, upon request by PRAC following the assessment of post-authorisation measure “LEG 014”. The Package Leaflet is being updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in the Netherlands and Portugal in the Package Leaflet.”

WS1647/G
Mirapexin-EMEA/H/C/000134/WS1647/0091/G
Sifrol-EMEA/H/C/000133/WS1647/0082/G
Boehringer Ingelheim International GmbH, Lead Rapporteur: Mark Ainsworth

WS1648
Docetaxel Zentiva-EMEA/H/C/000808/

WS1648/0060
Taxotere-EMEA/H/C/000073/WS1648/0133
Aventis Pharma S.A., Lead Rapporteur: Alexandre Moreau, “Update of sections 4.4 and 4.8 of the SmPC in order to add a warning about cases of severe cutaneous reactions and to add acute generalized exanthematous pustulosis as an undesirable effect, respectively. The Package Leaflet is updated in accordance. In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet.”

WS1677
Aluvia-EMEA/H/W/000764/WS1677/0110
Kaletra-EMEA/H/C/000368/WS1677/0179
Norvir-EMEA/H/C/000127/WS1677/0156
AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Joseph Emmerich, “To update sections 4.3 and 4.5 of the SmPC to include a new contraindication with apalutamide, a moderate to strong CYP3A4 inducer, as well as to update section 4.5 of the SmPC on the potential interaction with encorafenib following an update to the Kaletra and Aluvia (lopinavir/ritonavir) and Norvir (ritonavir) Company Core Data Sheets (CCDS).
The Package Leaflet is also updated accordingly”

B.6.10. CHMP-PRAC assessed procedures

Avastin - bevacizumab - EMEA/H/C/000582/II/0110
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, “Submission of the final report from study NEJ026 listed as an obligation in the Annex II of the Product Information. This is an open-label, randomized, Phase III study conducted in Japan to compare erlotinib + bevacizumab combination therapy versus erlotinib monotherapy as first-line therapies for patients with NSCLC with EGFR gene mutations (exon 19 deletion or exon 21 L858R substitution).
The RMP version 30.0 has also been submitted.
In addition, the Package leaflet is updated to reflect information on sodium content in compliance with the revised Annex to the European Commission guideline on "Excipients in

the labelling and package leaflet of medicinal products for human use".”	
Bydureon - exenatide - EMEA/H/C/002020/II/0064 AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, “Update of sections 4.2 and 4.4 of the SmPC in order to remove the limitation of use in patients with moderate renal impairment (creatinine clearance [CrCl] 30 to 50 ml/min) based on pooled data from 8 EQW/EQWS studies undertaken in patients with mild renal impairment/chronic kidney disease stage 2 or moderate renal impairment/chronic kidney disease stage 3, and on supportive data from EXSCEL (Study D5551C00003/BCB109) including a subset of patients with moderate renal impairment. In addition, the MAH took the opportunity to introduce GFR as the main indicator of renal function rather than CrCl. The Package Leaflet has been updated accordingly and the MAH has taken the opportunity to implement some minor changes in the labelling. An updated RMP version 34 was provided with the application, which includes consequential changes as well as a proposal for the removal of Acute Renal Failure (ARF) as an Important Identified Risk based on the GVP V Rev2 guidance. In addition, upon request following the assessment of II/54, a Pan EU epidemiological study to monitor events of pancreatic cancer has been included as an additional planned pharmacovigilance activity.”	
Increlex - mecasermin - EMEA/H/C/000704/II/0060 Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, “Update of sections 4.1, 4.2, 4.3, 4.4, 4.8 and 4.9 of the SmPC in order to update the safety information on benign or malignant neoplasia based on the EU Registry Study, the Ipsen global safety database and literature review. The Package Leaflet is updated accordingly. The MAH also submitted the updated RMP version 11. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet”	
Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0048/G	

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, "C.1.4: Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information on the risk of Left ventricular dysfunction (LVD) based on the final results from study BO39807 listed as a category 3 study in the RMP. This is an observational study of cardiac events in patients with HER2-positive metastatic breast cancer who have a Left Ventricular Ejection Fraction (LVEF) between 40%-49% prior to initiating treatment with Kadcyla; The RMP version 10.0 has also been submitted.
C.I.13: Submission of the final report from study BO28408 listed as a category 3 study in the RMP addressing cardiac safety, safety in elderly patients, and immunogenicity. This is a randomised, multicenter, open-label, two-arm, phase III neoadjuvant study evaluating the efficacy and safety of trastuzumab emtansine plus pertuzumab compared with chemotherapy plus trastuzumab and pertuzumab for patients with HER2-Positive Breast Cancer."

Lokelma - sodium zirconium cyclosilicate - EMEA/H/C/004029/II/0013

AstraZeneca AB, Rapporteur: Romaldas Mačiulaitis, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to update the clinical information based final results from study DIALIZE. This was a Phase 3b, multicentre, prospective, randomised, double-blind, placebo-controlled study to reduce incidence of pre-dialysis hyperkalaemia with sodium zirconium cyclosilicate. The Package Leaflet and Labelling are updated accordingly. The RMP version 2.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement the new excipient statement for sodium in section 4.4 of the SmPC, section 2 of Labelling and section 2 of the Package Leaflet. Furthermore, minor editorial changes were introduced in section 2 of the Package leaflet."

Lonsurf - trifluridine / tipiracil - EMEA/H/C/003897/II/0016

Les Laboratoires Servier, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Annika Folin, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update information on

patients with severe renal impairment based on final results from study TO-TAS-102-107 (A Phase 1, Open-label Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of TAS-102 in Patients With Advanced Solid Tumors and Varying Degrees of Renal Impairment). The Package Leaflet is updated accordingly. The updated RMP version 6.3 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the RMP in line with the template revision 2 of the good Pharmacovigilance practice module V guideline."

NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0030/G

Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Submission of the Guardian 4 (NN7008-3809) Clinical Trial in Previously Untreated Patients (PUPs) and the Guardian 9 (NN7008-4239) PK Clinical Trial.
In addition, the MAH has updated the SmPC to align with the 'EMA Core SmPC for human plasma derived and recombinant coagulation factor VIII products, revision 3' and Annex to the European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use'. Further, some administrative updates have also been applied."

Ondexxya - andexanet alfa - EMEA/H/C/004108/II/0002

Portola Netherlands B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst, "C.I.13: Submission of the Final Study Report for, ANNEXA-4 Study ("Prospective, Open-Label Study of Andexanet Alfa in Patients Receiving a Factor Xa Inhibitor Who Have Acute Major Bleeding") listed as category 2 study in the RMP. This is an interventional non-randomized, multicentre, prospective, open-label, single-group study in patients with acute major bleeding. The results of ANNEXA-4 were requested to be submitted as Specific Obligation in the context of Conditional Marketing Authorisation. The RMP version 1.1 has also been submitted."

Orkambi - lumacaftor / ivacaftor - EMEA/H/C/003954/II/0049

Vertex Pharmaceuticals (Ireland) Limited,

Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Rhea Fitzgerald, “Update of section 4.8 of the SmPC with the safety data from the Phase 3, open-label, rollover study for Studies 109 and 011 Part B (Study 011B) designed to evaluate the long-term safety and tolerability of Orkambi treatment for 96 weeks in patients with cystic fibrosis, 6 years of age and older, homozygous for F508del.”

Rapiscan - regadenoson - EMEA/H/C/001176/II/0034/G

GE Healthcare AS, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, “Grouping of variations:
- Update of sections 4.4 and 4.8 of the SmPC regarding myocardial ischaemia (myocardial infarction, ventricular arrhythmias and cardiac arrest) based on a review of the safety database and CCDS update
- Update of sections 4.4, 4.5, 4.8, 4.9 and 5.1 of the SmPC regarding co-administration with methylxanthines due to the risk of seizure and hypersensitivity including anaphylaxis based on a review of the safety database and CCDS update
- Update of section 5.1 of the SmPC regarding the use of regadenoson in patients with inadequate stress test based on results from study 3606-CL-3004 and CCDS update.
The RMP version (11.1) has also been submitted in order to fulfil LEG 016.”

Stayveer - bosentan - EMEA/H/C/002644/II/0028

Janssen-Cilag International NV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, “Update of Annex IID to remove the prescriber kit from the additional risk minimisation measures and also to remove the obligation to implement a formal "Controlled Distribution System" in EU countries further to a request from PRAC in the context of LEG 10.2 which concluded in March 2019. Section 4.2 of the SmPC is updated to include the statement that patients should be given the Package Leaflet and the Patient Alert Card which are included in the pack.
In addition the MAH took the opportunity to align the PI with the EC guideline on excipients (EMA/CHMP/302620/2017).
Version 11 of the RMP is updated accordingly.”

TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0062

Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, “Update of sections 4.4 and 4.8 of the SmPC to add a warning on the risk of herpes zoster based on cumulative review data submitted in the ongoing PSUSA/00010143/201903. The Package Leaflet is updated accordingly.”

TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0063

Biogen Netherlands B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, “Update of sections 4.4 and 4.8 of the SmPC to reflect PML in the setting of mild lymphopenia based on data submitted in the ongoing PSUSA/00010143/201903. The Package Leaflet is updated accordingly.
Additionally, the Product Information has been updated in line with QRD template (version 10.1).”

Tracleer - bosentan - EMEA/H/C/000401/II/0092

Janssen-Cilag International NV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, “Update of Annex IID to remove the prescriber kit from the additional risk minimisation measures and also to remove the obligation to implement a formal "Controlled Distribution System" in EU countries further to a request from PRAC in the context of LEG 86.2 which concluded in March 2019. Section 4.2 of the SmPC is updated to include the statement that patients should be given the Package Leaflet and the Patient Alert Card which are included in the pack.
In addition the MAH took the opportunity to align the PI with the EC guideline on excipients (EMA/CHMP/302620/2017).
Version 11 of the RMP is updated accordingly.”

UDENYCA - pegfilgrastim - EMEA/H/C/004413/II/0003

ERA Consulting GmbH, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, “To update section 4.6 of the SmPC to update the safety information based on feasibility data regarding the pregnancy and lactation registry listed as a category 3 study in the RMP; this is a non-interventional registry. The Package Leaflet

is updated accordingly. The updated RMP version 1.5 has also been submitted."

Zelboraf - vemurafenib - EMEA/H/C/002409/II/0054
Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Annika Folin, "Update of sections 4.4 and 4.5 of the SmPC in order to add information and a precaution regarding concomitant strong CYP3A4 inhibitors based on final results from study GO29475 (MEA-011), a category 3 study in the RMP; the Package Leaflet is updated accordingly. The RMP version 12.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PL in line with the excipients guideline (EMA/CHMP/302620/2017) by adding information about the product's sodium content."

B.6.11. PRAC assessed procedures

PRAC Led
AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0025
sanofi-aventis groupe, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Submission of the patients and HCPs final survey reports to assess the effectiveness of the education materials; the survey reports are part of the additional pharmacovigilance activities in the RMP (category 3 studies). Within this submission the MAH is proposing a revised patient card with the following revisions: the patient card was restructured (general guidance, possible side effects, pregnancy), details related to the Accelerated Elimination Procedure were deleted and symptoms related to liver and infections are described."

PRAC Led
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0081
UCB Pharma S.A., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "C.I.13: Submission of the final report from study (British Society for Rheumatology Biologics Register (BSRBR), RA0022) listed as a category 3 study in

the RMP. This is a UK registry which aims to monitor the long term safety of TNF-α drugs and other targeted therapies in rheumatoid arthritis patients.
Submission of the interim report from study (RABBIT registry, RA0020) listed as a category 3 study in the RMP. This is a German biologic registry, long-term observational cohort study of the safety and effectiveness of biologic agent in rheumatoid arthritis."

PRAC Led

Luveris - lutropin alfa - EMEA/H/C/000292/II/0082

Merck Europe B.V., Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP for Luveris 75 IU powder and solvent for injections version 3.1, 28 Nov 2018 in order to:
- adapt the RMP template to Good Pharmacovigilance Practice (GVP) Module V, rev 2.
- delete reference to Luveris 450 IU solution for injection in pre-filled pen, following the withdrawal of this presentation (EU/1/00/155/007).
- removal of important identified risks "Ovarian Hyperstimulation Syndrome (OHSS)" and "Mild to severe hypersensitivity reactions including anaphylactic reactions and shock" and important potential risks "Thromboembolic (TE) events", "Reproductive system cancer", "Ectopic pregnancy", "Multiple pregnancies", "Congenital anomaly" and "off label use"). For the missing information of "Hypogonadotropic hypogonadal women with severe LH and FSH deficiency of advanced maternal age (older than 40 years)", the advanced maternal age has been changed from 40 to 42 years.
- amendment and update of the epidemiology and non-clinical sections of the RMP, as per the most recent data. The clinical trial section and exclusion criteria in pivotal clinical studies section have been updated for recombinant human luteinizing hormone (rhLH).
- update with the patient exposure data up to the data lock point (DLP) of 28 November 2018.
- Other minor changes (e.g. reporting rates in RMP tables)"

PRAC Led

Selincro - nalmefene -
EMEA/H/C/002583/II/0025
H. Lundbeck A/S, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, “submission for the Final Study Reports for the PASS 15649A: Use of Nalmefene (Selincro) in European databases: Cohort design using longitudinal electronic medical records or claims databases and PASS 14910A a non-interventional multicountry prospective cohort study to investigate the pattern of use of Selincro and frequency of selected adverse reactions in routine clinical practice.”

PRAC Led
SIMBRINZA - brinzolamide / brimonidine -
EMEA/H/C/003698/II/0019
Novartis Europharm Limited, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, “Submission of an updated RMP version 3.0 in order to remove metabolic acidosis/renal impairment as an important potential risk from the list of safety concerns and in addition update the Risk management plan to comply with the new GVP module V rev 2 RMP template.”

PRAC Led
Slenyto - melatonin -
EMEA/H/C/004425/II/0010
RAD Neurim Pharmaceuticals EEC SARL, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, “The removal of “Delay of sexual maturation and development” as an “Important potential risk” from the EU-RMP.”

PRAC Led
Yondelis - trabectedin -
EMEA/H/C/000773/II/0058, Orphan
Pharma Mar, S.A., Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, “Update of section 4.4 of the SmPC in order to add a warning based on results from study Cardiac Safety Report [Protocols ET743-SAR-3007, ET743-OVA-301, ET743-OVC-3006; Phase 3. JNJ-17027907; R270741 (trabectedin)] following the PSUSA procedure EMEA/H/C/PSUSA/00003001/201809; the Package Leaflet is updated accordingly.”

PRAC Led

WS1655

Aerius-EMEA/H/C/000313/WS1655/0091

Azomyr-EMEA/H/C/000310/WS1655/0095

Neoclarityn-EMEA/H/C/000314/WS1655/0089

Merck Sharp & Dohme B.V., Duplicate, Duplicate of Allex (SRD), Azomyr, Opulis (SRD), Lead Rapporteur: Koenraad Norga, Lead PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Bart Van der Schueren, "C.I.13: Submission of the final report from study (EUPAS15038) listed as a category 3 study in the RMP. This is a non-interventional non-imposed PASS study designed to assess the potential risk of desloratadine exposure on seizures, supraventricular tachycardia, and atrial fibrillation or flutter."

B.6.12. CHMP-CAT assessed procedures

YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0011, Orphan, ATMP

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

YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0012, Orphan, ATMP

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

B.6.13. CHMP-PRAC-CAT assessed procedures

B.6.14. PRAC assessed ATMP procedures

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

WS1634

Advate-EMEA/H/C/000520/WS1634/0102

ADYNOVI-EMEA/H/C/004195/WS1634/0007

Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus

WS1658/G

Eucreas-EMEA/H/C/000807/WS1658/0075/G
Galvus-EMEA/H/C/000771/WS1658/0063/G
Icandra-EMEA/H/C/001050/WS1658/0078/G
Jalra-EMEA/H/C/001048/WS1658/0065/G
Xiliarx-EMEA/H/C/001051/WS1658/0062/G
Zomarist-EMEA/H/C/001049/WS1658/0077/G
Novartis Europharm Limited, Lead Rapporteur: Kristina Dunder

WS1669
Ryzodeg-EMEA/H/C/002499/WS1669/0035
Tresiba-EMEA/H/C/002498/WS1669/0042
Xultophy-EMEA/H/C/002647/WS1669/0032
Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder

WS1672
Mirapexin-EMEA/H/C/000134/WS1672/0092
Sifrol-EMEA/H/C/000133/WS1672/0083
Boehringer Ingelheim International GmbH, Lead Rapporteur: Mark Ainsworth, “To delete the dosage strength of 1.1mg for Pramipexole tablets.”

WS1675
Abseamed-EMEA/H/C/000727/WS1675/0085
Binocrit-EMEA/H/C/000725/WS1675/0084
Epoetin alfa Hexal-EMEA/H/C/000726/WS1675/0084
Sandoz GmbH, Lead Rapporteur: Alexandre Moreau, “To update sections 4.2, 4.4, 4.8 and 5.1 of the SmPC to align the PI with the NAP originator Eprex. The PL was updated accordingly. In addition, Annex II was updated following procedure EMEA/H/C/IG0970/G.”

WS1682
Filgrastim Hexal-EMEA/H/C/000918/WS1682/0051
Zarzio-EMEA/H/C/000917/WS1682/0052
Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege, “To update section 2 of the

Package Leaflet in order to align the PI with its NAP originator Neupogen. Editorial changes are also proposed to the HU, IS, LT, PL and SV annexes.”	
WS1688 **Abseamed-EMEA/H/C/000727/WS1688/0086** **Binocrit-EMEA/H/C/000725/WS1688/0085** **Epoetin alfa Hexal-EMEA/H/C/000726/WS1688/0085** Sandoz GmbH, Lead Rapporteur: Alexandre Moreau	

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

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

B.7.2. Monthly Line listing for Type I variations

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

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

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

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

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

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

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

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

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

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

F.1. Parallel Distribution - Pursuant to Article 9 of Council Regulation (EC) No. 2743 / 98 of 14 December 1998, as amended

F.2. Request for scientific opinion on justification of exceptional circumstance and for imperative grounds of public health

G. ANNEX G

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

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

G.2. Ongoing procedures

G.3. PRIME

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

G.3.1. List of procedures concluding at 22-25 July 2019 CHMP plenary:

G.3.2. List of procedures starting in July 2019 for September 2019 CHMP adoption of outcomes

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