23 July 2018
EMA/504524/2018 Corr.[1]
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 23-26 July 2018

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

23 July 2018, 13:00 – 19:30, room 2A

24 July 2018, 08:30 – 19:30, room 2A

25 July 2018, 08:30 – 19:30, room 2A

26 July 2018, 08:30 – 15:00, room 2A

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.

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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).

[1] Correction in section 3.7

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Table of contents

1. Introduction 8

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

1.2. Adoption of agenda 8

1.3. Adoption of the minutes 8

2. Oral Explanations 8

2.1. Pre-authorisation procedure oral explanations 8

2.1.1. paclitaxel - Orphan - EMEA/H/C/004154 8

2.1.2. patisiran - Orphan - EMEA/H/C/004699 8

2.1.3. durvalumab - EMEA/H/C/004771 9

2.2. Re-examination procedure oral explanations 9

2.2.1. Dexxience - betrixaban - EMEA/H/C/004309 9

2.2.2. Eladynos - abaloparatide - EMEA/H/C/004157 9

2.3. Post-authorisation procedure oral explanations 9

2.3.1. Blincyto - blinatumomab - Orphan - EMEA/H/C/003731/II/0011 9

2.3.2. Xarelto - rivaroxaban - EMEA/H/C/000944/II/0058 10

2.3.3. WS1278 OPDIVO - nivolumab - EMEA/H/C/003985/WS1278/0042 Yervoy - ipilimumab - EMEA/H/C/002213/WS1278/0053 10

2.3.4. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0042 10

2.4. Referral procedure oral explanations 10

3. Initial applications 11

3.1. Initial applications; Opinions 11

3.1.1. paclitaxel - Orphan - EMEA/H/C/004154 11

3.1.2. encorafenib - EMEA/H/C/004580 11

3.1.3. deferiprone - EMEA/H/C/004710 11

3.1.4. gefitinib - EMEA/H/C/004826 11

3.1.5. adalimumab - EMEA/H/C/004429 12

3.1.6. tildrakizumab - EMEA/H/C/004514 12

3.1.7. durvalumab - EMEA/H/C/004771 12

3.1.8. vigabatrin - PUMA - EMEA/H/C/004534 12

3.1.9. lenalidomide - EMEA/H/C/004857 12

3.1.10. voretigene neparvovec - Orphan - ATMP - EMEA/H/C/004451 13

3.1.11. binimetinib - EMEA/H/C/004579 13

3.1.12. melatonin - PUMA - EMEA/H/C/004425 13

3.1.13. patisiran - Orphan - EMEA/H/C/004699 13

3.1.14. pegfilgrastim - EMEA/H/C/003961 14

3.1.15. tezacaftor / ivacaftor - Orphan - EMEA/H/C/004682 14

3.1.16. pegfilgrastim - EMEA/H/C/004413 14
3.1.17. abemaciclib - EMEA/H/C/004302 14
3.1.18. eravacycline - EMEA/H/C/004237 15
3.2. Initial applications; List of outstanding issues (Day 180; Day 120 for procedures with accelerated assessment timetable) 15
3.2.1. ropeginterferon alfa-2b - Orphan - EMEA/H/C/004128 15
3.2.2. buprenorphine - EMEA/H/C/004651 15
3.2.3. doxorubicin hydrochloride - EMEA/H/C/004110 15
3.2.4. galcanezumab - EMEA/H/C/004648 15
3.2.5. pacritinib - Orphan - EMEA/H/C/004793 16
3.2.6. paclitaxel - EMEA/H/C/004441 16
3.2.7. mogamulizumab - Orphan - EMEA/H/C/004232 16
3.2.8. influenza vaccine surface antigen inactivated prepared in cell cultures - Article 28 - EMEA/H/C/004814 16
3.2.9. pegfilgrastim - EMEA/H/C/004802 16
3.3. Initial applications; List of questions (Day 120; Day 90 for procedures with accelerated assessment timetable) 17
3.3.1. atazanavir - EMEA/H/C/004859 17
3.3.2. turoctocog alfa pegol - Orphan - EMEA/H/C/004883 17
3.3.3. cemiplimab - EMEA/H/C/004844 17
3.3.4. ciprofloxacin - EMEA/H/C/004394 17
3.3.5. miglustat - EMEA/H/C/004904 17
3.3.6. pegvaliase - Orphan - EMEA/H/C/004744 17
3.3.7. sotagliflozin - EMEA/H/C/004889 18
3.4. Update on on-going initial applications for Centralised procedure 18
3.4.1. zanamivir - EMEA/H/C/004102 18
3.4.2. fremanezumab - EMEA/H/C/004833 18
3.5. Re-examination of initial application procedures under Article 9(2) of Regulation no 726/2004 18
3.5.1. Dexxience - betrixaban - EMEA/H/C/004309 18
3.5.2. Nerlynx - neratinib - EMEA/H/C/004030 19
3.6. Initial applications in the decision-making phase 19
3.7. Withdrawals of initial marketing authorisation application 19
3.7.1. axalimogene filolisbac - ATMP - EMEA/H/C/004473 19
4. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008 19
4.1. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Opinion 19
4.1.1. Inhixa - enoxaparin sodium - EMEA/H/C/004264/X/0018 19
4.1.2. Inhixa - enoxaparin sodium - EMEA/H/C/004264/X/0026 20

4.1.3. Renvela - sevelamer carbonate - EMEA/H/C/000993/X/0039 20
4.1.4. Sevelamer carbonate Zentiva - sevelamer carbonate - EMEA/H/C/003971/X/0011 20
4.2. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 180 list of outstanding issues 20
4.2.1. Gilenya - fingolimod - EMEA/H/C/002202/X/0044/G 20
4.3. Extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008; Day 120 List of question 21
4.3.1. Dupixent - dupilumab - EMEA/H/C/004390/X/0004/G 21
4.3.2. Orencia - abatacept - EMEA/H/C/000701/X/0117/G 21
4.3.3. Xeljanz - tofacitinib - EMEA/H/C/004214/X/0012 22
4.4. Update on on-going extension application according to Annex I of Commission Regulation (EC) No 1234/2008 22
4.5. Re-examination procedure of extension of marketing authorisation according to Annex I of Commission Regulation (EC) No 1234/2008 22

5. Type II variations - variation of therapeutic indication procedure according to Annex I of Commission Regulation (EC) No 1234/2008 22

5.1. Type II variations - variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008; Opinions or Requests for supplementary information 22
5.1.1. Blincyto - blinatumomab - Orphan - EMEA/H/C/003731/II/0011 22
5.1.2. Blincyto - blinatumomab - Orphan - EMEA/H/C/003731/II/0018 23
5.1.3. Coagadex - human coagulation factor X - Orphan - EMEA/H/C/003855/II/0007 23
5.1.4. Darzalex - daratumumab - Orphan - EMEA/H/C/004077/II/0011 23
5.1.5. Hemlibra - emicizumab - EMEA/H/C/004406/II/0002 24
5.1.6. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/II/0063/G 24
5.1.7. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0042 25
5.1.8. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0043 25
5.1.9. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0047 26
5.1.10. NovoSeven - eptacog alfa (activated) - EMEA/H/C/000074/II/0104 26
5.1.11. Nucala - mepolizumab - EMEA/H/C/003860/II/0013/G 26
5.1.12. Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0049 27
5.1.13. Xarelto - rivaroxaban - EMEA/H/C/000944/II/0058 27
5.1.14. Xtandi - enzalutamide - EMEA/H/C/002639/II/0039/G 27
5.1.15. WS1274 Mekinist - trametinib - EMEA/H/C/002643/WS1274/0023 Tafinlar - dabrafenib - EMEA/H/C/002604/WS1274/0031 28
5.1.16. WS1278 OPDIVO - nivolumab - EMEA/H/C/003985/WS1278/0042 Yervoy - ipilimumab - EMEA/H/C/002213/WS1278/0053 29
5.1.17. WS1372 OPDIVO - nivolumab - EMEA/H/C/003985/WS1372/0053 Yervoy - ipilimumab - EMEA/H/C/002213/WS1372/0057 29
5.1.18. WS1406 Abseamed-EMEA/H/C/000727/WS1406/0070, Binocrit-EMEA/H/C/000725/WS1406/0070, Epoetin alfa Hexal-EMEA/H/C/000726/WS1406/0069 . 29

5.2. Update on on-going Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008 30

5.3. Re-examination of Type II variation; variation of therapeutic indication procedure according to Commission Regulation (EC) No 1234/2008 30

6. Ancillary medicinal substances in medical devices 30

6.1. Ancillary medicinal substances in medical devices; Opinions/ Day 180 list of outstanding issues / Day 120 list of questions 30

6.2. Update of Ancillary medicinal substances in medical devices 30

7. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use) 30

7.1. Procedure under Article 83(1) of Regulation (EC) 726/2004 (Compassionate Use) 30

8. Pre-submission issues 31

8.1. Pre-submission issue 31

8.1.1. emapalumab - Orphan - H0004386 31

8.1.2. larotrectinib sulphate - H0004919 31

8.1.3. onasemnogene abeparvovec - Orphan - ATMP - H0004750 31

8.1.4. Autologous haematopoietic stem cells transduced with lentiviral vector encoding the human beta-A-T87Q-globin gene - Orphan - ATMP - H0003691 31

8.2. Priority Medicines (PRIME) 32

8.2.1. List of applications received 32

8.2.2. Recommendation for PRIME eligibility 32

9. Post-authorisation issues 32

9.1. Post-authorisation issues 32

9.1.1. Victrelis – boceprevir – EMEA/H/C/2332 32

9.1.2. Intanza 15 microgram/strain - influenza vaccine (split virion, inactivated) - EMEA/H/C/000957 32

9.1.3. Sovaldi - sofosbuvir - EMEA/H/C/002798/R/0050 32

9.1.4. VELCADE - bortezomib - EMEA/H/C/000539/II/0088 33

10. Referral procedures 33

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

10.1.1. XOFIGO - EMEA/H/A-20/1459 33

10.2. Requests for CHMP Opinion under Article 5(3) of Regulation (EC) No 726/2004 . 34

10.2.1. Gentamicin – EMEA/H/A-5(3)/1468 34

10.3. Procedure under Articles 5(2) and 10 of Regulation (EC) No 726/2004 34

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 34

10.4.1. Paclitaxel Hetero - EMEA/H/A-29(4)/1466 34

10.4.2. Syner-KINASE 10 000 IU - EMEA/H/A-29(4)/1472 34
10.5. Harmonisation - Referral procedure under Article 30 of Directive 2001/83/EC 35
10.5.1. Septanest and associated names – Articaine (hydrochloride)/ Adrenaline (tartrate) - EMEA/H/A-30/1461 35
10.6. Community Interests - Referral under Article 31 of Directive 2001/83/EC 35
10.6.1. Omega-3-acid-ethyl esters- containing medicinal products for oral use – EMEA/H/A-31/146435
10.6.2. Valsartan-containing medicinal products - EMEA/H/A-31/1471 35
10.6.3. Gadolinium-containing contrast agents (GdCA): Gadobutrol (NAP); gadodiamide (NAP); gadopentetic acid (NAP); gadoteric acid (NAP); gadoteridol (NAP); gadoxetic acid (NAP) - EMEA/H/A-31/1097 36
10.7. Re-examination Procedure under Article 32(4) of Directive 2001/83/EC 36
10.8. Procedure under Article 107(2) of Directive 2001/83/EC 36
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 37
10.10. Procedure under Article 29 of Regulation (EC) 1901/2006 37
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 37

11. Pharmacovigilance issue 37
11.1. Early Notification System 37

12. Inspections 37
12.1. GMP inspections 37
12.2. GCP inspections 37
12.3. Pharmacovigilance inspections 37
12.4. GLP inspections 37

13. Innovation Task Force 38
13.1. Minutes of Innovation Task Force 38
13.2. Innovation Task Force briefing meetings 38
13.3. Requests for CHMP Opinion under Article 57(1)J and (1)P of Regulation (EC) No 726/2004 38
13.4. Nanomedicines activities 38

14. Organisational, regulatory and methodological matters 38
14.1. Mandate and organisation of the CHMP 38
14.1.1. Concepts of significant benefit (follow-up to CHMP Work Plan 2017) 38
14.1.2. EMA Implementation plan of the new medical device and in vitro diagnostic regulation 38
14.1.3. Rules of Procedure for standing working parties 38
14.1.4. Telematics strategy 2020-2025: Concept Paper 38
14.2. Coordination with EMA Scientific Committees 39

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC) 39
14.2.2. Committee for Advanced Therapies (CAT) 39
14.2.3. Committee for Herbal Medicinal Products (HMPC) 39
14.2.4. Paediatric Committee (PDCO) 39
14.2.5. Committee for Orphan Medicinal Products (COMP) 40
14.2.6. Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) 40
14.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups 40
14.3.1. Scientific Advice Working Party (SAWP) 40
14.3.2. Name Review Group (NRG) 40
14.3.3. Biologics Working Party (BWP) 40
14.3.4. Rheumatology/Immunology Working Party (RIWP) 41
14.3.5. Blood Products Working Party (BPWP) 41
14.3.6. SmPC Advisory Group 41
14.3.7. Guideline Consistency Group (GCG) 41
14.3.8. Biosimilar Medicinal Product Working Party (BMWP) 42
14.3.9. Oncology Working Party 42
14.3.10. Pharmacokinetics Working Party (PKWP) 42
14.3.11. Quality Working Party (QWP) 42
14.4. Cooperation within the EU regulatory network 42
14.5. Cooperation with International Regulators 42
14.5.1. SADC and ECOWAS joint assessment meetings 42
14.5.2. International Council on Harmonisation (ICH) 42
14.6. Contacts of the CHMP with external parties and interaction with the Interested Parties to the Committee 43
14.7. CHMP work plan 43
14.8. Planning and reporting 43
14.9. Others 43

15. Any other business 43
15.1. Relocation information to delegates 43
15.2. Preparedness of the system and capacity increase 43

16. Explanatory notes 44

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 23-26 July 2018. See July 2018 CHMP minutes (to be published post September 2018 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 23-26 July 2018

1.3. Adoption of the minutes

CHMP minutes for 25-28 June 2018.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. paclitaxel - Orphan - EMEA/H/C/004154

Oasmia Pharmaceutical AB; treatment of ovarian cancer

Scope: Oral explanation

Action: Oral explanation to be held on 24 July 2018 at time 16:00

List of Outstanding Issues adopted on 26.04.2018, 14.09.2017, 18.05.2017. List of Questions adopted on 23.06.2016.

See 3.1

2.1.2. patisiran - Orphan - EMEA/H/C/004699

Accelerated assessment

Alnylam Netherlands B.V.; treatment of hereditary transthyretin-mediated amyloidosis

Scope: Oral explanation

Action: Oral explanation to be held on 23 July 2018 at time 16:00

List of Outstanding Issues adopted on 26.06.2018. List of Questions adopted on 24.04.2018.

See 3.1

2.1.3. durvalumab - EMEA/H/C/004771

treatment of locally advanced, unresectable non-small cell lung cancer (NSCLC)

Scope: Oral explanation

Action: Oral explanation to be held on 24 July 2018 at time 18:00

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 25.01.2018.

See 3.1

2.2. Re-examination procedure oral explanations

2.2.1. Dexxience - betrixaban - EMEA/H/C/004309

Portola Pharma UK Limited; treatment of prophylaxis of venous thromboembolism (VTE)

Scope: Oral explanation

Action: Oral explanation to be held on 24 July 2018 at time 09:00

Opinion adopted on 22.03.2018.

See 3.5

2.2.2. Eladynos - abaloparatide - EMEA/H/C/004157

Radius International Ltd; treatment of osteoporosis

Scope: Oral explanation, Report from Ad-hoc Expert Group meeting

Action: Oral explanation to be held on 24 July 2018 at time 11:00

Opinion adopted on 22.03.2018.

2.3. Post-authorisation procedure oral explanations

2.3.1. Blincyto - blinatumomab - Orphan - EMEA/H/C/003731/II/0011

Amgen Europe B.V.

Rapporteur: Alexandre Moreau, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Eva Jirsová

Scope: Oral explanation

Action: Oral explanation to be held on 24 July 2018 at time 14:00

Request for Supplementary Information adopted on 26.04.2018, 14.12.2017, 22.06.2017.

See 5.1

2.3.2. Xarelto - rivaroxaban - EMEA/H/C/000944/II/0058

Bayer AG

Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue

Scope: Oral explanation

Action: Possible oral explanation to be held on 25 July 2018 at time 11:00

Request for Supplementary Information adopted on 31.05.2018, 22.02.2018.

See 5.1

2.3.3. WS1278 OPDIVO - nivolumab - EMEA/H/C/003985/WS1278/0042 Yervoy - ipilimumab - EMEA/H/C/002213/WS1278/0053

Bristol-Myers Squibb Pharma EEIG

Lead Rapporteur: Paula Boudewina van Hennik, Lead Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Oral explanation

Action: Oral explanation to be held on 25 July 2018 at time 9:00

Request for Supplementary Information adopted on 31.05.2018, 22.02.2018.

See 5.1

2.3.4. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0042

Merck Sharp & Dohme B.V.

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: Oral explanation

Action: Oral explanation to be held on 25 July 2018 at time 16:00

Request for Supplementary Information adopted on 28.06.2018, 26.04.2018.

See 5.1

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. paclitaxel - Orphan - EMEA/H/C/004154

Oasmia Pharmaceutical AB; treatment of ovarian cancer

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.04.2018, 14.09.2017, 18.05.2017. List of Questions adopted on 23.06.2016.

See 2.1

3.1.2. encorafenib - EMEA/H/C/004580

in combination with binimetinib is indicated for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.12.2017.

3.1.3. deferiprone - EMEA/H/C/004710

treatment of iron overload in thalassemia major

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 09.11.2017.

3.1.4. gefitinib - EMEA/H/C/004826

treatment of non-small cell lung cancer

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.12.2017.

3.1.5. adalimumab - EMEA/H/C/004429

treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.04.2018. List of Questions adopted on 14.09.2017.

3.1.6. tildrakizumab - EMEA/H/C/004514

treatment of adults with moderate-to-severe plaque psoriasis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 20.07.2017.

3.1.7. durvalumab - EMEA/H/C/004771

treatment of locally advanced, unresectable non-small cell lung cancer (NSCLC)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 25.01.2018.

3.1.8. vigabatrin - PUMA - EMEA/H/C/004534

Treatment in monotherapy of infantile spasms (West's syndrome) and resistant partial epilepsy in infants and children

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.06.2018, 26.04.2018. List of Questions adopted on 14.12.2017.

3.1.9. lenalidomide - EMEA/H/C/004857

treatment of multiple myeloma

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on

14.12.2017.

3.1.10. voretigene neparvovec - Orphan - ATMP - EMEA/H/C/004451

Spark Therapeutics Ireland Ltd; treatment of patients with vision loss due to Leber congenital amaurosis or retinitis pigmentosa inherited retinal dystrophy

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 25.05.2018. List of Questions adopted on 08.12.2017.

The draft list of experts for the ad hoc expert group meeting on 5 July 2018 was adopted via written procedure on 5th July 2018.

3.1.11. binimetinib - EMEA/H/C/004579

in combination with encorafenib is indicated for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.12.2017.

3.1.12. melatonin - PUMA - EMEA/H/C/004425

treatment of insomnia in children with Autism Spectrum Disorders and neurogenetic diseases

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.09.2017.

3.1.13. patisiran - Orphan - EMEA/H/C/004699

Accelerated assessment

Alnylam Netherlands B.V.; treatment of hereditary transthyretin-mediated amyloidosis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.06.2018. List of Questions adopted on

24.04.2018.

See 2.1

3.1.14. pegfilgrastim - EMEA/H/C/003961

treatment of neutropenia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.09.2017.

3.1.15. tezacaftor / ivacaftor - Orphan - EMEA/H/C/004682

Vertex Pharmaceuticals (Europe) Ltd.; treatment of cystic fibrosis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.06.2018, 31.05.2018, 22.03.2018. List of Questions adopted on 14.12.2017.

3.1.16. pegfilgrastim - EMEA/H/C/004413

treatment of neutropenia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 28.06.2018, 14.12.2017. List of Questions adopted on 23.03.2017.

3.1.17. abemaciclib - EMEA/H/C/004302

treatment of hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer

Scope: Opinion

Action: For adoption

Oral explanation held on 25 June 2018. List of Outstanding Issues adopted on 31.05.2018, 26.04.2018. List of Questions adopted on 14.12.2017.

3.1.18. eravacycline - EMEA/H/C/004237

treatment of complicated intra-abdominal infections (cIAI) in adults

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.12.2017.

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

3.2.1. ropeginterferon alfa-2b - Orphan - EMEA/H/C/004128

AOP Orphan Pharmaceuticals AG; treatment of polycythemia vera

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.06.2017.

3.2.2. buprenorphine - EMEA/H/C/004651

treatment of opioid dependence within a framework of medical, social and psychological treatment

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 25.01.2018.

3.2.3. doxorubicin hydrochloride - EMEA/H/C/004110

treatment of breast and ovarian cancer

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 14.09.2017.

3.2.4. galcanezumab - EMEA/H/C/004648

prophylaxis of migraine

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.03.2018.

3.2.5. pacritinib - Orphan - EMEA/H/C/004793

CTI Life Sciences Limited; treatment of disease-related splenomegaly and control of symptoms in patients with primary myelofibrosis (PMF), post-polycythemia vera myelofibrosis (PPV-MF), or post-essential thrombocythemia myelofibrosis (PET-MF) who have thrombocytopenia (platelet counts ≤100,000 /µL).

Scope: List of outstanding issues, request from applicant dated 10 July 2018 for extension to the clock stop to respond to the List of outstanding issues

Action: For adoption

List of Questions adopted on 09.11.2017.

3.2.6. paclitaxel - EMEA/H/C/004441

treatment of metastatic breast cancer

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 31.05.2018. List of Questions adopted on 14.12.2017.

3.2.7. mogamulizumab - Orphan - EMEA/H/C/004232

Kyowa Kirin Limited; treatment of cutaneous T-cell lymphoma

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.02.2018.

3.2.8. influenza vaccine surface antigen inactivated prepared in cell cultures - Article 28 - EMEA/H/C/004814

prophylaxis of influenza in adults and children from 4 years of age

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.03.2018.

3.2.9. pegfilgrastim - EMEA/H/C/004802

treatment of neutropenia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 22.02.2018.

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

3.3.1. atazanavir - EMEA/H/C/004859

treatment of HIV-1 infection

Scope: List of questions

Action: For adoption

3.3.2. turoctocog alfa pegol - Orphan - EMEA/H/C/004883

Novo Nordisk A/S; Treatment and prophylaxis of bleeding in patients with haemophilia A

Scope: List of questions

Action: For adoption

3.3.3. cemiplimab - EMEA/H/C/004844

as monotherapy, indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma

Scope: List of questions

Action: For adoption

3.3.4. ciprofloxacin - EMEA/H/C/004394

treatment of non-cystic fibrosis bronchiectasis (NCFBE) patients with chronic lung infection with Pseudomonas aeruginosa (P. aeruginosa)

Scope: List of questions

Action: For adoption

3.3.5. miglustat - EMEA/H/C/004904

treatment of adult patients with mild to moderate type 1 Gaucher disease and only in the treatment of patients for whom enzyme replacement therapy is unsuitable

Scope: List of questions

Action: For adoption

3.3.6. pegvaliase - Orphan - EMEA/H/C/004744

BioMarin International Limited; treatment of adults with phenylketonuria (PKU) who have

inadequate blood phenylalanine control

Scope: List of questions

Action: For adoption

3.3.7. sotagliflozin - EMEA/H/C/004889

indicated as an adjunct to insulin therapy to improve glycaemic control in adults with type 1 diabetes mellitus

Scope: List of questions

Action: For adoption

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

3.4.1. zanamivir - EMEA/H/C/004102

treatment of influenza A or B virus infection

Scope: Request by the applicant dated 13 July 2018 for extension of clock-stop to respond to the List of Questions adopted in April 2018

Action: For adoption

List of Questions adopted on 26.04.2018.

3.4.2. fremanezumab - EMEA/H/C/004833

prevention of episodic and chronic migraine

Scope: Request by the applicant dated 13 July 2018 for extension of clock-stop to respond to the List of Questions adopted in May 2018

Action: For adoption

List of Questions adopted on 31.05.2018.

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

3.5.1. Dexxience - betrixaban - EMEA/H/C/004309

Portola Pharma UK Limited; treatment of prophylaxis of venous thromboembolism (VTE)

Scope: Re-examination of Opinion

Report from SAG CVS

Opinion adopted on 22.03.2018.

See 2.2

3.5.2. Nerlynx - neratinib - EMEA/H/C/004030

Puma Biotechnology Limited; extended adjuvant treatment of adult patients with early-stage HER2-overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab based therapy

Scope: Re-examination of Opinion, final opinion documents

Action: For information

Oral explanation held on 26 June 2018. Opinion adopted on 22.02.2018.

The final opinion documents were adopted via written procedure on 12.07.2018

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. axalimogene filolisbac - ATMP - EMEA/H/C/004473

treatment of cervical cancer

Scope: Withdrawal of initial marketing authorisation application

Action: For information

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. Inhixa - enoxaparin sodium - EMEA/H/C/004264/X/0018

Techdow Europe AB

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

Scope: “Extension application to add two new strengths of 12,000 IU (120 mg)/0.8 mL and 15,000 IU (150 mg)/1 mL for enoxaparin sodium solution for injection in pre-filled syringe, for subcutaneous, extracorporeal and intravenous administration.”

Action: For adoption

List of Outstanding Issues adopted on 28.06.2018, 31.05.2018. List of Questions adopted on 14.12.2017.

4.1.2. Inhixa - enoxaparin sodium - EMEA/H/C/004264/X/0026

Techdow Europe AB

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

Scope: "Extension application to add two new strengths of 30,000 IU (300 mg)/3 mL and 50,000 IU (500 mg)/5 mL for enoxaparin sodium solution for injection in vial, for subcutaneous, extracorporeal and intravenous administration."

Action: For adoption

List of Outstanding Issues adopted on 28.06.2018. List of Questions adopted on 22.03.2018.

4.1.3. Renvela - sevelamer carbonate - EMEA/H/C/000993/X/0039

Genzyme Europe BV

Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Laurence de Fays

Scope: "Extension application to add a new strength of 0.8 g powder for oral suspension."

Action: For adoption

List of Questions adopted on 22.02.2018.

4.1.4. Sevelamer carbonate Zentiva - sevelamer carbonate - EMEA/H/C/003971/X/0011

Genzyme Europe BV

Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Laurence de Fays

Scope: "Extension application to add a new strength of 0.8 g powder for oral suspension."

Action: For adoption

List of Questions adopted on 22.02.2018.

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. Gilenya - fingolimod - EMEA/H/C/002202/X/0044/G

Novartis Europharm Limited

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension application to introduce a new strength of hard capsules (0.25 mg) to the currently approved presentations of Gilenya, grouped with a type II variation (extension of indication) to add a new indication for the treatment of paediatric patients of 10 years of age and above with relapsing multiple sclerosis (RMS). As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 5.3, 6 and 8 of the SmPC are updated. The Package Leaflet and

Labelling are updated in accordance. In addition, Annex II is updated to be brought in line with the latest QRD template version 10."

Action: For adoption

List of Questions adopted on 22.03.2018.

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. Dupixent - dupilumab - EMEA/H/C/004390/X/0004/G

sanofi-aventis groupe

Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Kimmo Jaakkola

Scope: "Extension application to add a new strength of 200 mg solution for injection in pre-filled syringe with safety system (PFS-S) and pre-filled pen (PFP), grouped with a type II variation (C.I.6.a) to add the following indications:
- Add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older, who are inadequately controlled with medium-to-high dose inhaled corticosteroids (ICS) plus another medicinal product for maintenance treatment, including those with or without an eosinophilic phenotype;
- Maintenance therapy to improve lung function;
- Maintenance therapy to reduce oral steroid use and improve lung function in steroid-dependent asthma patients;
Based on the pivotal studies DRI12544, QUEST and VENTURE.
As a consequence, SmPC sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 have been updated and the Package Leaflet has been updated accordingly.
The RMP (version 2.0) is uppdated accordingly.
In addition, the MAH proposed to merge the SmPCs for the 200 mg and 300 mg strengths."

Action: For adoption

4.3.2. Orencia - abatacept - EMEA/H/C/000701/X/0117/G

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka

Scope: "Extension application to add 2 new strengths of 50 mg and 87.5 mg for solution for injection in a pre-filled syringe with needle guard, for subcutaneous (SC) administration, grouped with a type II variation (C.I.6.a) to include paediatric use of polyarticular Juvenile Idiopathic Arthritis (2 years and above) for solution for injection (50 mg, 87.5 mg and 125 mg).
The above-described changes are grouped
The RMP (version 25.0) is updated in accordance.

In addition, the applicant took the opportunity to implement minor editorial changes in the product information."

Action: For adoption

4.3.3. Xeljanz - tofacitinib - EMEA/H/C/004214/X/0012

Pfizer Limited

Rapporteur: Robert James Hemmings, PRAC Rapporteur: Sabine Straus

Scope: "Extension application to introduce a new pharmaceutical form (prolonged-release tablet) associated with a new strength (11 mg), and presented in pack sizes of 28, 30, 90 and 91 tablets.
The extension of indication includes a change in pharmacokinetics.
An updated RMP (version 4.0) has been provided."

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. Blincyto - blinatumomab - Orphan - EMEA/H/C/003731/II/0011

Amgen Europe B.V.

Rapporteur: Alexandre Moreau, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Eva Jirsová

Scope: "Extension of Indication to include the treatment of adults with minimal residual disease (MRD) positive B-cell precursor acute lymphoblastic leukaemia (ALL)for BLINCYTO; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, and to update the safety information. The

Labelling is updated in accordance.
RMP version 4.0 is included in this submission."

Action: For adoption

Request for Supplementary Information adopted on 26.04.2018, 14.12.2017, 22.06.2017.

See 2.3

5.1.2. Blincyto - blinatumomab - Orphan - EMEA/H/C/003731/II/0018

Amgen Europe B.V.

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Eva Jirsová

Scope: "Extension of Indication to include children 1 month and older to the authorised population for the treatment of adults with Philadelphia chromosome-negative relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL) for BLINCYTO;
as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated in order to include the new population, updated the posology and update the safety information. The Package Leaflet is updated in accordance.
RMP version 6.0 has been submitted"

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018, 22.03.2018, 12.10.2017.

5.1.3. Coagadex - human coagulation factor X - Orphan - EMEA/H/C/003855/II/0007

Bio Products Laboratory Limited

Rapporteur: Andrea Laslop, PRAC Rapporteur: Julie Williams

Scope: "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to include safety and efficacy data in children aged less than 12 years of age based on final results from the study Ten02, a phase III open-label multicentre study to confirm the safety, pharmacokinetics and efficacy of BPL's high purity factor X in the prophylaxis of bleeding in factor X deficient children under the age of 12 years, provided in accordance with the agreed paediatric investigational plan. The Package Leaflet is updated accordingly. The RMP version 7.0 has also been submitted."

Action: For adoption

5.1.4. Darzalex - daratumumab - Orphan - EMEA/H/C/004077/II/0011

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 include the combination with bortezomib, melphalan and prednisone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant for Darzalex; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in

accordance. The RMP version 3.1 (in version 2 of the RMP template) has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of the Lithuanian and Slovenian local representatives in the Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 22.03.2018.

5.1.5. Hemlibra - emicizumab - EMEA/H/C/004406/II/0002

Roche Registration GmbH

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of Indication to include routine prophylaxis of bleeding episodes in patients with hemophilia A without factor VIII inhibitors, for Hemlibra. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated with efficacy and safety information of the pivotal trials:
- Study BH30071 (HAVEN 3) - an ongoing, multicenter, open-label, randomized Phase III clinical study evaluating the efficacy, safety and PK of emicizumab prophylaxis at doses of 1.5 mg/kg/week (QW) and 3 mg/kg/every 2 weeks (Q2W) versus no prophylaxis in adults and adolescent patients (age of 12 or above) with haemophilia A without inhibitors against factor VIII (FVIII).
- Study BO39182 (HAVEN 4) - an ongoing multicenter, open-label, non-randomized Phase III study evaluating the efficacy, safety and PK of emicizumab given as the dose of 6 mg/kg/every 4 weeks (Q4W) in adults and adolescent patients (age of 12 or above) with hemophilia A with or without FVIII inhibitors.
- Study BH29992 (HAVEN 2) - a multicenter, open-label, non-randomized Phase III study evaluating the efficacy, safety and PK of emicizumab at the QW dose in pediatric patients (<12 years old or 12-17 years old and <40kg) with hemophilia A with FVIII inhibitors.
The Package Leaflet and the Risk Management Plan (v.2.0) is updated in accordance.
In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor corrections and clarity to sections 4.4, 4.5 and 4.6 of the SmPC."

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

Action: For adoption

5.1.6. Kalydeco - ivacaftor - Orphan - EMEA/H/C/002494/II/0063/G

Vertex Pharmaceuticals (Europe) Ltd

Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Dolores Montero Corominas

Scope: "1) C.I.6.a (type II) - Extension of Indication to include the combination regimen of the ivacaftor 150 mg evening dose and tezacaftor/ivacaftor;
2) B.IIe.5.a.2 (type IB) - to add a blister card pack presentation containing 28-tablets for the 150 mg film-coated tablets (EU/1/12/782/005);
3) B.IIe.5.a.2 (type IB) - to add a blister pack presentation containing 28-tablets for the 150 mg film-coated tablets (EU/1/12/782/006).
As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 6.5 and 8 of the SmPC are updated.

Annex A, the Package Leaflet and Labelling are updated in accordance.
An updated RMP (version 6.0) is included."

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018, 31.05.2018, 22.03.2018, 14.12.2017.

5.1.7. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0042

Merck Sharp & Dohme B.V.

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include treatment as monotherapy of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) on or after platinum-containing chemotherapy based on the results from KEYNOTE-040 (KN040) with supportive data from two additional single arm studies (KEYNOTE-012/ KEYNOTE-055). KN040 is a randomized, multi-center, pivotal phase III study investigating KEYTRUDA as a monotherapy versus standard treatment (methotrexate, docetaxel or cetuximab) in 495 patients with recurrent or metastatic HNSCC who have previously progressed on prior platinum. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to include in SmPC section 5.2 the description of pembrolizumab PK results on time-dependent change in clearance using a time-dependent pharmacokinetic (TDPK) model structure rather than the static PK model structure.
An updated RMP version 15.1 was provided as part of the application."

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018, 26.04.2018.

See 2.3

5.1.8. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0043

Merck Sharp & Dohme B.V.

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include 1st line treatment of non-squamous non-small cell lung cancer (NSCLC) in combination with pemetrexed and platinum chemotherapy based on the efficacy and safety data from pivotal study KEYNOTE-189, supported by data from KEYNOTE-021 cohorts C and G.
KEYNOTE-189 is a phase 3, randomized, placebo-controlled study undertaken to evaluate the efficacy and safety of pembrolizumab +pemetrexed + carboplatin or cisplatin (pembro combo) versus saline placebo + pemetrexed + carboplatin or cisplatin (control) in previously untreated subjects with advanced/metastatic nonsquamous NSCLC with no EGFR or ALK genomic tumor aberrations.
As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated and the Package Leaflet is updated in accordance.
An updated RMP version 16.2 was provided as part of the application."

Action: For adoption

Request for Supplementary Information adopted on 28.06.2018.

5.1.9. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0047

Merck Sharp & Dohme B.V.

Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include (as monotherapy) adjuvant treatment of melanoma in adults with lymph node involvement who have undergone complete resection, based on study KEYNOTE-054; a randomized, double-blind, phase 3 study conducted in collaboration with the European Organisation for Research and Treatment of Cancer (EORTC), undertaken to evaluate adjuvant therapy with pembrolizumab compared to placebo in patients with resected high-risk melanoma (Stage IIIA [> 1 mm lymph node metastasis], IIIB and IIIC). As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC have been updated and the Package Leaflet has been updated accordingly. An updated RMP version 17.1 was provided as part of the application."

Action: For adoption

5.1.10. NovoSeven - eptacog alfa (activated) - EMEA/H/C/000074/II/0104

Novo Nordisk A/S

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Nithyanandan Nagercoil

Scope: "Extension of Indication to extend patient population of NovoSeven for use in patients with Glanzmann's thrombasthenia without antibodies to platelets, or where platelets are not readily available, based on a prospective observational registry and literature references. As a consequence, sections 4.1 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in section 4.8 of the SmPC and in Package Leaflet."

Action: For adoption

5.1.11. Nucala - mepolizumab - EMEA/H/C/003860/II/0013/G

GlaxoSmithKline Trading Services Limited

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Type II-C.I.6-Extension of Indication to include children and adolescents aged 6 to 17 years for Nucala; as a consequence, Sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC and Sections 1, 2, 3, 4 and Information for Healthcare Professionals in the Package Leaflet are updated accordingly.
In addition to the proposed SmPC/PL updates specific to the paediatric indication, as Nucala is a biological medicine, GSK is including wording in the NUCALA SmPC (Section 4.4) and PL (Information for Health Care Professionals) that the name and batch number of the

administered product should be clearly recorded in the patient file.

Action: For adoption

Request for Supplementary Information adopted on 22.03.2018.

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

Novartis Europharm Limited

Rapporteur: 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; 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."

Action: For adoption

5.1.13. Xarelto - rivaroxaban - EMEA/H/C/000944/II/0058

Bayer AG

Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue

Scope: "Extension of Indication to include the prevention of stroke, myocardial infarction and cardiovascular death, and for the prevention of acute limb ischaemia and mortality in adult patients with coronary artery disease (CAD) or peripheral artery disease (PAD) for Xarelto 2.5 mg co-administered with acetylsalicylic acid; as a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance.
In addition, section 4.8 of the SmPC is updated for all other dose strengths (10/15/20 mg) of Xarelto with relevant exposure information based on the provided clinical data.
The updated RMP version 11.1 has also been submitted."

Report from SAG CVS

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018, 22.02.2018.

See 2.3

5.1.14. Xtandi - enzalutamide - EMEA/H/C/002639/II/0039/G

Astellas Pharma Europe B.V.

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Eva A. Segovia

Scope: "C.I.4: Update of sections 4.4, 4.7, 4.8 and 5.2 of the SmPC in order to amend the warning on possible association with seizure, to amend the effects on driving or operating machines, to amend the identified adverse reactions and to amend the 'Race' subsection

regarding pharmacokinetic properties based on the results from the completed studies PROSPER, a Phase 3 Randomized Controlled Study, designed to investigate the Safety and Efficacy of Enzalutamide in Patients with Non-Metastatic Castration-Resistant Prostate Cancer; and Asian PREVAIL, a Multinational Phase 3, Randomized, Double-blind, Placebo-controlled Efficacy and Safety Study of Oral Enzalutamide in Chemotherapy-naive Subjects with Progressive Metastatic Prostate Cancer Who Have Failed Androgen Deprivation Therapy; and the updated integrated clinical safety database.
The Package Leaflet is updated in accordance.
C.I.6.a: Extension of Indication to include patients with non-metastatic castration-resistant prostate cancer (CRPC) for Xtandi;
as a consequence, sections 4.1 and 5.1 of the SmPC are updated, based on the supportive clinical study results of MDV3100-14 (PROSPER), a Phase 3 Randomized Controlled Study, designed to investigate the Safety and Efficacy of Enzalutamide in Patients with Non-Metastatic Castration-Resistant Prostate Cancer; MDV3100-09 (STRIVE), a Multicenter Phase 2 Study to investigate the Safety and Efficacy of Enzalutamide Versus Bicalutamide in Men With Non-Mtastatic or Metastatic Castration-Resistant Prostate Cancer; and based on supportive non-clinical data from 7 new reports.
The Package Leaflet is updated in accordance.
An update RMP version 12.1 was submitted in order to include the changes related to the extension of indication."

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018.

5.1.15. WS1274
Mekinist - trametinib - EMEA/H/C/002643/WS1274/0023
Tafinlar - dabrafenib - EMEA/H/C/002604/WS1274/0031

Novartis Europharm Limited

Lead Rapporteur: Paula Boudewina van Hennik, Lead Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include the combination adjuvant treatment with trametinib and dabrafenib of adult patients with stage III melanoma with a BRAF V600 mutation, following complete resection. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 of the Mekinist and Tafinlar SmPCs are updated. The Package Leaflet and the Risk Management plan (version 14.0 for Mekinist and version 9.0 for Tafinlar, according to GVP module V revision 2) are updated in accordance. In addition, the Worksharing applicant (WSA) took the opportunity to correct some typos throughout the Mekinist and Tafinlar product information, to include a cross reference to the Mekinist SmPC in section 4.6 of the Tafinlar SmPC regarding fertility, to update the list of local representatives for Bulgaria, Hungary, Estonia, Latvia and Lithuania in the Package Leaflet of both products."

SAG report

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018, 22.02.2018.

5.1.16. WS1278
OPDIVO - nivolumab - EMEA/H/C/003985/WS1278/0042
Yervoy - ipilimumab - EMEA/H/C/002213/WS1278/0053

Bristol-Myers Squibb Pharma EEIG

Lead Rapporteur: Paula Boudewina van Hennik, Lead Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of indication to include the combination treatment with nivolumab and ipilimumab of adult patients with intermediate/poor-risk advanced renal cell carcinoma. As a consequence sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the Opdivo and Yervoy SmPCs are updated. The Package Leaflet and the Risk Management Plan (version 19.0 for Yervoy and version 13.0 for Opdivo) are updated in accordance. In addition, the Worksharing applicant (WSA) took the opportunity to correct some typos throughout the Yervoy and Opdivo product information."

Action: For adoption

Request for Supplementary Information adopted on 31.05.2018, 22.02.2018.

See 2.3

5.1.17. WS1372
OPDIVO - nivolumab - EMEA/H/C/003985/WS1372/0053
Yervoy - ipilimumab - EMEA/H/C/002213/WS1372/0057

Bristol-Myers Squibb Pharma EEIG

Lead Rapporteur: Jorge Camarero Jiménez, Lead Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include first-line treatment of adult patients with metastatic Non-Small Cell Lung Carcinoma (NSCLC) for OPDIVO and Yervoy; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add information from the pivotal study CA209227 (an open-label, randomised phase 3 trial of nivolumab, or nivolumab plus ipilimumab, or nivolumab plus platinum doublet chemotherapy versus platinum doublet chemotherapy in subjects with chemotherapy-naïve stage IV or recurrent NSCLC). The Package Leaflet and RMP (version 14.0 for Opdivo and version 21.0 for Yervoy) are updated in accordance. In addition, the MAH has taken the opportunity to introduce minor editorial and formatting revisions in the PI."

Action: For adoption

5.1.18. WS1406 Abseamed-EMEA/H/C/000727/WS1406/0070, Binocrit-EMEA/H/C/000725/WS1406/0070, Epoetin alfa Hexal-EMEA/H/C/000726/WS1406/0069

Sandoz GmbH,
Lead Rapporteur: Alexandre Moreau, Lead PRAC Rapporteur: Ghania Chamouni,

Scope: "Extension of indication to include the treatment of symptomatic anaemia

(haemoglobin concentration of ≤ 10 g/dl) in adults with low- or intermediate-1-risk primary myelodysplastic syndromes (MDS) who have low serum erythropoietin (< 200 mU/ml) for Binocrit, Epoetin alfa Hexal and Abseamed; as a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated with safety and efficacy information. The Package Leaflet and the risk management plan (version 17.0) are updated in accordance. In addition, the worksharing applicant (WSA) took the opportunity to align information with the reference medicinal product and with the EC guideline on Excipients, to improve the quality and readability of the translations in the product information and to update the Annex A in line with EMA guideline."

Action: For adoption

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

No items

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

No items

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. emapalumab - Orphan - H0004386

Novimmune B.V., Treatment of Primary Haemophagocytic Lymphohistiocytosis (HLH)

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

Action: For adoption

8.1.2. larotrectinib sulphate - H0004919

for the treatment of adult and paediatric patients with locally advanced or metastatic solid tumours (excluding primary Central Nervous System tumours) with a Neurotrophic Tyrosine Receptor Kinase (NTRK) gene fusion after prior standard therapy or as initial therapy when there is no adequate treatment option

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

Action: For adoption

8.1.3. onasemnogene abeparvovec - Orphan - ATMP - H0004750

AveXis EU Ltd; Treatment of paediatric patients diagnosed with SMA Type 1
indicated for the one-time-only treatment of pediatric patients with spinal muscular atrophy (SMA) Type 1

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

Action: For adoption

8.1.4. Autologous haematopoietic stem cells transduced with lentiviral vector encoding the human beta-A-T87Q-globin gene - Orphan - ATMP - H0003691

bluebird bio GmbH; Treatment of adolescents and adults with transfusion-dependent β-thalassemia (TDT) who do not have a β0 mutation at both alleles of the β-globin (HBB) gene (i.e., patients with a non-β0/β0 genotype)

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. Victrelis – boceprevir – EMEA/H/C/2332

Merck Sharp & Dohme Ltd; treatment of chronic hepatitis C (HCV)

Rapporteur: Joseph Emmerich, Co-Rapporteur: Johann Lodewijk Hillege

Scope: Withdrawal

Action: For information

9.1.2. Intanza 15 microgram/strain - influenza vaccine (split virion, inactivated) - EMEA/H/C/000957

Sanofi Pasteur Europe

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Kristina Dunder

Scope: Withdrawal

Action: For information

9.1.3. Sovaldi - sofosbuvir - EMEA/H/C/002798/R/0050

Gilead Sciences International Limited

Rapporteur: Filip Josephson, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Julie Williams

Scope: Renewal

Action: For adoption

9.1.4. VELCADE - bortezomib - EMEA/H/C/000539/II/0088

Janssen-Cilag International NV

Rapporteur: Daniela Melchiorri

Scope: "Update of sections 4.2 and 5.1 of the SmPC in order to add a new dosing schedule for VELCADE (bortezomib) in combination with melphalan and prednisone (VMP) for the treatment of patients with newly diagnosed multiple myeloma, who are not eligible for high-dose chemotherapy with hematopoetic stem cell transplant.

The proposed new dosing schedule is supported by analyses comparing the current approved VcMP schedule (from 26866138MMY3002 [VISTA] study) with pooled modified less intensive ("once-weekly") VcMP schedules (from 54767414MMY3007 [ALCYONE], GIMENA MM-03-05 [GIMENA]). Additional supportive efficacy and safety data come from GEM2005MAS65 [PETHEMA].

The PL (section 3) is amended accordingly.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the PL."

Action: For adoption

Request for Supplementary Information adopted on 22.03.2018.

10. Referral procedures

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

10.1.1. XOFIGO - EMEA/H/A-20/1459

Bayer AG

Rapporteurs for the Article 20 referral: PRAC Rapporteur: Patrick Batty; PRAC Co-rapporteur: Martin Huber

CHMP Rapporteur: Harald Enzmann; CHMP Co-Rapporteur: Daniela Melcchiorri;

Scope: Review of the benefit-risk balance following notification by the European Commission of a referral under Article 20 of Regulation (EC) No 726/2004 based on pharmacovigilance data

Action: For adoption

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

10.2.1. Gentamicin – EMEA/H/A-5(3)/1468

MAHs: various

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Jorge Camarero Jiménez

Scope: CHMP list of outstanding issues

Action: For adoption

Review of histamine levels in Gentamicin-containing solutions for injection/infusion

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

No items

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

10.4.1. Paclitaxel Hetero - EMEA/H/A-29(4)/1466

Hetero Europe S.L.

Rapporteur: Fátima Ventura, Co-Rapporteur: Paula Boudewina van Hennik

Scope: CHMP list of outstanding issues /CHMP opinion

Action: For adoption

Decentralised Procedure number: PT/H/1256/001/DC, notification by the Portuguese Agency dated 29 March 2018 notifying of the start of a referral under Article 29(4) of Directive 2001/83/EC.

10.4.2. Syner-KINASE 10 000 IU - EMEA/H/A-29(4)/1472

Syner-Medica Ltd

Rapporteur: TBC, Co-Rapporteur: TBC

Scope: Start of procedure, appointment of Rapporteurs, list of questions

Action: For adoption

RMS: UK; CMS: DE, ES, FR, NL; Mutual Recognition Procedure number: UK/H/6520/01-05/MR, Disagreements regarding benefit/risk balance, safety and manufacturing.

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

10.5.1. Septanest and associated names – Articaine (hydrochloride)/ Adrenaline (tartrate) - EMEA/H/A-30/1461

Septodont group of companies and associated companies

Rapporteur: Romaldas Maciulaitis, Co-rapporteur: Fatima Ventura

Scope: List of questions, timetable

Action: For adoption

Harmonisation exercise for Septanest and associated names. Summary of Product Characteristics and Module 3 harmonisation was triggered by the MAH.

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

10.6.1. Omega-3-acid-ethyl esters- containing medicinal products for oral use – EMEA/H/A-31/1464

MAHs: various

Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise

Scope: Request for an extension to the clock stop to respond to the list of outstanding issues adopted in June CHMP

Action: For adoption

Review of the benefit-risk balance following notification by the MPA in Sweden on 15 March 2018 of a referral under Article 31 of Directive 2001/83/EC.

10.6.2. Valsartan-containing medicinal products - EMEA/H/A-31/1471

MAHs: various

Rapporteur: TBC, Co-Rapporteur: TBC,

Scope: Start of procedure, list of questions, timetable, appointment of Rapporteurs

Action: For adoption

Referral notification from European Commission regarding an API manufacturer (Zhejiang Huahai Pharmaceutical, China), who has detected the presence of a previously undetected impurity, N-nitrosodimethylamine (NDMA, also known as dimethylnitrosamine) in the valsartan API manufactured at its site in Chuannan. Zhejiang Huahai is one of the API manufacturers that are supplying valsartan for medicinal products authorised in the EU.

The CHMP appointed Daniela Melchiorri as Rapporteur (interest level 2) and Martina Weise as Co-rapporteur (interest level 2) during the July CHMP ORGAM meeting.

The CHMP adopted a list of questions to the MAHs and API manufacturers with a specific timetable.

Notification: 5 July 2018

Start of the procedure (CHMP):16 July 2018

List of questions: 16 July 2018

Submission of responses: 30 July 2018

Re-start of the procedure: 23 August 2018

Rapporteur/Co-rapporteur assessment report(s) circulated to CHMP: 10 September 2018

Comments: 13 September 2018

Updated Rapporteur/co-rapporteur assessment reports circulated to CHMP: 14 September 2018

CHMP list of outstanding issues /CHMP opinion: 20 September 2018

10.6.3. Gadolinium-containing contrast agents (GdCA): Gadobutrol (NAP); gadodiamide (NAP); gadopentetic acid (NAP); gadoteric acid (NAP); gadoteridol (NAP); gadoxetic acid (NAP) - EMEA/H/A-31/1097

Applicant: various

Lead Rapporteur: Patrick Batty

Scope: Annual cumulative reviews on NSF cases submission as a post-authorisation measure resulting from the 2010 Article 20 and Article 31 referral procedures for gadolinium-containing contrast agents

Timetable

Action: For adoption

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 2018 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

No items

13.2. Innovation Task Force briefing meetings

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. Concepts of significant benefit (follow-up to CHMP Work Plan 2017)

Action: For discussion

14.1.2. EMA Implementation plan of the new medical device and in vitro diagnostic regulation

Action: For discussion

Follow-up from June ORGAM

14.1.3. Rules of Procedure for standing working parties

Action: For discussion

14.1.4. Telematics strategy 2020-2025: Concept Paper

Action: For discussion

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 9-12 July 2018

Action: For information

List of Union Reference Dates and frequency of submission of Periodic Safety Update Reports (EURD list) for July 2018

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 18-20 July 2018
Action: For information

Revised draft Guideline on quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells (EMA/CAT/GTWP/671639/2018 Rev. 1)

CAT Rapporteur: Marcos Timon

Action: For adoption for 12 months public consultation

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 23-24 July 2018

Action: For information

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at July 2018 PDCO

Action: For information

Report from the PDCO meeting held on 24-27 July 2018

Action: For information

Joint CHMP/PDCO session

Agenda for joint session

Action: For discussion

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 17-19 July 2018

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 2018

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 9-12 July 2018. 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.

Nomination of a replacement SAWP member and his/her alternate following resignation of Jan Sjoberg

Action: For adoption

14.3.2. Name Review Group (NRG)

No items

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP July 2018 meeting to CHMP for adoption:

- 15 reports on products in scientific advice and protocol assistance
- 13 reports on products in pre-authorisation procedures
- 1 report on products in post-authorisation procedures
- 1 report on products in plasma master file

Action: For adoption

Response to CMDh question on requirements for Module 3 for the transfer of test methods

to already approved QC testing site for a biological medicinal product (EMA/CHMP/BWP/492172/2018)

CHMP: Sol Ruiz

Action: For adoption

14.3.4. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus

Election of vice-chair to RIWP

Action: For adoption

Response from RIWP and PKWP to CMDh questions on Classification as Narrow Therapeutic Index (NTI) drug and advice on requirements for bioequivalence studies – colchicine

Action: For adoption

14.3.5. Blood Products Working Party (BPWP)

Chair: Jacqueline Kerr

Guideline on core SmPC for human albumin solution (EMA/CHMP/BPWP/494462/2011/Rev.1)

Action: For adoption

Guideline on the clinical investigation of recombinant and human plasma-derived factor VIII products (EMA/CHMP/BPWP/144533/2009 rev. 2)

Action: For adoption

Guideline on core SmPC for human plasma derived and recombinant coagulation factor VIII products rev. 3 (EMA/CHMP/BPWP/1619/1999 rev. 3)

Action: For adoption

14.3.6. SmPC Advisory Group

Proposal for the development of an eLearning product information review curriculum: call for volunteers

Action: For discussion

Follow-up from June CHMP Plenary and July ORGAM meeting

14.3.7. Guideline Consistency Group (GCG)

Chair: Barbara van Zwieten-Boot

Election of Chair to the Guideline Consistency Group

Action: For adoption

14.3.8. Biosimilar Medicinal Product Working Party (BMWP)

Chair: Elena Wolff-Holz/Niklas Ekman

Guideline on similar biological medicinal products containing recombinant granulocyte-colony stimulating factor (rG-CSF) (EMA/483392/2018 Rev 1)

Action: For adoption

14.3.9. Oncology Working Party

Chair: Pierre Demolis/Paolo Foggi

Guideline on the use of minimal residual disease as a clinical endpoint in multiple myeloma studies (EMA/CHMP/183565/2018)

Action: For adoption for 3 month public consultation

14.3.10. Pharmacokinetics Working Party (PKWP)

PKWP response to CMDh request on referral procedure vaginal ring

Action: For adoption

14.3.11. Quality Working Party (QWP)

Letter to EDQM to seek input from the European Phamacopoeia Inhalation Working Party (EMA/CHMP/CVMP/QWP/126810/2018)

Action: For adoption

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

14.5.1. SADC and ECOWAS joint assessment meetings

Action: For information

14.5.2. International Council on Harmonisation (ICH)

ICH M9 Guideline: Biopharmaceutics Classification System-based Biowavers – Step1

Action: Draft guideline for adoption and release for 6 month public consultation

Report on ICH June 2018 meeting in Kobe, Japan

Action: For information

CESHARP: Call for expression of interest of one expert

Action: For information

Continuous Manufacturing (ICH Q13): nomination of experts

Action: For adoption

Analytical Procedure Development and Revision of Q2 (R1) Analytical Validation: nomination of experts

Action: For adoption

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. Relocation information to delegates

Action: For information

15.2. Preparedness of the system and capacity increase

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)*

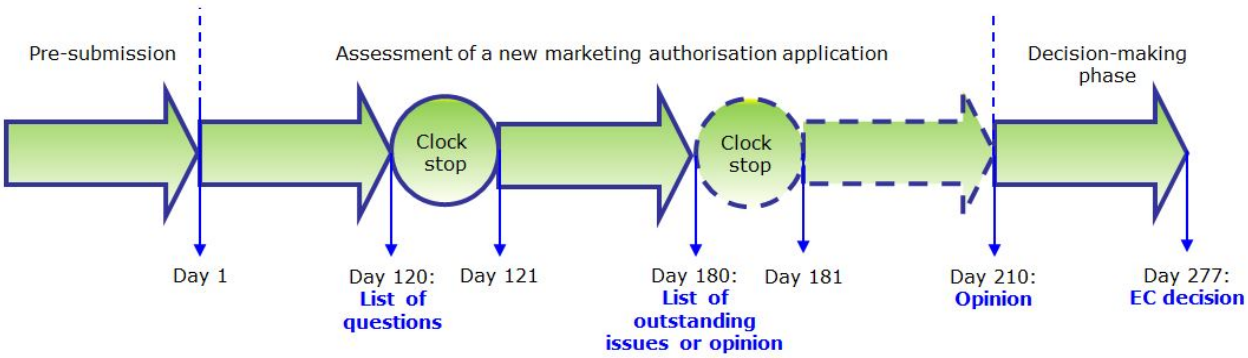
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

23 July 2018
EMA/CHMP/446480/2018

Annex to 23-26 July 2018 CHMP Agenda

Pre submission and post authorisation issues

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

B. POST-AUTHORISATION PROCEDURES OUTCOMES 3
B.1. Annual re-assessment outcomes 3
B.1.1. Annual reassessment for products authorised under exceptional circumstances 3
B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES 4
B.2.1. Renewals of Marketing Authorisations requiring 2nd Renewal 4
B.2.2. Renewals of Marketing Authorisations for unlimited validity 4
B.2.3. Renewals of Conditional Marketing Authorisations 5
B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES 6
B.4. EPARs / WPARs 8
B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES 9
B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects 9
B.5.2. CHMP assessed procedures scope: Non-Clinical and Clinical aspects 16
B.5.3. CHMP-PRAC assessed procedures 31
B.5.4. PRAC assessed procedures 39
B.5.5. CHMP-CAT assessed procedures 44
B.5.6. CHMP-PRAC-CAT assessed procedures 44
B.5.7. PRAC assessed ATMP procedures 44
B.5.8. Unclassified procedures and worksharing procedures of type I variations 45
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 47

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B.6.4. Annual Re-assessments: timetables for adoption 47
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 48
B.6.7. Type II Variations scope of the Variations: Extension of indication 48
B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects 49
B.6.9. CHMP assessed procedures scope: Non-Clinical and Clinical aspects 51
B.6.10. CHMP-PRAC assessed procedures 61
B.6.11. PRAC assessed procedures 64
B.6.12. CHMP-CAT assessed procedures 68
B.6.13. CHMP-PRAC-CAT assessed procedures 68
B.6.14. PRAC assessed ATMP procedures 68
B.6.15. Unclassified procedures and worksharing procedures of type I variations 68
B.7. DOCUMENTS TABLED IN MMD AFTER THE CHMP PLENARY 70
B.7.1. Yearly Line listing for Type I and II variations 70
B.7.2. Monthly Line listing for Type I variations 70
B.7.3. Opinion on Marketing Authorisation transfer (MMD only) 70
B.7.4. Notifications in accordance with Article 61(3) of Council Directive 2001/83/EC (MMD only) 70
B.7.5. Request for supplementary information relating to Notification of Type I variation (MMD only) 70
B.7.6. Notifications of Type I Variations (MMD only) 70

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) 70

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) 70

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES 70
E.1. PMF Certification Dossiers: 70
E.1.1. Annual Update 70
E.1.2. Variations: 71
E.1.3. Initial PMF Certification: 71
E.2. Time Tables – starting & ongoing procedures: For information 71

F. ANNEX F - Decision of the Granting of a Fee Reduction/Fee Waiver 71
F.1. Parallel Distribution - Pursuant to Article 9 of Council Regulation (EC) No. 2743/98 of 14 December 1998, as amended 71
F.2. Request for scientific opinion on justification of exceptional circumstance and for imperative grounds of public health 71

G. ANNEX G 71
G.1. Final Scientific Advice (Reports and Scientific Advice letters): 71
G.2. Ongoing procedures 71
G.3. PRIME 71
G.3.1. List of procedures concluding at 23-26 July 2018 CHMP plenary: 71
G.3.2. List of procedures starting in July 2018 for August 2018 CHMP adoption of outcomes 71

H. ANNEX H - Product Shared Mailboxes – e-mail address.....71

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

Report on Eligibility to Centralised Procedure for July 2018: **For adoption**

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

Final Outcome of Rapporteurship allocation for July 2018: **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/0006, Orphan
Leadiant GmbH, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Adam Przybylkowski

Elaprase - idursulfase - EMEA/H/C/000700/S/0075
Shire Human Genetic Therapies AB, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty

Firdapse - amifampridine - EMEA/H/C/001032/S/0053, Orphan
BioMarin International Limited, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams
Request for Supplementary Information adopted on 28.06.2018.

Qarziba - dinutuximab beta - EMEA/H/C/003918/S/0006, Orphan
EUSA Pharma (UK) Limited, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Brigitte

Keller-Stanislawski

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Fortacin - lidocaine / prilocaine -
EMEA/H/C/002693/R/0023
Recordati Ireland Ltd, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Dolores Montero Corominas
Request for Supplementary Information adopted on 31.05.2018.

Sovaldi - sofosbuvir -
EMEA/H/C/002798/R/0050
Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, Co-Rapporteur: Alar Irs, PRAC Rapporteur: Julie Williams

TECFIDERA - dimethyl fumarate -
EMEA/H/C/002601/R/0053
Biogen Idec Ltd, Rapporteur: Martina Weise, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Martin Huber

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Brintellix - vortioxetine -
EMEA/H/C/002717/R/0019
H. Lundbeck A/S, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Laurence de Fays

Diacomit - stiripentol -
EMEA/H/C/000664/R/0021
BIOCODEX, Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Julie Williams

Grastofil - filgrastim -
EMEA/H/C/002150/R/0020
Apotex Europe BV, Rapporteur: Robert James Hemmings, Co-Rapporteur: Sol Ruiz, PRAC Rapporteur: Patrick Batty

Izba - travoprost -
EMEA/H/C/002738/R/0011
Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Almath Spooner

Kadcyla - trastuzumab emtansine -
EMEA/H/C/002389/R/0039
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Doris Stenver
Request for Supplementary Information adopted on 31.05.2018.

Levetiracetam Hospira - levetiracetam -
EMEA/H/C/002783/R/0018
Hospira UK Limited, Generic, Generic of Keppra, Rapporteur: Juris Pokrotnieks, PRAC Rapporteur: Laurence de Fays

Neuraceq - florbetaben (18F) -
EMEA/H/C/002553/R/0025
Life Radiopharma Berlin GmbH, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Patrick Batty

Tivicay - dolutegravir -
EMEA/H/C/002753/R/0040
ViiV Healthcare B.V., Rapporteur: Filip Josephson, Co-Rapporteur: Joseph Emmerich, PRAC Rapporteur: Julie Williams

Xigduo - dapagliflozin / metformin -
EMEA/H/C/002672/R/0044
AstraZeneca AB, Rapporteur: Kristina Dunder, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Julie Williams

B.2.3. Renewals of Conditional Marketing Authorisations

Adcetris - brentuximab vedotin -
EMEA/H/C/002455/R/0058, Orphan
Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus

Lartruvo - olaratumab -
EMEA/H/C/004216/R/0010, Orphan
Eli Lilly Nederland B.V., Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus

NINLARO - ixazomib -
EMEA/H/C/003844/R/0012, Orphan
Takeda Pharma A/S, Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Ulla Wändel Liminga

Venclyxto - venetoclax -
EMEA/H/C/004106/R/0013, Orphan

AbbVie Deutschland GmbH & Co. KG,
Rapporteur: Filip Josephson, PRAC Rapporteur:
Patrick Batty

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 9-12 July 2018 PRAC:

Signal of autoimmune hepatitis

Abacavir, dolutegravir, lamivudine, zidovudine, atazanavir, cobicistat, darunavir, emtricitabine, tenofovir alafenamide, didanosine, rilpivirine, efavirenz, tenofovir disoproxil, elvitegravir, rilpivirine, enfuvirtide, etravirine, fosamprenavir, indinavir, zidovudine, lopinavir, maraviroc, nevirapine, raltegravir, saquinavir, stavudine, tipranavir - ZIAGEN, TRIUMEQ, KIVEXA, TRIZIVIR, REYATAZ, EVOTAZ, PREZISTA, REZOLSTA, SYMTUZA, TIVICAY, JULUCA, STOCRIN, SUSTIVA, ATRIPLA, GENVOYA, STRIBILD, EMTRIVA, ODEFSEY, EVIPLERA, DESCOVY, TRUVADA, FUZEON, INTELENCE, TELZIR, CRIXIVAN, EPIVIR, COMBIVIR, KALETRA, CELSENTRI, VIRAMUNE, ISENTRESS; EDURANT, NORVIR, INVIRASE, ZERIT, VIREAD, APTIVUS

PRAC recommendation on a variation: **For adoption**

Signal of lupus-like syndrome and related terms

Human normal immunoglobulin - FLEBOGAMMA DIF, HIZENTRA, HYQVIA, KIOVIG, PRIVIGEN

PRAC recommendation on a variation: **For adoption**

Signal of interaction possibly leading to decreased levothyroxine efficacy and hypothyroidism

Ritonavir; lopinavir; levothyroxine – NORVIR; KALETRA; VIEKIRAX

Follow-up from February PRAC meeting - justification from MAH for not following the PRAC recommendation: **For information**

PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its July 2018 meeting:

EMEA/H/C/PSUSA/00003085/201712
(ustekinumab)
CAPS:
Stelara (EMEA/H/C/000958) (ustekinumab), Janssen-Cilag International NV, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, "01 January 2017 - 31 December 2017"

EMEA/H/C/PSUSA/00010028/201712
(concentrate of proteolytic enzymes enriched in bromelain)
CAPS:
NexoBrid (EMEA/H/C/002246) (concentrate of proteolytic enzymes enriched in bromelain), MediWound Germany GmbH, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, "18 December 2016 to 17 December 2017"

EMEA/H/C/PSUSA/00010128/201712
(ponatinib)
CAPS:
Iclusig (EMEA/H/C/002695) (ponatinib), Incyte Biosciences Distribution B.V., Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, "14 December 2016 – 13 December 2017"

EMEA/H/C/PSUSA/00010341/201712
(secukinumab)
CAPS:
Cosentyx (EMEA/H/C/003729) (secukinumab), Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, PRAC Rapporteur: Eva A. Segovia, "26 DEC 2016 - 25 DEC 2017"

EMEA/H/C/PSUSA/00010379/201801
(nivolumab)
CAPS:
OPDIVO (EMEA/H/C/003985) (nivolumab), Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, "04 July 2017 to 03 January 2018"

EMEA/H/C/PSUSA/00010391/201712
(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, isotope of mass 177), I.D.B. Holland B.V., Rapporteur: Nithyanandan Nagercoil NAPS: **NAPs** - EU , PRAC Rapporteur: Almath Spooner, "20.06.2017 - 19.12.2017"	

B.4. EPARs / WPARs

Cablivi - caplacizumab - EMEA/H/C/004426, Orphan Ablynx NV, indicated for the treatment of acquired thrombotic thrombocytopenic purpura (aTTP)., New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Duzallo - allopurinol / lesinurad - EMEA/H/C/004412 Grunenthal GmbH, gout, Fixed combination application (Article 10b of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Kymriah - tisagenlecleucel - EMEA/H/C/004090, Orphan, ATMP Novartis Europharm Limited, treatment of B cell acute lymphoblastic leukaemia (ALL) and diffuse large B cell lymphoma (DLBCL), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Mepsevii - vestronidase alfa - EMEA/H/C/004438, Orphan Ultragenyx Germany GmbH, Mepsevii is indicated for the treatment of Mucopolysaccharidosis VII (MPS VII; Sly syndrome) for patients of all ages, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Nerlynx - neratinib - EMEA/H/C/004030 Puma Biotechnology Limited, extended adjuvant treatment of adult patients with early-stage HER2-overexpressed/amplified breast cancer who have received prior adjuvant trastuzumab based therapy, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Raligize - axalimogene filolisbac - EMEA/H/C/004473, ATMP FGK Representative Service GmbH, treatment of cervical cancer, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.

WPAR	
Ulipristal Acetate Gedeon Richter - ulipristal acetate - EMEA/H/C/005017 Gedeon Richter Plc., treatment of uterine fibroids, Informed Consent of Esmya, Informed consent application (Article 10c of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
VEYVONDI - vonicog alfa - EMEA/H/C/004454, Orphan Baxalta Innovations GmbH, Treatment of von Willebrand Disease (VWD), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Vyxeos - daunorubicin / cytarabine - EMEA/H/C/004282, Orphan Jazz Pharmaceuticals Ireland Limited, treatment of adults with high-risk acute myeloid leukaemia (AML), Known active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480, Orphan, ATMP Kite Pharma EU B.V., treatment of diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL) and transformed follicular lymphoma (TFL), New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.

B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

Adcetris - brentuximab vedotin - EMEA/H/C/002455/II/0056/G, Orphan Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 05.07.2018.	Request for supplementary information adopted with a specific timetable.
ATryn - antithrombin alfa - EMEA/H/C/000587/II/0033/G Laboratoire Francais du Fractionnement et des Biotechnologies, Rapporteur: Alexandre Moreau Opinion adopted on 19.07.2018. Request for Supplementary Information adopted on 03.05.2018, 15.02.2018.	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Benepali - etanercept - EMEA/H/C/004007/II/0035 Samsung Bioepis UK Limited, Rapporteur: Andrea Laslop Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 17.05.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
BiResp Spiromax - budesonide / formoterol - EMEA/H/C/003890/II/0024/G Teva Pharma B.V., Duplicate, Duplicate of DuoResp Spiromax, Rapporteur: Nithyanandan Nagercoil Request for Supplementary Information adopted on 21.06.2018.	
Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0068/G UCB Pharma S.A., Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 15.03.2018.	
Circadin - melatonin - EMEA/H/C/000695/II/0053/G RAD Neurim Pharmaceuticals EEC Ltd., Rapporteur: Bruno Sepodes Opinion adopted on 05.07.2018.	Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cuprior - trientine - EMEA/H/C/004005/II/0001/G GMP-Orphan SA, Rapporteur: Jayne Crowe	
Cyramza - ramucirumab - EMEA/H/C/002829/II/0024/G Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik	
Cyramza - ramucirumab - EMEA/H/C/002829/II/0025 Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 19.07.2018.	Request for supplementary information adopted with a specific timetable.
DuoResp Spiromax - budesonide / formoterol - EMEA/H/C/002348/II/0024/G Teva Pharma B.V., Rapporteur: Nithyanandan Nagercoil Request for Supplementary Information adopted on 21.06.2018.	
Dupixent - dupilumab - EMEA/H/C/004390/II/0006/G	Request for supplementary information adopted with a specific timetable.

sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 19.07.2018.	
Entyvio - vedolizumab - EMEA/H/C/002782/II/0029 Takeda Pharma A/S, Rapporteur: Greg Markey Request for Supplementary Information adopted on 17.05.2018.	
Episalvan - birch bark extract - EMEA/H/C/003938/II/0010 Amryt AG, Rapporteur: Kristina Dunder Opinion adopted on 05.07.2018.	Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Eptifibatide Accord - eptifibatide - EMEA/H/C/004104/II/0004 Accord Healthcare Limited, Generic, Generic of Integrilin, Rapporteur: Jayne Crowe Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 07.06.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Evicel - human fibrinogen / human thrombin - EMEA/H/C/000898/II/0059 Omrix Biopharmaceuticals N. V., Rapporteur: Jan Mueller-Berghaus	
EXJADE - deferasirox - EMEA/H/C/000670/II/0061 Novartis Europharm Limited, Rapporteur: Alexandre Moreau	
Eylea - aflibercept - EMEA/H/C/002392/II/0046 Bayer AG, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 31.05.2018.	
Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0082 AstraZeneca AB, Rapporteur: Bart Van der Schueren Request for Supplementary Information adopted on 28.06.2018.	
Fuzeon - enfuvirtide - EMEA/H/C/000514/II/0051/G Roche Registration GmbH, Rapporteur: Kristina Dunder	
Gardasil - human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant,	

adsorbed) - EMEA/H/C/000703/II/0077 MSD Vaccins, Rapporteur: Kristina Dunder	
Gardasil - human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) - EMEA/H/C/000703/II/0078 MSD Vaccins, Rapporteur: Kristina Dunder	
Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0025 MSD Vaccins, Rapporteur: Kristina Dunder	
Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0028, Orphan Roche Registration GmbH, Rapporteur: Sinan B. Sarac Opinion adopted on 19.07.2018.	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Gliolan - aminolevulinic acid - EMEA/H/C/000744/II/0016/G medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Bruno Sepodes Request for Supplementary Information adopted on 17.05.2018.	
Herzuma - trastuzumab - EMEA/H/C/002575/II/0005 Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus	
Imatinib Teva - imatinib - EMEA/H/C/002585/II/0033 Teva B.V., Generic, Generic of Glivec, Rapporteur: Jorge Camarero Jiménez Opinion adopted on 05.07.2018. Request for Supplementary Information adopted on 03.05.2018.	Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0046 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 21.06.2018.	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0051/G Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 19.07.2018.	Request for supplementary information adopted with a specific timetable.

Kineret - anakinra - EMEA/H/C/000363/II/0060 Swedish Orphan Biovitrum AB (publ), Rapporteur: Mark Ainsworth	
Lemtrada - alemtuzumab - EMEA/H/C/003718/II/0021/G Genzyme Therapeutics Ltd, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth Opinion adopted on 19.07.2018. Request for Supplementary Information adopted on 07.06.2018.	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Litak - cladribine - EMEA/H/C/000504/II/0015 Lipomed GmbH, Rapporteur: Robert James Hemmings Opinion adopted on 05.07.2018.	Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Lynparza - olaparib - EMEA/H/C/003726/II/0022 AstraZeneca AB, Rapporteur: Alexandre Moreau	
Naglazyme - galsulfase - EMEA/H/C/000640/II/0070 BioMarin International Limited, Rapporteur: Greg Markey Request for Supplementary Information adopted on 12.04.2018.	
NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0026/G Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 19.07.2018.	Request for supplementary information adopted with a specific timetable.
Olanzapine Apotex - olanzapine - EMEA/H/C/001178/II/0034 Apotex Europe BV, Generic, Generic of Zyprexa, Rapporteur: John Joseph Borg Opinion adopted on 05.07.2018.	Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Repatha - evolocumab - EMEA/H/C/003766/II/0026/G Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 19.07.2018.	Request for supplementary information adopted with a specific timetable.
Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0023/G CSL Behring GmbH, Rapporteur: Kristina Dunder	

Request for Supplementary Information adopted on 28.06.2018.	
Rotarix - human rotavirus, live attenuated - EMEA/H/C/000639/II/0106/G GlaxoSmithKline Biologicals S.A., Rapporteur: Bart Van der Schueren	
Simponi - golimumab - EMEA/H/C/000992/II/0082/G Janssen Biologics B.V., Rapporteur: Kristina Dunder Opinion adopted on 05.07.2018. Request for Supplementary Information adopted on 31.05.2018.	Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Strensiq - asfotase alfa - EMEA/H/C/003794/II/0030/G, Orphan Alexion Europe SAS, Rapporteur: Greg Markey Opinion adopted on 12.07.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0126 GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder Opinion adopted on 19.07.2018.	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0127/G GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 19.07.2018.	Request for supplementary information adopted with a specific timetable.
Trulicity - dulaglutide - EMEA/H/C/002825/II/0030 Eli Lilly Nederland B.V., Rapporteur: Greg Markey	
Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0008 Pfizer Limited, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 05.07.2018.	Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Vaniqa - eflornithine - EMEA/H/C/000325/II/0051 Almirall S.A, Rapporteur: Peter Kiely Opinion adopted on 19.07.2018. Request for Supplementary Information adopted on 26.04.2018, 22.03.2018, 26.10.2017.	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Xiapex - collagenase clostridium histolyticum - EMEA/H/C/002048/II/0099 Swedish Orphan Biovitrum AB (publ), Rapporteur: Martina Weise	
Yervoy - ipilimumab - EMEA/H/C/002213/II/0058/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik Request for Supplementary Information adopted on 12.07.2018.	Request for supplementary information adopted with a specific timetable.
Zerbaxa - ceftolozane / tazobactam - EMEA/H/C/003772/II/0015/G Merck Sharp & Dohme B.V., Rapporteur: Robert James Hemmings Opinion adopted on 05.07.2018. Request for Supplementary Information adopted on 26.04.2018.	Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1339/G **Fertavid-EMEA/H/C/001042/WS1339/0038/G** **Puregon-EMEA/H/C/000086/WS1339/0096/G** Merck Sharp & Dohme B.V., Lead Rapporteur: Nithyanandan Nagercoil Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 15.03.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1393/G **Hexacima-EMEA/H/C/002702/WS1393/0080/G** **Hexaxim-EMEA/H/W/002495/WS1393/0085/G** **Hexyon-EMEA/H/C/002796/WS1393/0084/G** Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 19.07.2018.	Request for supplementary information adopted with a specific timetable.
WS1404 **Nuwiq-EMEA/H/C/002813/WS1404/0022** **Vihuma-EMEA/H/C/004459/WS1404/0004** Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 05.07.2018.	Request for supplementary information adopted with a specific timetable.

WS1415
Blitzima-
EMEA/H/C/004723/WS1415/0015
Ritemvia-
EMEA/H/C/004725/WS1415/0015
Rituzena-
EMEA/H/C/004724/WS1415/0016
Truxima-
EMEA/H/C/004112/WS1415/0016
Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz

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

Abraxane - paclitaxel - EMEA/H/C/000778/II/0089 Celgene Europe Limited, Rapporteur: Paula Boudewina van Hennik, "Update of section 4.6 and 5.3 of the SmPC based on information available for the paclitaxel active substance in available literature and product information. No additional non-clinical data was submitted." Opinion adopted on 19.07.2018.	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
BESPONSA - inotuzumab ozogamicin - EMEA/H/C/004119/II/0006, Orphan Pfizer Limited, Rapporteur: Robert James Hemmings, "Update of sections 4.8 and 5.1 of the SmPC based on the supplemental Clinical Study Report for the pivotal phase 3 Study B1931022 (Study 1022) that was prepared following last patient last visit. The Package Leaflet is updated accordingly. The MAH took the opportunity to make minor editorial changes for added clarity in sections 4.2, 4.4, 4.8, 5.1, 5.3 and 6.6 of the SmPC and Package Leaflet."	
Cayston - aztreonam - EMEA/H/C/000996/II/0073, Orphan Gilead Sciences Ireland UC, Rapporteur: Johann Lodewijk Hillege, "Submission of the final report from study GX US 205-0128, listed as a category 3 study in the RMP. This is a prospective, observational, 5 year registry study carried out to monitor the susceptibility to aztreonam of Pseudomonas aeruginosa isolates from patients with Cystic Fibrosis in the US. The population eligible for the registry included paediatric subjects, and the final study population included approximately 26% of subjects of less than 18 years of age.	

No changes to the SmPC are proposed based on the results from this non-interventional, registry study."	
Dacogen - decitabine - EMEA/H/C/002221/II/0035, Orphan Janssen-Cilag International N.V., Rapporteur: Alexandre Moreau, "Update of section 4.4, and 4.8 of the SmPC in order to add the adverse events "Hepatic Function abnormal" and "Hyperbilirubinaemia" with the frequency common and to include clinical recommendations in patients developing signs or symptoms of hepatic impairment based on a cumulative review of post-marketing data; the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the contact details of the local representative in Portugal in the Package Leaflet. Furthermore, the term "(for pH adjustment)" has been removed from the Annex IIIA in accordance with the revision 2 of the European Commission guideline on Excipients in the labelling and package leaflet of medicinal products for human use."	
DaTSCAN - ioflupane (123i) - EMEA/H/C/000266/II/0055 GE Healthcare Ltd, Rapporteur: Robert James Hemmings, "Update of section 4.8 of the SmPC in order to add Erythema, pruritus, rash, urticaria, hyperhidrosis, Dyspnea, Vomiting and Blood pressure decreased as undesirable effects all with a not known frequency. The Package leaflet has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 11 of the SmPC in line with ICRP Publication 128, Radiation Dose to Patients from "Radiopharmaceuticals: a Compendium of Current Information Related to Frequently Used Substances, 2015". The Marketing authorisation holder (MAH) took also the opportunity to bring the PI in line with the latest QRD template version 10.0."	
Dukoral - cholera vaccine (inactivated, oral) - EMEA/H/C/000476/II/0058 Valneva Sweden AB, Rapporteur: Kristina Dunder, "Update of the 'instructions for use' in the Package Leaflet in order to increase clarity	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

and reduce the risk of medication errors. Minor corresponding editorial changes have been implemented in section 4.2 of the SmPC. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10, to update Annex II with regards to PSUR requirements, to correct the description of the container of the vaccine suspension and to introduce minor linguistic and layout improvements to the Annexes."
Opinion adopted on 19.07.2018.

Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0024/G
MSD Vaccins, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to update the information following results from long-term follow-up (LTFU) studies. Specifically:

- a long-term effectiveness sub-section is added, based on the first interim reports from the 9vHPV studies V503-021-01 and V503-002-20 (two category 3 studies included in the pharmacovigilance plan of the 9vHPV vaccine - MEA-004 and MEA 005, respectively).

- update of the immunogenicity sub-section based on the data from the two 9vHPV studies listed above as well as final results from studies V503-001-04 and V503-010-01.

- update of the qHPV clinical data based on the efficacy/effectiveness results and/or immunogenicity results of the qHPV studies V501-015-21 (4th interim report), V501-019-21 (final study report), V501-020-21 (final study report) and the extension of study V501-167."
Request for Supplementary Information adopted on 31.05.2018.

Humira - adalimumab - EMEA/H/C/000481/II/0179
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to add Lichenoid skin reactions with a rare frequency following a signal detection request (EPITT ref. No. 19128) for cumulative review (SDA106). The Package Leaflet is updated accordingly"

Request for Supplementary Information adopted on 31.05.2018.	
HyQvia - human normal immunoglobulin - EMEA/H/C/002491/II/0040/G Baxalta Innovations GmbH, Rapporteur: Jan Mueller-Berghaus, “Update of section 4.8 of the SmPC to include aseptic meningitis as adverse reaction. The PL is updated accordingly. Update of section 4.2 of the SmPC to include the option of handpush administration of the rHuPH20 component (in addition to administration with a pump). This change is a correction in order to harmonize with the PIL.” Request for Supplementary Information adopted on 25.05.2018.	
IBRANCE - palbociclib - EMEA/H/C/003853/II/0011 Pfizer Limited, Rapporteur: Filip Josephson, “Update of section 5.1 of the SmPC to update the clinical efficacy data from pivotal Phase 3 Study A5481008 (PALOMA-2), a study of IBRANCE in combination with letrozoleto, to include the results from recent analyses of the study with a data cutoff date of 31 May 2017. In addition, the MAH took the oportunity to update section 4.2 to include that when coadministered with an aromatase inhibitor, the later should be administered according to the dose schedule reported in the Summary of Product Characteristics.” Request for Supplementary Information adopted on 17.05.2018.	
Inflectra - infliximab - EMEA/H/C/002778/II/0061 Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey, “To submit the final report from study CT-P13 3.4, listed as a category 3 study in the RMP. A Randomized, Double-Blind, Parallel-Group, Phase 3 Study to Demonstrate Noninferiority in Efficacy and to Assess Safety of CT-P13 Compared to Remicade in Patients with Active Crohn’s Disease.” Opinion adopted on 19.07.2018. Request for Supplementary Information adopted on 17.05.2018.	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Isentress - raltegravir - EMEA/H/C/000860/II/0073	

Merck Sharp & Dohme B.V., Rapporteur: Greg Markey, “Update of sections 4.6 and 5.3 of the SmPC, upon request by PRAC following the assessment of the latest PSUR (PSUSA/00010373/201703), to include revised safety information about pregnancy and risk of malformative or foetal toxicity (LEG). The Package Leaflet has been updated accordingly.” Request for Supplementary Information adopted on 12.04.2018.	
Lemtrada - alemtuzumab - EMEA/H/C/003718/II/0023 Genzyme Therapeutics Ltd, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth, “Update of section 4.8 of the SmPC in order to update the table of frequencies of adverse reactions in accordance with the SmPC guideline following request from PRAC in procedure EMEA/H/C/PSUSA/00010055/201703. This procedure also included an update in section 4.4 to add warning on acute acalculous cholecystit following a cumulative review of the cases. The Package Leaflet is updated accordingly.” Request for Supplementary Information adopted on 12.07.2018.	Request for supplementary information adopted with a specific timetable.
Lucentis - ranibizumab - EMEA/H/C/000715/II/0069 Novartis Europharm Limited, Rapporteur: Kristina Dunder, “Update of section 5.1 of the SmPC in order to include information on the diabetic retinopathy score (DRSS) in diabetic macular edema patients (DME) based on pooled data from studies RFB002D2301 (RESTORE), RFB002D2303 (REVEAL) and RFB002D2305 (REFINE).” Request for Supplementary Information adopted on 28.06.2018, 22.02.2018.	
Orgalutran - ganirelix - EMEA/H/C/000274/II/0041 Merck Sharp & Dohme B.V., Rapporteur: Outi Mäki-Ikola, “Update of section 4.3 of the SmPC to expand the existing contraindication regarding hypersensitivity to include also wording regarding dry natural rubber/latex and sections 4.4 and 6.5 of the SmPC to clarify that this product is in contact with dry natural rubber/latex. The labelling and Package Leaflet have been updated accordingly. In addition, the MAH took the opportunity to update the contact	

details of the local representative in Belgium in the Package Leaflet."	
Ozempic - semaglutide - EMEA/H/C/004174/II/0001 Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, "Update of section 5.1 of the SmPC in order to reflect final results from the SUSTAIN 7 trial (NN9535-4216), a 40-week open-label trial comparing the safety and efficacy of 0.5 mg of Ozempic to 0.75 mg of dulaglutide and 1 mg of Ozempic to 1.5 mg of dulaglutide in patients on metformin with type-2 diabetes." Request for Supplementary Information adopted on 25.05.2018.	
Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (H5N1) (live attenuated, nasal) - EMEA/H/C/003963/II/0015 AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.6 of the SmPC with regards to pregnancy information based on the review and summary of pregnancy data from published literature and MAH pharmacovigilance database. The MAH took the opportunity to include editorial changes in section 4.8 and 5.1 of the SmPC."	
Perjeta - pertuzumab - EMEA/H/C/002547/II/0039 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC and relevant section of the PL to include tumour lysis syndrome (TLS) as a rare adverse reaction." Opinion adopted on 05.07.2018.	Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Praluent - alirocumab - EMEA/H/C/003882/II/0040 sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Submission of the final clinical study report of study R727-CL-1018 (study title: A Phase 2 Pilot Study with a Randomized Double-Blind Treatment Phase to Evaluate the Pharmacodynamics and Safety of Alirocumab in Patients with Autosomal Dominant Hypercholesterolemia and Gain-of-Function Mutations in 1 or Both Alleles of the PCSK9 Gene or Loss-of-Function Mutations in 1 or More Alleles of the Apolipoprotein B Gene), as per	Request for supplementary information adopted with a specific timetable.

MEA012." Request for Supplementary Information adopted on 19.07.2018.	
Remsima - infliximab - EMEA/H/C/002576/II/0052 Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey, "To submit the final report from study CT-P13 3.4, listed as a category 3 study in the RMP. A Randomized, Double-Blind, Parallel-Group, Phase 3 Study to Demonstrate Noninferiority in Efficacy and to Assess Safety of CT-P13 Compared to Remicade in Patients with Active Crohn's Disease." Opinion adopted on 19.07.2018. Request for Supplementary Information adopted on 17.05.2018.	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Revestive - teduglutide - EMEA/H/C/002345/II/0043, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Mark Ainsworth, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC based on the final CSR of study TED-C14-006 ("a 24-Week Double-blind, Safety, Efficacy, and Pharmacodynamic Study Investigating Two Doses of Teduglutide in Pediatric Subjects Aged 1 Year Through 17 Years With Short Bowel Syndrome who are Dependent on Parenteral Support"; a category 3 study in the RMP). The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 31.05.2018.	
Savene - dexrazoxane - EMEA/H/C/000682/II/0036 Clinigen Healthcare Ltd, Rapporteur: Alexandre Moreau, "Update of section 4.4 and 4.6 of the SmPC in order to add a warning on mutagenic activity of dexrazoxane and to update the contraception recommendations based on toxicological data and literature review, the Package Leaflet is updated accordingly. In addition the MAH took the opportunity to make an administrative amendment to the description of the pharmaceutical form for Savene in order to align with the relevant EDQM standard terms." Request for Supplementary Information adopted on 14.06.2018.	
Somavert - pegvisomant -	Request for supplementary information adopted

EMEA/H/C/000409/II/0084 Pfizer Limited, Rapporteur: Joseph Emmerich, "Update of sections 4.2 and 4.4 of the SmPC to introduce posology recommendations to recommend an assessment of baseline levels of liver tests (LTs) [serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum total bilirubin (TBIL), and alkaline phosphatase (ALP)] prior initiation of treatment with Somavert following analysis of the interim result for study "A6291010 (ACROSTUDY) - A multicenter, post marketing surveillance study of pegvisomant therapy in patients with acromegaly – extension" as requested in procedure EMEA/H/C/000409/MEA 061.1. The PL has been updated accordingly." Request for Supplementary Information adopted on 12.07.2018.	with a specific timetable.
Spinraza - nusinersen - EMEA/H/C/004312/II/0004, Orphan Biogen Idec Ltd, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.4 and 4.8 of the SmPC to include new safety information related to communicating hydrocephalus. The PIL and the RMP (new version 10.0) are updated accordingly. Section 4.2 of the SmPC is updated to move an existing wording on the route of administration of the product in order to improve readability." Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 14.06.2018, 12.04.2018, 08.02.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Stelara - ustekinumab - EMEA/H/C/000958/II/0063 Janssen-Cilag International NV, Rapporteur: Greg Markey, "Update of section 4.8 of the SmPC in order to revise the immunogenicity rate in patients with psoriasis from "less than 8%" to "up to 12.4 %" following based on new data generated from a Phase 3b study in psoriasis patients, CNTO1275PSO3009 (PSTELLAR) - A Study of Ustekinumab to Evaluate a "Subject-tailored" Maintenance Dosing Approach in Subjects With Moderate-to-Severe Plaque Psoriasis (PSTELLAR). In addition, the MAH took the opportunity to update section 4.4 of the SmPC and package	

leaflet with additional warning of the excipient sodium to align with the recent updates to the Annex of the EC guideline on excipients in labelling." Request for Supplementary Information adopted on 31.05.2018, 22.03.2018.	
Sustiva - efavirenz - EMEA/H/C/000249/II/0145/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Bruno Sepodes, "Update of sections 4.3 and 4.5 of the SmPC in order to add contraindication with elbasvir/grazoprevir due to the potential for significant decreases in plasma concentrations of elbasvir and grazoprevir, based on the post-approval and literature data, the Package Leaflet is updated accordingly. Update of sections 4.4 and 4.5 to include warnings in relation to the co-administration of efavirenz and sofosbuvir/velpatasvir; efavirenz and vepatasvir/sofosbuvir/voxilaprevir and efavirenz and glecaprevir/pibrentasvir; based on the post-approval and literature data, the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet."	
Tivicay - dolutegravir - EMEA/H/C/002753/II/0034 ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC to add the new ADR 'acute hepatic failure' with a frequency of rare based on post-marketing and clinical trial data. The Package Leaflet has been updated accordingly." Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 17.05.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tivicay - dolutegravir - EMEA/H/C/002753/II/0041/G ViiV Healthcare B.V., Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC with Week 24 data (secondary analysis) from the pivotal Phase III studies, 204861 [GEMINI-1] and 205543 [GEMINI-2] in ART-naïve adult subjects. The Package Leaflet has been updated accordingly."	
Triumeq - dolutegravir / abacavir /	Positive Opinion adopted by consensus on

lamivudine - EMEA/H/C/002754/II/0053 ViiV Healthcare UK Limited, Rapporteur: Filip Josephson, "Update of section 4.8 of the SmPC to add the new ADR 'acute hepatic failure' with a frequency of rare based on post-marketing and clinical trial data, and to implement minor changes for increased clarity. The Package Leaflet has been updated accordingly." Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 17.05.2018.	12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Truvada - emtricitabine / tenofovir disoproxil - EMEA/H/C/000594/II/0147 Gilead Sciences Ireland UC, Rapporteur: Greg Markey, "Update of sections 4.8 and 5.1 of the Truvada SmPC based on the final results from study Study ATN-113 (CO-US-164-0455): listed as a category 3 study in the RMPl; this is a Project PeEPare - An open label demonstration project and phase II safety study of pre-exposure prophylaxis use among 15 to 17 year old men who have sex with men (YMSM) in the United States." Request for Supplementary Information adopted on 25.05.2018.	
Vargatef - nintedanib - EMEA/H/C/002569/II/0021 Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, "Update of section 4.8 of the SmPC in order to add 'pruritus' as a new adverse drug reaction with a frequency 'common' following a routine review of post-marketing data. The Package Leaflet is updated accordingly."	
VELCADE - bortezomib - EMEA/H/C/000539/II/0088 Janssen-Cilag International NV, Rapporteur: Daniela Melchiorri, "Update of sections 4.2 and 5.1 of the SmPC in order to add a new dosing schedule for VELCADE (bortezomib) in combination with melphalan and prednisone (VMP) for the treatment of patients with newly diagnosed multiple myeloma who are not eligible for high-dose chemotherapy with hematopoetic stem cell transplant. The proposed new dosing schedule is supported by analyses comparing the current approved	

VcMP schedule (from 26866138MMY3002 [VISTA] study) with pooled modified less intensive ("once-weekly") VcMP schedules (from 54767414MMY3007 [ALCYONE], GIMENA MM-03-05 [GIMENA]). Additional supportive efficacy and safety data come from GEM2005MAS65 [PETHEMA]. The PL (section 3) is amended accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the PL." Request for Supplementary Information adopted on 22.03.2018.	
Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/II/0047 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Submission of the final report from study (M14-567) listed as a category 3 study in the RMP. This is a randomized, open-label study to evaluate the safety and efficacy of the co-administration of ombitasvir/ABT-450/Ritonavir (ombitasvir/ABT-450/r) with sofosbuvir (SOF) with or without ribavirin (RBV) in subjects with genotype 2 chronic hepatitis C virus (HCV) infection or genotype 3 HCV infection with or without Cirrhosis."	
Vimpat - lacosamide - EMEA/H/C/000863/II/0070/G UCB Pharma S.A., Rapporteur: Filip Josephson, "C.I.4 - Update of sections 4.8, 5.1, and 5.2 of the SmPC in order to update clinical efficacy and safety data in the paediatric population with the results from study SP0969: a phase 3, multicentre, double-blind, randomized, placebo-controlled, parallel-group study to evaluate the efficacy and safety of lacosamide as adjunctive therapy in subjects with epilepsy ≥4 years to <17 years of age with uncontrolled partial-onset seizures; 3 new ADRs (nasopharyngitis, pharyngitis, and pyrexia) have been added based on the results of the above mentioned study; C.I.4 - Update of section 5.2 of the SmPC in order to update the pharmacokinetic data in the paediatric population based on results from the CL0430 population pharmacokinetic (PK) analyses;	

C.I.4 - Update of section 4.8 of the SmPC in order to update the incidence of decreased appetite, lethargy, and abnormal behaviour in the paediatric population based on results from the updated safety data for Pool SPX-1 with clinical cut-off date of 01 November 2016. The Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some editorial changes in the PI. The MAH also took the opportunity to revise Annex A as requested." Request for Supplementary Information adopted on 21.06.2018, 22.03.2018.	
Visudyne - verteporfin - EMEA/H/C/000305/II/0097 Novartis Europharm Limited, Rapporteur: Alexandre Moreau, "Update of SPC in sections 4.4 Warning and precautions for use and 4.8. Undesirable effects to include information "Cases of anaphylactic reactions have been observed in patients receiving Visudyne. If an anaphylactic or other serious allergic reaction occurs during or following infusion, administration of Visudyne should be discontinued immediately and appropriate therapy be initiated." with frequency 'not known' . The Package Leaflet have been updated accordingly"	
Votubia - everolimus - EMEA/H/C/002311/II/0051, Orphan Novartis Europharm Limited, Rapporteur: Harald Enzmann, "Update of sections 4.8 (all pharmaceutical pharms) and 5.1 (dispersible tablets only) of the SmPC in order to update the safety and efficacy information based on final results from study CRAD001M2304, listed as a category 3 study in the RMP; this is a three-arm, randomized, double-blind, placebo-controlled study of the efficacy and safety of two trough-ranges of everolimus as adjunctive therapy in patients with tuberous sclerosis complex (TSC) who have refractory partial-onset seizures. The Package Leaflet is updated accordingly." Opinion adopted on 12.07.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Xyrem - sodium oxybate -	

EMEA/H/C/000593/II/0075

UCB Pharma S.A., Rapporteur: Bruno Sepodes, "Update of section 4.9 of the SmPC in order to include safety information on hypernatremia based on a cumulative review of post-marketing data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in sections 4.2 and 4.4 of the SmPC and in the Package Leaflet, as well as to align the annexes with the latest QRD template v.10. Moreover, the Package Leaflet was updated to include information on hypoaesthesia."

WS1346

Aprovel-
EMEA/H/C/000141/WS1346/0170
CoAprovel-
EMEA/H/C/000222/WS1346/0185
Irbesartan Hydrochlorothiazide Zentiva-
EMEA/H/C/000783/WS1346/0099
Irbesartan Zentiva-
EMEA/H/C/000785/WS1346/0078
Karvea-EMEA/H/C/000142/WS1346/0174
Karvezide-
EMEA/H/C/000221/WS1346/0187

Sanofi Clir SNC, Lead Rapporteur: Concepcion Prieto Yerro, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information for irbesartan and for irbesartan/ hydrochlorothiazide linked to irbesartan INN by adding "Psoriasis : the use of irbesartan in patients with psoriasis or a history of psoriasis should be carefully weighed as it may exacerbate psoriasis" and include new undesirable effects "anaphylactic reaction including anaphylactic shock", "psoriasis", "photosensitivity"; and update of the corresponding section of PL.
In addition, the Worksharing applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10."
Request for Supplementary Information adopted on 25.05.2018.

WS1348

Exviera-EMEA/H/C/003837/WS1348/0035
Viekirax-
EMEA/H/C/003839/WS1348/0042

AbbVie Deutschland GmbH & Co. KG, Lead

Rapporteur: Filip Josephson, “Submission of the final report from study (M14-227) listed as a category 3 study in the RMP. This is a Phase 3b study designed to evaluate the safety and efficacy of ombitasvir/paritaprevir/ritonavir and dasabuvir in HCV infected patients with Child-Pugh B decompensated cirrhosis.” Request for Supplementary Information adopted on 12.04.2018.	
WS1351 **Eviplera-EMEA/H/C/002312/WS1351/0090** **Stribild-EMEA/H/C/002574/WS1351/0091** **Truvada-EMEA/H/C/000594/WS1351/0146** **Viread-EMEA/H/C/000419/WS1351/0185** Gilead Sciences International Limited, Lead Rapporteur: Joseph Emmerich, “Update of section 4.4 of the SmPC for Viread, Truvada and Stribild and Section 4.5 of the SmPC for Viread, Truvada, Eviplera and Stribild in order to add the results from study Study GS-US-367-1657, listed as a a category 3 study in the RMP; this is a Phase 1 Multiple Dose Study to Evaluate the Pharmacokinetic Drug-Drug Interaction Potential between Sofosbuvir/Velpatasvir/GS-9857 Fixed-Dose Combination and HIV Antiretroviral in Healthy Subjects. The corresponding section 2 of the Package Leaflet for Viread, Truvada and Stribild has been updated. In addition, the Worksharing applicant (WSA) took the opportunity to make administrative updates to Section 4.1 and 4.5 of the Stribild SmPC and to implement some linguistic amendments (MLAs) to the translations of the product information annexes.” Opinion adopted on 19.07.2018. Request for Supplementary Information adopted on 17.05.2018.	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1380 **Ebymect-EMEA/H/C/004162/WS1380/0033** **Edistride-EMEA/H/C/004161/WS1380/0027** **Forxiga-EMEA/H/C/002322/WS1380/0046**	

Xigduo-EMEA/H/C/002672/WS1380/0045 AstraZeneca AB, Lead Rapporteur: Kristina Dunder, "Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to reflect the final study results from study D1690C00024 (DERIVE); A Multicentre, Double-Blind, Placebo-Controlled, Parallel Group, Randomized, Phase III Study to Evaluate the Glycaemic Efficacy and Renal Safety of Dapagliflozin in Patients with Type 2 Diabetes Mellitus and Moderate Renal Impairment (CKD 3A) Who Have Inadequate Glycaemic Control. In addition, the Worksharing applicant took the opportunity to implement minor editorial changes in Edistride, Ebymect and Xigduo SmPCs, as well as Ebymect Labelling. The Package Leaflets for Xigduo and Ebymect are updated accordingly."	
WS1392 **ProQuad-EMEA/H/C/000622/WS1392/0125** MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC in order to add the adverse reaction (ADR) meningitis with a frequency "not known" and to add a clarifying foot note for immunocompromised or immunocompetent individuals applicable to the ADR meningitis, herpes zoster and encephalitis. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to make some editorial changes in the product information and to update the list of local representatives in the package leaflet." Request for Supplementary Information adopted on 05.07.2018.	Request for supplementary information adopted with a specific timetable.
WS1400 **Exviera-EMEA/H/C/003837/WS1400/0039** **Viekirax-EMEA/H/C/003839/WS1400/0046** AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Filip Josephson, "Submission of the final report from study M14-224: An Open-Label Study to Evaluate the Safety, Efficacy and Pharmacokinetics of Ombitasvir/ABT-450/Ritonavir (Ombitasvir/ABT-450/r) and Dasabuvir Co-administered With or Without Sofosbuvir (SOF) and Ribavirin (RBV) in Direct-Acting Antiviral Agent (DAA) Treatment-Experienced Adults With Genotype 1 Chronic	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Hepatitis C Virus (HCV) Infection, listed as a category 3 study in the RMP." Opinion adopted on 19.07.2018.	
WS1401 **Genvoya-** **EMEA/H/C/004042/WS1401/0047** **Stribild-EMEA/H/C/002574/WS1401/0094** **Tybost-EMEA/H/C/002572/WS1401/0044** Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings, "Update of section 4.6 the SmPC for Tybost, Stribild and Genvoya based on pharmacokinetics data in pregnancy from IMPAACT study P1026s (ClinicalTrials.gov ID NCT00042289); this is an ongoing, nonrandomized, open-label, parallel-group, multi-centre phase 4 prospective study of antiretroviral (ARV) pharmacokinetics (PK) and safety in HIV-1 infected pregnant women that includes an arm for EVG/COBI. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 12.07.2018.	Request for supplementary information adopted with a specific timetable.

B.5.3. CHMP-PRAC assessed procedures

Dacogen - decitabine - **EMEA/H/C/002221/II/0033, Orphan** Janssen-Cilag International N.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of section sections 4.2, 4.8, 5.1 and 5.2 of the SmPC to reflect the results from paediatric study DACOGENAML2004 titled 'Phase 1-2 Safety and Efficacy Study of DACOGEN in sequential administration with Cytarabine in children with relapsed or refractory acute myeloid leukemia', provided as per the requirement of article 46. The RMP version 3.1 (in line with the revision 2 of the RMP template) has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.4 of the SmPC to align the safety warning related to sodium excipient with the Annex to the revised European Commission guideline on `Excipients in the labelling and package leaflet of medicinal products for human use'. The	

Package Leaflet is updated in accordance. Moreover, the contact details of the local representative in Slovenia have been updated in the Package Leaflet." Request for Supplementary Information adopted on 31.05.2018.	
Erivedge - vismodegib - EMEA/H/C/002602/II/0039/G Roche Registration GmbH, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "C.I.4 Update of SmPC section 4.4 in order to update the special warnings and precautions for use on the effects of post-natal development and 4.8. in order to include a new adverse event (precocious puberty) observed in children in post marketing. C.I.11.z To submit the final study report for observational study ML28296 (post approval commitment MEA 18) and reflect the newly available information in the RMP version 13.0. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some editorial changes in the product information." Opinion adopted on 12.07.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Herzuma - trastuzumab - EMEA/H/C/002575/II/0006 Celltrion Healthcare Hungary Kft., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski	
Invokana - canagliflozin - EMEA/H/C/002649/II/0034 Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "Update of sections 4.1, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information on cardiovascular events following final results from CANVAS Program (DIA3008 and DIA4003); the Package Leaflet is updated accordingly. Study DIA3008 is phase 3 Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of JNJ-28431754 on Cardiovascular Outcomes in Adult Subjects With Type 2 Diabetes Mellitus Study DIA4004 is phase 4 Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of Canagliflozin on Renal Endpoints in Adult Subjects With Type	

2 Diabetes Mellitus The RMP version 7.2 has also been submitted." Request for Supplementary Information adopted on 31.05.2018, 25.01.2018.	
Ocrevus - ocrelizumab - EMEA/H/C/004043/II/0002 Roche Registration GmbH, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Julie Williams, "Update of sections 4.4 and 4.5 of the SmPC in order to include information on vaccination based on interim results from study BN29739 listed as a category 3 study in the RMP; this is a phase IIIb, multicentre, randomised, parallel-group, open-label study to evaluate the effects of ocrelizumab on immune response in patients with relapsing forms of multiple sclerosis. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted." Request for Supplementary Information adopted on 12.07.2018, 17.05.2018.	Request for supplementary information adopted with a specific timetable.
Olumiant - baricitinib - EMEA/H/C/004085/II/0006 Eli Lilly Nederland B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Patrick Batty, "Update of section 4.8 of the SmPC in order to include pneumonia as adverse drug reaction with frequency 'common' following PRAC outcome on signal of pneumonia. The Package Leaflet is updated accordingly. The RMP version 6.0 has also been submitted as part of this application." Request for Supplementary Information adopted on 28.06.2018.	
Remicade - infliximab - EMEA/H/C/000240/II/0209 Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the current warning on colon cancer and dysplasia of Section 4.4 of the SmPC based on final report of the OPUS Registry (Prospective, Observational, Non-Interventional, Post-marketing Safety Surveillance Program in Subjects with UC; P04808) as per MEA 121. In addition, the MAH is taking the opportunity to add a warning on screening tests for tuberculosis to align it with current medical practice, add a reminder on the patient alert card in package leaflet and include some	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

editorial changes in line with the QRD template." Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 17.05.2018, 11.01.2018.	
Remicade - infliximab - EMEA/H/C/000240/II/0214 Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the RMP (v 17.0) and Annex II-D of the Product Information to remove the Educational material for health care professionals. In addition, the MAH is taking the opportunity to update the package leaflet with some missing warnings and ADRs already reflected in the SmPC, as requested by CHMP, and to introduce some minor QRD related changes."	
Stayveer - bosentan - EMEA/H/C/002644/II/0023 Marklas Nederlands BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Caroline Laborde, "Update of Annex II.D and the RMP (version 9.2) following the submission of the final (13th) study report of the DUO Registry (a Category 3 non-interventional post-approval safety study and additional risk minimisation measure in the bosentan European Risk Management Plan). The MAH took the opportunity to include some editorial changes in the SmPC and to update the list of local representatives in the PL." Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 14.06.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
TAGRISSO - osimertinib - EMEA/H/C/004124/II/0024 AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Sabine Straus, "Update of sections 4.2 and 5.2 of the SmPC based on the results from Study D5160C00008, undertaken to determine the pharmacokinetics, safety and tolerability of AZD9291 following a single oral dose to patients with advanced solid tumours and normal hepatic function or mild or moderate hepatic impairment. An updated RMP version 11 was agreed during the procedure." Opinion adopted on 19.07.2018. Request for Supplementary Information adopted on 14.06.2018, 17.05.2018.	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Tarceva - erlotinib - EMEA/H/C/000618/II/0058 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Update of sections 4.2, and 5.1 of the SmPC based on phase III clinical study MO22162 (CURRENTS) comparing a higher dose of Tarceva (300 mg) over the recommended daily dose (150 mg) in current smokers with locally advanced or metastatic non-small cell lung cancer (NSCLC) in the second-line setting after failure of chemotherapy. The Package Leaflet is updated accordingly. The RMP version 7.0 has been submitted, as part of this application. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in sections 4.4, 4.5, 4.6, 4.7, 4.8 and 5.2 of the SmPC."	
Tasigna - nilotinib - EMEA/H/C/000798/II/0095, Orphan Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Update of section 4.6 of the SmPC to include the recommendation that women should not breast-feed during Tasigna treatment and for 2 weeks after the last dose. The Package Leaflet has been updated accordingly. Further, the MAH took the opportunity to implement minor editorial changes, corrections and/or additions in the SmPC and Package Leaflet based on data already submitted and assessed previously, including the alignment of section 4 of the Package Leaflet with section 4.8 of the SmPC, the completeness of the list of excipients in SmPC section 6.1 and minor changes to SmPC sections 4.4 and 4.5. Furthermore, the MAH took the opportunity to update the contact details in the list of local representatives in the Package Leaflet." Opinion adopted on 19.07.2018. Request for Supplementary Information adopted on 14.06.2018.	Positive Opinion adopted by consensus on 19.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tracleer - bosentan - EMEA/H/C/000401/II/0086 Actelion Registration Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Caroline Laborde, "Update of Annex II.D and the RMP (version 9.2) following the submission of the final (13th) study report of the DUO Registry (a Category 3 non-interventional post-approval	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

safety study and additional risk minimisation measure in the bosentan European Risk Management Plan). The MAH took the opportunity to include some editorial changes in the SmPC and to update the list of local representatives in the PL." Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 14.06.2018.	
Tremfya - guselkumab - EMEA/H/C/004271/II/0002/G Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski "Update of sections 1, 2 , 3, 5.1, 6.4, 6.5, 6.6, of the SmPC with details of a new presentation, based on the results from study CNTO1959PSO3006; this is study is an open-label, randomized, study to assess the design features of an investigational prefilled syringe-facilitated injection device (PFS-FID) and the ability of subjects with rheumatoid arthritis or psoriasis to self-administer Placebo with the PFS-FID. The Package Leaflet and Labelling are updated accordingly. The RMP version 2.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet." Opinion adopted on 12.07.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Truberzi - eluxadoline - EMEA/H/C/004098/II/0005/G Allergan Pharmaceuticals International Ltd, Rapporteur: Harald Enzmann, PRAC Rapporteur: Adam Przybylkowski, "C.I.13: Submission of the final report from study ELX-PH-08 listed as a category 3 study. This is an in vitro evaluation study aimed to investigate the effects on treating primary cultures of cryopreserved human hepatocytes with eluxadoline on the expression of cytochrome P450 (CYP) enzymes C.I.13: Submission of the final report from study 3030-102-002 listed as a category 3 study. This is a randomised, open label study aimed to evaluate the effect of eluxadoline as a potential time dependent inhibitor of CYP3A4 with the substrate midazolam.	Request for supplementary information adopted with a specific timetable.

C.I.11.a: To update the RMP for Truberzi to version v2.0 to update the important identified risk from “SO spasm” to “SO spasm (Sphincter of Oddi dysfunction, SOD)” and to include pancreatitis as an important identified risks. This change has been agreed by the CHMP/PRAC in the outcome of EMEA/H/C/PSUSA/00010528/201703.” Request for Supplementary Information adopted on 12.07.2018, 17.05.2018, 08.03.2018.	
Varuby - rolapitant - EMEA/H/C/004196/II/0007/G Tesaro UK Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adam Przybylkowski, “- Update of SmPC section 4.5 regarding interaction with OCT1 substrates following the submission of the non-clinical study: in vitro evaluation of the substrate and inhibitor potential of rolapitant for efflux and update of transporters (17TESAP2R1). - Update of SmPC section 4.5 regarding interaction with UGT substrates following the submission of the 2 non-clinical studies: evaluation of potential UGT inhibition by rolapitant in cryopreserved human hepatocytes (170594) and evaluation of potential rolapitant metabolism by recombinantly expressed human UGT enzymes (TSRP/REP/07CRD75486/2017) - Update of SmPC section 4.5 following the submission of the open-label, single-d0se study to assess the effects of rolapitant (oral) on the pharmacokinetics of caffeine (CYP1A2) in healthy subjects (1000-01-001) The RMP version 1.2 has also been submitted.” Request for Supplementary Information adopted on 12.07.2018.	Request for supplementary information adopted with a specific timetable.
Vokanamet - canagliflozin / metformin - EMEA/H/C/002656/II/0034 Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Menno van der Elst, “Update of sections 4.1, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information on cardiovascular events following final results from CANVAS Program (DIA3008 and DIA4003); the Package Leaflet is updated accordingly. Study DIA3008 is phase 3 Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of JNJ-28431754	

on Cardiovascular Outcomes in Adult Subjects With Type 2 Diabetes Mellitus Study DIA4004 is phase 4 Randomized, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of Canagliflozin on Renal Endpoints in Adult Subjects With Type 2 Diabetes Mellitus The RMP version 7.2 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet andto bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 31.05.2018, 25.01.2018.	
WS1335 **Rixathon-** **EMEA/H/C/003903/WS1335/0010** **Riximyo-** **EMEA/H/C/004729/WS1335/0010** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus, Lead PRAC Rapporteur: Doris Stenver, "Submission of final study reports for studies GP13-302 (a randomized, double-blind, parallel-group safety study with the aim to specifically address a potential safety risk of a switch from treatment with originator rituximab (Mabthera/Rituxan) to treatment with GP2013) and GP13-201 (a 52-week multicenter, randomized, double-blind, parallel-arm, comparative study in patients with active Reumathoid Arthritis (RA) refractory or intolerant to standard DMARDs and one or up to three anti-TNFs therapies). The RMP (version 3.1) has been updated accordingly." Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 12.04.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1396 **Kisplyx-EMEA/H/C/004224/WS1396/0011** **Lenvima-** **EMEA/H/C/003727/WS1396/0015** Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren, Lead PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 4.5 of the SmPC to include that there is no significant drug-drug interaction risk with midazolam,	Request for supplementary information adopted with a specific timetable.

based on the results of study E7080-A001-109 (A Phase 1 Study to determine DDI of lenvatinib and midazolam, a cytochrome P450 3A4 (CYP3A4) substrate, in subjects with advanced solid tumors). The RMP is updated (version 10.4)"
Request for Supplementary Information adopted on 12.07.2018.

WS1406
Abseamed-
EMEA/H/C/000727/WS1406/0070
Binocrit-
EMEA/H/C/000725/WS1406/0070
Epoetin alfa Hexal-
EMEA/H/C/000726/WS1406/0069
Sandoz GmbH, Lead Rapporteur: Alexandre Moreau, Lead PRAC Rapporteur: Ghania Chamouni, "Extension of indication to include the treatment of symptomatic anaemia (haemoglobin concentration of ≤ 10 g/dl) in adults with low- or intermediate-1-risk primary myelodysplastic syndromes (MDS) who have low serum erythropoietin (< 200 mU/ml) for Binocrit, Epoetin alfa Hexal and Abseamed; as a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated with safety and efficacy information. The Package Leaflet and the risk management plan (version 17.0) are updated in accordance. In addition, the worksharing applicant (WSA) took the opportunity to align information with the reference medicinal product and with the EC guideline on Excipients, to improve the quality and readability of the translations in the product information and to update the Annex A in line with EMA guideline."

B.5.4. PRAC assessed procedures

PRAC Led
Bosulif - bosutinib -
EMEA/H/C/002373/II/0030
Pfizer Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "Submission of an updated RMP version 4.3 in line with changes requested by the CHMP following variation II/25/G in fulfilment of PAM (REC 014). In addition, the MAH took the opportunity to extend due date of SOB (Specific Obligation).

Annex II has been updated accordingly."	
PRAC Led **Inflectra - infliximab -** **EMEA/H/C/002778/II/0060** Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "To update the RMP for Inflectra to version 8.0 to introduce the new RMP template, update some milestones of the Pharmacovigilance plan and delete some safety concerns form the educational material to Health Care Profesionals." Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 17.05.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Lucentis - ranibizumab -** **EMEA/H/C/000715/II/0070/G** Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "1. Type II- C.I.13: Submission of the final report from study LUMINOUS study (CRFB002A2406), an observational, multicenter study to assess the long term safety and effectiveness of ranibizumab in routine clinical practice, in fulfilment of the post-authorisation measures MEA 036, MEA 048 and MEA 054. Consequentially, the RMP has been updated to reflect these changes. 2. Type II-C.I.11: Submission of an updated RMP version 17.0 (RMP template Rev. 2) according to GVP Module V to include changes not consequential to LUMINOUS study. In addition, the MAH is proposing the removal of the use of educational materials and targeted follow-up checklists listed in Annex II-D of the Product Information." Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 14.06.2018, 12.04.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **MabThera - rituximab -** **EMEA/H/C/000165/II/0144** Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Update the RMP to remove the additional risk minimization	Request for supplementary information adopted with a specific timetable.

measure of Educational Outreaches for the important identified risk of Infusion Related Reactions and Acute Infusion Related Reactions (IRR). Therefore, the RMP has been updated accordingly to version 16.0." Request for Supplementary Information adopted on 12.07.2018, 12.04.2018.	
PRAC Led **Neulasta - pegfilgrastim - EMEA/H/C/000420/II/0099** Amgen Europe B.V., Rapporteur: Robert James Hemmings, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Robert James Hemmings, "Submission of an updated RMP version 5.1 in order to add study 20160176, a retrospective cohort study of female breast cancer patients aged 66 years and over selected from the US SEER-Medicare database to estimate the risk of acute myeloid leukemia/myelodysplastic syndrome for breast cancer patients, as a new Pharmacovigilance activity (category 3). In addition the MAH submitted the draft protocol for study 20160176." Request for Supplementary Information adopted on 12.07.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0078** Pfizer Limited, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "To update the RMP (version 8.1). The update includes changes approved in procedure II-49 and II-73. The RMP is also being revised to align with current EU RMP template, as per GVP Module V Rev. 2 including proposals for the removal of some Important Potential Risks: Guillain-Barré syndrome, Purpura, Vasculitis, Acute disseminated encephalomyelitis, Brachial neuritis, Anaphylaxis, Administration via the intravascular, intradermal or subcutaneous route, and Administration to patients with thrombocytopenia or any coagulation disorder with a risk of haemorrhage. The MAH also proposes removal of the missing information: Use in patients with chronic diseases and Use during lactation" Opinion adopted on 12.07.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led	Positive Opinion adopted by consensus on

Remsima - infliximab - EMEA/H/C/002576/II/0051 Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "To update the RMP for Remsima to version 8.0 to introduce the new RMP template, update some milestones of the Pharmacovigilance plan and delete some safety concerns form the educational material to HCP." Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 17.05.2018.	12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **TAGRISSO - osimertinib - EMEA/H/C/004124/II/0023** AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Sabine Straus, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 9 in order to remove the category 3 PASS Study D5160C00022 (ASTRIS) from the Pharmacovigilance plan." Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 14.06.2018, 17.05.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Tasigna - nilotinib - EMEA/H/C/000798/II/0092, Orphan** Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of an updated RMP version 21.1 in order to delete the important identified risk 'Myelosuppression', to implement changes in the definition of the identified risks 'Hepatotoxicity' and 'Fluid retention', and to reflect the discontinuation of the educational material as additional risk minimisation measure. Annex II has been updated accordingly." Opinion adopted on 12.07.2018. Request for Supplementary Information adopted on 12.04.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Volibris - ambrisentan - EMEA/H/C/000839/II/0055** Glaxo Group Ltd, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Dolores Montero Corominas, PRAC-CHMP liaison: Concepcion	Request for supplementary information adopted with a specific timetable.

Prieto Yerro, “C.I.11: Submission of an updated RMP (version 7.6) in order to remove the provision of the educational materials for healthcare professionals given the availability of the SmPC and the experience of using ambrisentan as requested by the PRAC in the PSUR procedure PSUSA/00000129/201706. The Annex II of the product information is updated accordingly. In addition, the MAH also took the opportunity to update the Annex II as requested by the Portuguese Agency following the approval of the last update to the educational materials (risks of decreases in haemoglobin or haematocrit, renal impairment, peripheral oedema and fluid retention, and hypersensitivity reaction) and to correct typographical errors in the Annex II of the product information.” Request for Supplementary Information adopted on 12.07.2018.	
PRAC Led **Zavesca - miglustat - EMEA/H/C/000435/II/0062/G, Orphan** Actelion Registration Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, “C.I.13: Submission of the final report of the 9th NPC registry report including an RMP update within the context of variation EMEA/H/C/000435/II/0056 C.I.11: Submission of an updated RMP version 14 in order to remove the important identified risks: reduced platelet counts and weight loss based on the current ongoing PSUR procedure for miglustat (EMEA/H/C/PSUSA/00002062/201710)” Opinion adopted on 12.07.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Led **WS1370** **Zoledronic acid Mylan-** **EMEA/H/C/002482/WS1370/0015** Mylan S.A.S, Generic, Generic of Zometa, Lead PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, “The RMP has been updated to the latest template. In addition the MAH has included “and other anatomical sites” in addition to “Osteonecrosis of the jaw” as an important identified risk, to be in line with CHMP assessment report for zoledronic acid, procedure number EMEA/H/C/PSUSA/00003149/201608, dated 21 April 2017.” Request for Supplementary Information adopted on 10.07.2018.	Request for supplementary information adopted with a specific timetable.
Tamiflu - oseltamivir - **EMEA/H/C/000402/II/0133** Roche Registration GmbH, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, “Update of the RMP (v.16) to discontinue the guided questionnaires (GQ) for neurological and psychiatric adverse events (NPAE), hepatobiliary disorders and hypothermia.” Opinion adopted on 12.07.2018.	Positive Opinion adopted by consensus on 12.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.5. CHMP-CAT assessed procedures

Zalmoxis - allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - **EMEA/H/C/002801/II/0009/G, Orphan, ATMP** MolMed S.p.A, Rapporteur: Johannes Hendrikus Ovelgonne, CHMP Coordinator: Paula Boudewina van Hennik Request for Supplementary Information adopted on 20.04.2018.	

B.5.6. CHMP-PRAC-CAT assessed procedures

B.5.7. PRAC assessed ATMP procedures

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

WS1353/G **Hexacima-** **EMEA/H/C/002702/WS1353/0079/G** **Hexaxim-** **EMEA/H/W/002495/WS1353/0084/G** **Hexyon-** **EMEA/H/C/002796/WS1353/0083/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Furthermore, the MAH took the opportunity to introduce editorial changes in module 3.2.S.2.3." Request for Supplementary Information adopted on 19.07.2018, 17.05.2018.	Request for supplementary information adopted with a specific timetable.
WS1365/G **Ambirix-** **EMEA/H/C/000426/WS1365/0091/G** **Fendrix-** **EMEA/H/C/000550/WS1365/0063/G** **Infanrix hexa-** **EMEA/H/C/000296/WS1365/0240/G** **Twinrix Adult-** **EMEA/H/C/000112/WS1365/0125/G** **Twinrix Paediatric-** **EMEA/H/C/000129/WS1365/0126/G** GlaxoSmithKline Biologicals, Lead Rapporteur: Bart Van der Schueren This WS procedure includes the NAPs/MRP products listed in Annex B." Opinion adopted on 05.07.2018.	Positive Opinion adopted by consensus on 05.07.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1377/G **Infanrix hexa-** **EMEA/H/C/000296/WS1377/0241/G** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren	
WS1385 **Izba-EMEA/H/C/002738/WS1385/0009** **Travatan-** **EMEA/H/C/000390/WS1385/0058** Novartis Europharm Limited, Lead Rapporteur: Concepcion Prieto Yerro, "To provide an updated Environmental Risk Assessment (ERA) dossier for travoprost-containing products Travatan and Izba, pursuant to the post-authorisation recommendation provided by the Agency in the framework of the following procedures: · Travatan extension of indication -	

Procedure No. EMEA/H/C/000390/II/0046
· Izba initial MAA - Procedure No. EMEA/H/C/002738/0000
Based on the updated ERA results, the MAH also proposes to update sections 5.3 Preclinical safety data in both Izba and Travatan SmPC as well as section 6.6 Special precautions for disposal in Travatan SmPC."
Request for Supplementary Information adopted on 07.06.2018.

WS1387
Infanrix hexa-
EMEA/H/C/000296/WS1387/0242
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1405
Fiasp-EMEA/H/C/004046/WS1405/0006
NovoMix-
EMEA/H/C/000308/WS1405/0094
NovoRapid-
EMEA/H/C/000258/WS1405/0122
Ryzodeg-
EMEA/H/C/002499/WS1405/0027
Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder

WS1408
Enbrel-EMEA/H/C/000262/WS1408/0221
LIFMIOR-
EMEA/H/C/004167/WS1408/0016
Pfizer Limited, Lead Rapporteur: Robert James Hemmings

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

sodium oxybate - EMEA/H/C/004962
, medium to long-term maintenance of alcohol abstinence and treatment of mild to moderate alcohol withdrawal syndrome

dapagliflozin / saxagliptin / metformin

hydrochloride - EMEA/H/C/004910

, - to improve glycaemic control when metformin with or without sulphonylurea (SU) does not provide adequate glycaemic control and where simultaneous addition of dapagliflozin and saxagliptin is considered necessary - to improve glycaemic control when metformin with or without sulphonylurea (SU) and either dapagliflozin or saxagliptin does not provide adequate glycaemic control - when already being treated with dapagliflozin and saxagliptin and metformin.

deferasirox - EMEA/H/C/005014

, treatment of chronic iron overload, Generic, Generic of EXJADE

ravulizumab - EMEA/H/C/004954, Orphan

Alexion Europe SAS, treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH).

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

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

efmoroctocog alfa - EMEA/H/C/003964/X/0021

Rapporteur: Jan Mueller-Berghaus, “Extension application to introduce new strength of 4000 IU, 5000 IU and 6000 IU primarily enabling phophylactic dosing in adult patients.”
List of Questions adopted on 31.05.2018.

romosozumab - EMEA/H/C/004465

, Treatment of osteoporosis
List of Questions adopted on 26.04.2018.

trastuzumab - EMEA/H/C/004916

, treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)
List of Questions adopted on 22.03.2018.

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

clofarabine - EMEA/H/C/000613/S/0059

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

Granupas - para-aminosalicylic acid -
EMEA/H/C/002709/R/0026, Orphan
Eurocept International B.V., Rapporteur: Greg Markey, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Patrick Batty

Jardiance - empagliflozin -
EMEA/H/C/002677/R/0040
Boehringer Ingelheim International GmbH, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Dolores Montero Corominas

Mepact - mifamurtide -
EMEA/H/C/000802/R/0047, Orphan
Takeda France SAS, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Sabine Straus

Pregabalin Pfizer - pregabalin -
EMEA/H/C/003880/R/0025
Pfizer Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Sabine Straus

Vokanamet - canagliflozin / metformin -
EMEA/H/C/002656/R/0039
Janssen-Cilag International NV, Rapporteur: Martina Weise, Co-Rapporteur: Svein Rune Andersen, 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

Keytruda - pembrolizumab -
EMEA/H/C/003820/II/0057
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus, "Extension of Indication to include 1st line treatment of locally advanced or metastatic non-small cell lung cancer tumours expressing PD-L1 with a ≥ 1% tumour proportion score (TPS), based on data from study KEYNOTE-042; an international, randomized, open-label Phase 3 study investigating KEYTRUDA monotherapy compared to standard of care platinum-based chemotherapy in patients with locally advanced

or metastatic PD-L1 positive (TPS ≥ 1%) NSCLC, and on supportive data from the final planned analysis of KEYNOTE-024; a Phase 3 randomized open-label study of KEYTRUDA monotherapy compared to platinum-based chemotherapy in metastatic NSCLC with PD-L1 TPS ≥50%. As a result, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC have been updated. An updated RMP version 18.1 was provided as part of the application."

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Alprolix - eftrenonacog alfa - EMEA/H/C/004142/II/0020, Orphan
Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop

Bortezomib Accord - bortezomib - EMEA/H/C/003984/II/0014
Accord Healthcare Limited, Generic, Generic of VELCADE, Rapporteur: Milena Stain

Bortezomib Hospira - bortezomib - EMEA/H/C/004207/II/0008
Hospira UK Limited, Generic, Generic of VELCADE, Rapporteur: Milena Stain

Dupixent - dupilumab - EMEA/H/C/004390/II/0009/G
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus

Fabrazyme - agalsidase beta - EMEA/H/C/000370/II/0106
Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege

Kentera - oxybutynin - EMEA/H/C/000532/II/0047
Nicobrand Limited, Rapporteur: Bart Van der Schueren

Kyntheum - brodalumab - EMEA/H/C/003959/II/0004/G
LEO Pharma A/S, Rapporteur: Johann Lodewijk Hillege

Lemtrada - alemtuzumab - EMEA/H/C/003718/II/0025/G
Genzyme Therapeutics Ltd, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth

Lonquex - lipegfilgrastim -
EMEA/H/C/002556/II/0041/G
Sicor Biotech UAB, Rapporteur: Greg Markey

MULTAQ - dronedarone -
EMEA/H/C/001043/II/0041
sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege

Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine -
EMEA/H/C/002226/II/0082
Pfizer Limited, Rapporteur: Greg Markey

NovoSeven - eptacog alfa (activated) -
EMEA/H/C/000074/II/0106
Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik

Ocrevus - ocrelizumab -
EMEA/H/C/004043/II/0004
Roche Registration GmbH, Rapporteur: Mark Ainsworth

Privigen - human normal immunoglobulin -
EMEA/H/C/000831/II/0136/G
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

Reagila - cariprazine -
EMEA/H/C/002770/II/0008
Gedeon Richter Plc., Rapporteur: Kristina Dunder

Shingrix - herpes zoster vaccine (recombinant, adjuvanted) -
EMEA/H/C/004336/II/0007
GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren

Somavert - pegvisomant -
EMEA/H/C/000409/II/0086/G
Pfizer Limited, Rapporteur: Joseph Emmerich

Tamiflu - oseltamivir -
EMEA/H/C/000402/II/0135
Roche Registration GmbH, Rapporteur: Outi Mäki-Ikola

WS1452
Rixathon-
EMEA/H/C/003903/WS1452/0013
Riximyo-
EMEA/H/C/004729/WS1452/0013
Sandoz GmbH, Lead Rapporteur: Jan Mueller-

Berghaus

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

Alecensa - alectinib - EMEA/H/C/004164/II/0016

Roche Registration GmbH, Rapporteur: Filip Josephson, "Submission of the final study analysis on secondary ALK-mutation positive/negative samples and correlation with clinical outcome in fulfilment of a CHMP recommendation for alectinib, adopted during the initial Marketing Authorization. The application is based on an additional analysis generated from two studies (NP28673 and NP28761)."

Atripla - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/000797/II/0130

Bristol-Myers Squibb and Gilead Sciences Ltd., Rapporteur: Martina Weise, "Update of sections 4.3 and 4.5 of the SmPC in order to include drug-drug interaction data between efavirenz (EFV) and grazoprevir/elbasvir based on a review of the antiviral product Zepatier.

The Marketing authorisation holder (MAH) has taken the opportunity to introduce changes to the sodium wording in Section 4.4 of the SmPC and to align the text in Section 4.6 (Fertility, pregnancy and lactation) for Atripla with the currently approved wording in the Eviplera SmPC.

The Package Leaflet (PIL) has been updated accordingly.

In addition, the MAH has also taken the opportunity to implement some minor linguistic amendments (MLAs) to the translations of the product information annexes for the following languages: DE, FI, FR, IT, NL and NO."

Baraclude - entecavir - EMEA/H/C/000623/II/0059

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to include information regarding the newly detected resistance information showing reduced susceptibility to entecavir for

the rtA 181C substitution in combination with LVDr substitutions, rtL 180M + rtM204V. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10. The MAH also took the opportunity to add the sodium concentration for Baraclude 0.05 mg/ml oral solution in section 2 of the SmPC and section 2 of the PL according to the guideline on 'excipients in the labelling and package leaflet of medicinal products for human use'."

Brilique - ticagrelor - EMEA/H/C/001241/II/0041

AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2 and 4.4 of the SmPC in order to clarify the posology in patients having an acute coronary syndromes (ACS) event, to update the warning related to bradyarrhythmia based on already assessed studies and post-marketed use (clinical trials PLATO (D5130C05262), PEGASUS (D5132C00001), SOCRATES (D5134C00001) and EUCLID (D5135C00001)) and to introduce "stroke" as a possible even in case of premature discontinuation.
Furthermore the MAH took the opportunity to update the PI in relation to sodium content in line with QRD and to update the list of local representatives in the Package Leaflet."

Coagadex - human coagulation factor X - EMEA/H/C/003855/II/0009, Orphan

Bio Products Laboratory Limited, Rapporteur: Andrea Laslop, "Update of section section 5.2 of the SmPC in order to include data on long-term use based on final results from the study Ten05, a multicentre, retrospective data collection study on the use of BPL's high purity factor X in the treatment of patients with hereditary factor X deficiency on a compassionate use basis. In addition the Marketing authorisation holder (MAH) took the opportunity to update the number of patients treated with Coagadex in section 4.8 of the SmPC based on studies Ten01, Ten02 and Ten03 as well as to include some editorial changes in section 4.2 of the SmPC. Furthermore, the information on perioperative management in the Package Leaflet has been aligned with information in the

SmPC."

ILARIS - canakinumab -
EMEA/H/C/001109/II/0060
Novartis Europharm Limited, Rapporteur: Jan Mueller-Berghaus, "Update of section 5.1 of the SmPC based on the final clinical study report (CSR) from Study ACZ885G2306 (β-SPECIFIC 4 Patients: Study of Paediatric efficacy and safety with first-line use of canakinumab: An open-label canakinumab (ACZ885) dose reduction or dose interval prolongation efficacy and safety study in patients with Systemic Juvenile Idiopathic Arthritis (SJIA)). The submission of the final CSR addresses the post-authorisation measure MEA 036.3 (PAES) and the requirements of article 46 of the paediatric regulation."

Isentress - raltegravir -
EMEA/H/C/000860/II/0078/G
Merck Sharp & Dohme B.V., Rapporteur: Greg Markey, "Submission of the final reports from 3 in vitro studies evaluating the inhibitory effect of raltegravir at higher concentrations on OATP1B3, OCT1, OCT2, MATE1 and MATE2-K transporters and CYP2B6, CYP2D6, UGT2B7 enzyme activities, and a final CSR to assess the drug-drug interaction (DDI) potential of raltegravir at a 1,200 mg once daily clinical dose, according to the request from the CHMP following the assessment of X/59."

Keytruda - pembrolizumab -
EMEA/H/C/003820/II/0054
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Update of section 5.1 of the SmPC based on the final clinical study report (CSR) for KEYNOTE-045 (KN045); a phase III randomized clinical trial of pembrolizumab (MK-3475) versus paclitaxel, docetaxel or vinflunine in subjects with recurrent or progressive metastatic urothelial cancer. The submission addresses the post-authorisation measure 'ANX 020' and Annex IID has been updated accordingly."

Kyprolis - carfilzomib -
EMEA/H/C/003790/II/0030, Orphan
Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of section 4.4 of the SmPC in order to include a warning of the increased risk of cardiac failure in Asian patients

treated with carfilzomib based on postmarketing experience and 3 phase 3, randomized-controlled studies (CLARION-Study 2011-003; ENDEAVOR-Study 20130398 and A.R.R.O.W.-Study 20140355). In addition, the Marketing authorisation holder (MAH) took the opportunity to propose few minor typographical changes to SmPC."

Latuda - lurasidone - EMEA/H/C/002713/II/0021

Aziende Chimiche Riunite Angelini Francesco S.p.A., Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC to add new paediatric data available in children and adolescent patients (10-17 years of age) with bipolar I disorder, upon request by CHMP following the assessment of the paediatric study D1050326 submitted according to Art. 46 procedure (no. EMEA/H/C/002713/P46/008)."

LUTATHERA - lutetium (177Lu) oxodotreotide - EMEA/H/C/004123/II/0005, Orphan

Advanced Accelerator Applications, Rapporteur: Robert James Hemmings, "Update of the SmPC section 5.1 to include information on the quality of life based on analysis of Netter-I Quality of Life data."

Mircera - methoxy polyethylene glycol-epoetin beta - EMEA/H/C/000739/II/0067

Roche Registration GmbH, Rapporteur: Concepcion Prieto Yerro, "Update of sections 4.2., 5.1. and 5.2. of the SmPC in order to update the paediatric information based on results from phase II dose finding study NH 19707 (Dolphin): An Open-Label, Multi-Center, Multiple Dose Study to Determine the Optimum Starting Dose of Intravenous MIRCERA for Maintenance Treatment of Anemia in Pediatric Patients with Chronic Kidney Disease on Hemodialysis; listed as a category 3 study in the RMP. The Package Leaflet is updated accordingly."

Otezla - apremilast - EMEA/H/C/003746/II/0021

Celgene Europe Limited, Rapporteur: Peter Kiely, "Update of sections 4.2 and 5.1 of Otezla SmPC to include data (up to 5 years of treatment) from the following studies (CC-10004-PSA-002, -003, -004, -005 and CC-

10004-PSOR-008, - 009)) listed as a category 3 study in the RMP (MEA 002)."

Praluent - alirocumab - EMEA/H/C/003882/II/0041
sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Submission of the final clinical study report of study R727-CL-1119 (study title: A Randomized, Double-Blind, Double-Dummy, Active-Controlled Study to Evaluate the Efficacy and Safety of REGN727/SAR236553 in Patients with Primary Hypercholesterolemia Who Are Intolerant to Statins), as per MEA011."

Skilarence - dimethyl fumarate - EMEA/H/C/002157/II/0008/G
Almirall S.A, Rapporteur: Robert James Hemmings, "Submission of the final report from study AML/27. This is an in vitro study aimed to assess the potential of dimethyl fumarate to inhibit human hepatic cytochrome P450 (CYP) enzymes.

Submission of the final report from study AML/28. This is an in vitro study aimed to assess the potential interaction of dimethyl fumarate with p-glycoprotein (P-gp).

Submission of the final report from study Almirall-15-05May2017. This is an in vitro study aimed to assess the interaction of dimethyl fumarate with human BCRP efflux (ABC) transporters."

Translarna - ataluren - EMEA/H/C/002720/II/0045, Orphan
PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 4.5 of the SmPC in order to include information on Drug-Drug Interaction with sensitive probe substrate of organic anion transporting polypeptide 1B3 (OATP1B3) based on study PTC124-GD-042-HV (MEA016). The package leaflet is updated accordingly."

Translarna - ataluren - EMEA/H/C/002720/II/0046, Orphan
PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update information on patients with moderate to severe renal impairment based on results from study PTC124-GD-032-HV (MEA010). In

addition the MAH took the opportunity to amend section 5.2 to propose correction of the biotransformation statement. The Package leaflet is updated accordingly."

VELCADE - bortezomib - EMEA/H/C/000539/II/0090

Janssen-Cilag International NV, Rapporteur: Daniela Melchiorri, "Update of section 5.1 of the SmPC to update the information based on final long-term follow-up and overall survival data for LYM-3002, a Randomized, Open-label, Multicenter Phase 3 Study of the Combination of Rituximab, Cyclophosphamide, Doxorubicin, VELCADE, and Prednisone (VcR-CAP) or Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (R-CHOP) in Patients With Newly Diagnosed Mantle Cell Lymphoma who are not Eligible for a Bone Marrow Transplant.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of Local representatives in the Package Leaflet."

Venclyxto - venetoclax - EMEA/H/C/004106/II/0016, Orphan

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Submission of the report from study M13-982 listed as a category 3 study in the RMP. This is a Phase 2 Open-Label Study of the Efficacy of ABT199 (GDC-0199) in Subjects with Relapsed/Refractory or Previously Untreated Chronic Lymphocytic Leukemia Harboring the 17p Deletion."

Xadago - safinamide - EMEA/H/C/002396/II/0027

Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 4.5 of the SmPC in order to implement information regarding interaction of safinamide and rosuvastatin, following results from study CRO-PK-17-318. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Ireland in the Package Leaflet and to include editorial changes in the English, German and Spanish product information."

XALKORI - crizotinib - EMEA/H/C/002489/II/0055

Pfizer Limited, Rapporteur: Alexandre Moreau, "Update of section 4.2 of the SmPC in order to provide greater clarity in the crizotinib dosing regimen modification recommendations for patients who receive a reduced dose of crizotinib, either because of pre-existing moderate or severe hepatic impairment or severe renal impairment or because of a previous dose reduction while on treatment with crizotinib. The Package Leaflet has been updated accordingly."

XALKORI - crizotinib - EMEA/H/C/002489/II/0057

Pfizer Limited, Rapporteur: Alexandre Moreau, "Submission of a number of analysis pertaining to the mechanisms of tumor resistance to crizotinib due to secondary ROS1 kinase domain mutations in patients with ROS1-positive non-small cell lung cancer (NSCLC)."

XALKORI - crizotinib - EMEA/H/C/002489/II/0058

Pfizer Limited, Rapporteur: Alexandre Moreau, "Submission of the final study report for study A8081038, a multinational active safety surveillance study of crizotinib in Europe and the United States."

Xultophy - insulin degludec / liraglutide - EMEA/H/C/002647/II/0026

Novo Nordisk A/S, Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC in order to reflect data for use of Xulthopy in combination with sodium glucose co-transporter 2 inhibitors (SGLT2i) in patients inadequately controlled on SGLT2i ±other oral anti-diabetic drug.

The update is based on data from the clinical trial: NN9068-4229: "A Clinical Trial Comparing Glycaemic Control and Safety of Insulin Degludec/Liraglutide (IDegLira) versus Insulin Glargine (IGlar) as Add-on Therapy to SGLT2i in Subjects with Type 2 Diabetes Mellitus"."

Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0038

Pfizer Ireland Pharmaceuticals, Rapporteur: Greg Markey, "Update of section 4.2 of the SmPC to amend the recommended duration of ceftaroline fosamil intravenous (IV) infusion for standard dose regimens in adults and paediatrics to a range of 5 to 60 minutes from

the currently recommended infusion duration of 1 hour. The PIL is updated accordingly. In addition the MAH has also taken the opportunity to reformat section 4.2 of the SmPC Posology and method of administration and to incorporate minor editorial updates to sections 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC."	
Zostavax - shingles (herpes zoster) vaccine (live) - EMEA/H/C/000674/II/0117 MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, "Update of sections 4.5 and 5.1 of the SmPC to include that Zostavax can be given concomitantly with pneumococcal vaccine and to reflect the results of an observational post-marketing study comparing the effectiveness of Zostavax when co-administrated with a 23-valent pneumococcal polysaccharide vaccine (Bruxvoort K et al. 2018). The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet."	
WS1411/G **Aluvia-** **EMEA/H/W/000764/WS1411/0105/G** **Kaletra-** **EMEA/H/C/000368/WS1411/0171/G** **Norvir-** **EMEA/H/C/000127/WS1411/0150/G** AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Joseph Emmerich, "Update of section 4.5 of the SmPC in order to update the safety information on the interaction with ibrutinib based on the company core data sheets. The Package Leaflet is updated accordingly. Update of section 4.5 of the SmPC in order to update the safety information of ritonavir, lopinavir/ritonavir on the interaction with levothyroxine based on the PRAC signal final assessment report EMA/101535/2018 possibly leading to decreased levothyroxine efficacy and hypothyroidis."	
WS1417/G **Invega-** **EMEA/H/C/000746/WS1417/0060/G** **Trevicta-** **EMEA/H/C/004066/WS1417/0013/G** **Xeplion-**	

EMEA/H/C/002105/WS1417/0039/G
Janssen-Cilag International NV, Lead Rapporteur: Kristina Dunder, “Update of sections 4.4 and 4.5 of the SmPC in order to add information regarding concomitant use with psychostimulants (in line with the CMDh recommendations for risperidone) and of section 4.8 of the SmPC to add catatonia as a new side-effect categorised as `Rare'. The Package Leaflet is updated accordingly.”

WS1422
CONTROLOC Control-
EMEA/H/C/001097/WS1422/0030
PANTOLOC Control-
EMEA/H/C/001100/WS1422/0034
PANTOZOL Control-
EMEA/H/C/001013/WS1422/0032
SOMAC Control-
EMEA/H/C/001098/WS1422/0031
Takeda GmbH, Lead Rapporteur: Greg Markey, “Update of section 5.3 of the SmPC in order to update the safety information based on the final results of study 14GR325 “A pre- and postnatal developmental toxicity study of pantoprazole sodium (PF-05208751) by oral gavage in rats focused on postnatal evaluation of bone development” as required by the PRAC Recommendation of EMEA/H/C/PSUSA/00002285/201708.”

WS1429
Descovy-
EMEA/H/C/004094/WS1429/0032
Genvoya-
EMEA/H/C/004042/WS1429/0048
Odefsey-
EMEA/H/C/004156/WS1429/0033
Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings, “Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC with data in patients on chronic haemodialysis from the Study GS-US-292-1825; this is a Phase 3b Open-Label Study toEvaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of E/C/F/TAF Fixed Dose Combination (FDC) in HIV-1 Infected Subjects on Chronic Hemodialysis.
The Package Leaflet is updated accordingly.
In addition, the Worksharing applicant (WSA) took the opportunity to introduce changes to the lactose wording for Genvoya and Odefsey

and an administrative correction to the Genvoya Patient information leaflet (PIL) in order to add “lurasidone” to the second list of contra-indicated drugs appearing in the PIL.

The WSA has also taken the opportunity to introduce some minor administrative amendments throughout the product information for all three products as well as to implement some minor linguistic amendments (MLAs) to the translations of the respective product information annexes:
- Genvoya: DE, ES, FI, HR, HU, IS, IT, NO, SL and SV languages
- Descovy: DA, DE, ES, FR, HR, NL, NO, PT and SL languages
- Odefsey: CS, DE, LV, MT, NL, PL, SL and SV languages.”

WS1433
Clopidogrel Zentiva-
EMEA/H/C/000975/WS1433/0061
Clopidogrel/Acetylsalicylic acid Zentiva-
EMEA/H/C/001144/WS1433/0051
DuoPlavin-
EMEA/H/C/001143/WS1433/0050
Iscover-
EMEA/H/C/000175/WS1433/0133
Plavix-EMEA/H/C/000174/WS1433/0130
Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, “In response to PRAC recommendation for the signal of insulin autoimmune syndrome (EPITT ref 19155), update of section 4.8 of the SmPC to the new adverse reaction ‘insulin autoimmune syndrome’. The Package Leaflet are updated accordingly.”

WS1444
Kisplyx-EMEA/H/C/004224/WS1444/0012
Lenvima-
EMEA/H/C/003727/WS1444/0016
Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren, “Update of Sections 4.4 and 4.8 of the SmPC to add pneumothorax and nephrotic syndrome. The PIL is updated accordingly.”

WS1449
Relvar Ellipta-
EMEA/H/C/002673/WS1449/0038
Revinty Ellipta-
EMEA/H/C/002745/WS1449/0035

Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, “Update of section 4.8 of the SmPC in order to add hyperglycaemia as an adverse reaction based on a cumulative review of hyperglycaemia/new onset diabetes associated with fluticasone/vilanterol (FF/VI); the Package Leaflet is updated accordingly.
In addition, the Worksharing applicant (WSA) took the opportunity to update the Package Leaflet with a clarification on the adverse event “blurred vision” already included in the SmPC (WS-1224).”

WS1459
Clopidogrel Zentiva-
EMEA/H/C/000975/WS1459/0062
Clopidogrel/Acetylsalicylic acid Zentiva-
EMEA/H/C/001144/WS1459/0052
DuoPlavin-
EMEA/H/C/001143/WS1459/0051
Iscover-
EMEA/H/C/000175/WS1459/0134
Plavix-EMEA/H/C/000174/WS1459/0131
Sanofi Clir SNC, Lead Rapporteur: Bruno Sepodes, “Update of section 5.1 of the SmPC in order to reflect the clinical outcome data of 2 randomised investigator-sponsored studies regarding de-escalation of P2Y12 receptor inhibitor to clopidogrel in ACS.”

B.6.10. CHMP-PRAC assessed procedures

Brilique - ticagrelor -
EMEA/H/C/001241/II/0042
AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, “Update of sections 4.2, 4.9 and 5.2 of the SmPC in order to update the safety information in relation to renal impairment based on the final results from study D5130L00067; this is a single dose, randomized, open label, parallel group study conducted to compare the pharmacokinetics (PK), pharmacodynamics (PD), safety and tolerability of ticagrelor in haemodialysis patients to subjects with normal renal function. The RMP version 11 has also been submitted.”

CYLTEZO - adalimumab -
EMEA/H/C/004319/II/0004
Boehringer Ingelheim International GmbH,

Rapporteur: Milena Stain, PRAC Rapporteur: Ulla Wändel Liminga, "Submission of the final report from study 1297.3 listed as a category 3 study in the RMP. This is an interventional trial to generate long-term safety, efficacy, and immunogenicity data for the administration of the proposed biosimilar Cyltezo in patients with moderate to severe rheumatoid arthritis."

Kisqali - ribociclib - EMEA/H/C/004213/II/0003/G

Novartis Europharm Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver, "C.I.4: Update of section 5.2 of the SmPC in order to reflect on results from study CLEE011A2109: A Phase I, open label, multi-centre, parallel cohort, single dose study to evaluate the pharmacokinetics of LEE011 in healthy subjects with normal hepatic function and subjects with impaired hepatic function; C.I.4: Update of section 4.2 and 5.2 of the SmPC in order to reflect on results from study CLEE011A2116-Part I: A phase I, open label, multicentre, parallel-group, single dose two-staged study to evaluate the pharmacokinetics and safety of a single 400 mg oral dose of LEE011 in subjects with varying degrees of impaired renal function compared to matched healthy volunteers with normal renal function. The RMP version 2.0 has also been submitted."

NovoMix - insulin aspart - EMEA/H/C/000308/II/0095

Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.2, 4.5 and 5.1 of the SmPC to include data on the use of NovoMix® 30 combination use with GLP-1 receptor agonists. The PIL is updated accordingly. The RMP is laso updated (version 3)"

OFEV - nintedanib - EMEA/H/C/003821/II/0021, Orphan

Boehringer Ingelheim International GmbH, Rapporteur: Jayne Crowe, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of section 4.8 of the SmPC in order to include 'myocardial infarction' as a new adverse drug reaction with a frequency 'uncommon' in order to fulfil LEG 004.1, following the assessment of PSUSA/00010319/201704. The Package Leaflet is updated accordingly. The RMP version 6.0 (in

revision 2 of the template) has also been submitted."

Onivyde - irinotecan hydrochloride trihydrate - EMEA/H/C/004125/II/0008, Orphan

Baxalta Innovations GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: David Olsen, "Update of sections 1, 2, 4.2, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC in order to reflect the expression of strength based on irinotecan anhydrous free-base. The Labelling and Package Leaflet are updated accordingly. In addition the MAH took the opportunity to introduce minor editorial changes. The updated RMP version 2.1 has also been submitted."

Plegridy - peginterferon beta-1a - EMEA/H/C/002827/II/0046

Biogen Idec Ltd, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Julie Williams, "Update of sections 4.4 and 4.8 of the SmPC in order to add new warning and safety information about anaphylaxis. The RMP version 3.2 has also been submitted."

Ryzodeg - insulin human - EMEA/H/C/002499/II/0028

Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of section 5.1 of the SmPC based on new clinical data from a cardiovascular outcome trial EX1250-4080 (DEVOTE) conducted for insulin degludec. DEVOTE was a randomised, double-blind and event-driven clinical trial with a median duration of 2 years comparing the cardiovascular safety of insulin degludec versus insulin glargine (100 units/mL) in patients with type 2 diabetes mellitus at high risk of cardiovascular events.

Based on the long-term exposure and safety data from DEVOTE which are also relevant for insulin degludec/insulin aspart, the Ryzodeg SmPC is updated with data from the trial in alignment with a recent update of the SmPC for insulin degludec.

Section 6.5 of the SmPC is also being amended for an editorial improvement to more precisely describe the nature of the plunger stopper.

The RMP version 7 has also been submitted, with updates consequent to the data in support of the application."

Tamiflu - oseltamivir - EMEA/H/C/000402/II/0136

Roche Registration GmbH, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.2, 4.8, 5.1 and 5.2 to guide prescribers on the use of Tamiflu for treatment in immunocompromised (IC) patients based on studyt NV20234, a Phase III, double-blind, randomized, stratified, multicenter study of conventional and double dose oseltamivir for the treatment of influenza in IC patients.
The PL and RMP (v15) have been updated accordingly.
In addition, the MAH took the opportunity to correct some minor errors."

Toujeo - insulin glargine - EMEA/H/C/000309/II/0105/G

Sanofi-Aventis Deutschland GmbH, Duplicate, Duplicate of Lantus, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst

B.6.11. PRAC assessed procedures

PRAC Led

Humira - adalimumab - EMEA/H/C/000481/II/0182

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 14.0 in order to include a thorough review of the currently specified safety concerns in the Humira RMP, to updated in regards of previously assessed safety concerns and to make associated updates in line with GVP Module V."

PRAC Led

Kengrexal - cangrelor - EMEA/H/C/003773/II/0015

Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of an updated RMP version 2.0 in order to update the requirements for a study listed as category 3 in the RMP. In addition, the

MAH took the opportunity to revise the RMP in line with the RMP template version 2.0."

PRAC Led

MabThera - rituximab - EMEA/H/C/000165/II/0152

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final study report of the non-interventional drug utilisation study (DUS) BA28478 (MabThera drug utilisation study and patient alert card evaluation in non-oncology patients in Europe: an infusion centre-based approach). Consequently, update of sections 4.2 and 4.4 of the SmPC and Annex II.E to remove the patient alert card as an additional risk minimisation measure for the risks of PML and infections, for the non-oncology indications. The Package leaflet is updated in accordance. The RMP is laso updated (version 18). This submission is done in fulfilment of FUM-68.1 and FUM-71."

PRAC Led

Mycamine - micafungin - EMEA/H/C/000734/II/0038

Astellas Pharma Europe B.V., Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "Submission of an updated RMP version 20.0 in order to streamline and improve the educational programme and communication to physicians prescribing Mycamine as requested in variation II/0035."

PRAC Led

Neofordex - dexamethasone - EMEA/H/C/004071/II/0008

Laboratoires CTRS, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of an updated RMP version 4.0 in order to propose the removal a category 3 activity 'removal of the score line for subdivision of the 40mg tablet and consequent deletion of the 20mg posology'. In addition, the MAH updated the other category 3 activity 'Development of a 20mg oral dosage form'. The MAH implemented the RMP revision 2 format."

PRAC Led

Pegasys - peginterferon alfa-2a - EMEA/H/C/000395/II/0101

Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "Submission of an updated RMP version 9.0 in order to remove the NV25361 study (category 3 study). In addition, the YV25718 (study to establish the efficacy and safety of PEG-IFN monotherapy in children from 3 to less than 18 years of age with CHB) long term follow up milestone is amended from Q3 2020 to Q4 2021. The classification of some risks is also amended as per revision 2 of Module V of GVP including updates in the epidemiology section."

PRAC Led

Simponi - golimumab - EMEA/H/C/000992/II/0084

Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 18.0 in order to remove the Educational program for prescribing healthcare professionals as an additional risk minimization measure for Simponi, based upon the conclusion of the PRAC PSUR Assessment report (PSUSA/00001560/201704)."

PRAC Led

Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0188

Gilead Sciences International Limited, PRAC Rapporteur: Caroline Laborde, PRAC-CHMP liaison: Joseph Emmerich, "Submission of the final report from study GS-EU-174-0224 listed as a category 3 study in the RMP. This is a cross-sectional drug utilisation study in children and adolescents with Chronic Hepatitis B to assess whether physicians prescribing Viread to paediatric patients with Chronic Hepatitis B in the EU were following the relevant recommendations in the Viread SmPC and educational brochures."

PRAC Led

Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0190

Gilead Sciences International Limited, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Caroline Laborde, PRAC-CHMP liaison: Joseph Emmerich, "Submission of an updated RMP version 22.1 (in accordance with

the revised guidance in the Guideline on good pharmacovigilance practices Module V) to propose removing the additional risk minimization activities for HIV and HBV adults associated with the renal safety concern from the RMP."	
PRAC Led **Votubia - everolimus -** **EMEA/H/C/002311/II/0055, Orphan** Novartis Europharm Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "Submission of the final report from the non-interventional study CRAD001MIC03, listed as a category 3 study in the RMP. This is an international disease registry collecting data on manifestations, interventions and outcomes in patients with tuberous sclerosis complex."	
PRAC Led **Xeloda - capecitabine -** **EMEA/H/C/000316/II/0077** Roche Registration GmbH, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "To updated Xeloda RMP (version 9.1) in line with the product information changes recently approved within the variation EMEA/H/C/000163/II/0074. The following updates are incuded: Post-authorization exposure updated, Presentation of important identified risk Dihydropyrimidine dehydrogenase deficiency (DPD) updated and updates related to Section 4.4 of EU SmPC for DPD revised as part of procedure EMEA/H/C/316/II/0074. In addition MAH took the opportunity to introduce the new EU RMP template."	
PRAC Led **WS1402** **Bretaris Genuair-** **EMEA/H/C/002706/WS1402/0038** **Eklira Genuair-** **EMEA/H/C/002211/WS1402/0038** AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, Lead PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Robert James Hemmings, "Submission of an updated RMP version 7.0 in order to proposed changes in categorisation of safety concerns and missing information in the RMP as per the guidance provide for the revision 2 of the RMP and to	

provide the RMP under the revision 2 template."

PRAC Led
WS1403
Brimica Genuair-
EMEA/H/C/003969/WS1403/0023
Duaklir Genuair-
EMEA/H/C/003745/WS1403/0023
AstraZeneca AB, Lead Rapporteur: Nithyanandan Nagercoil, Lead PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Robert James Hemmings, "Submission of an updated RMP version 4.0 in order to proposed changes in categorisation of safety concerns and missing information in the RMP as per the guidance provide for the revision 2 of the RMP and to provide the RMP under the revision 2 template."

B.6.12. CHMP-CAT assessed procedures

Imlygic - talimogene laherparepvec -
EMEA/H/C/002771/II/0024, ATMP
Amgen Europe B.V., Rapporteur: Olli Tenhunen,

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

WS1407
HyQvia-EMEA/H/C/002491/WS1407/0042
Kiovig-EMEA/H/C/000628/WS1407/0083
Baxalta Innovations GmbH, Lead Rapporteur: Jan Mueller-Berghaus

WS1409
Keppra-EMEA/H/C/000277/WS1409/0172
UCB Pharma S.A., Lead Rapporteur: Koenraad Norga,

WS1410
Infanrix hexa-
EMEA/H/C/000296/WS1410/0243
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1416
Kisplyx-EMEA/H/C/004224/WS1416/0014

Lenvima-
EMEA/H/C/003727/WS1416/0018
Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren

WS1419
Abseamed-
EMEA/H/C/000727/WS1419/0073
Binocrit-
EMEA/H/C/000725/WS1419/0073
Epoetin alfa Hexal-
EMEA/H/C/000726/WS1419/0072
Sandoz GmbH, Lead Rapporteur: Alexandre Moreau

WS1424
Eviplera-
EMEA/H/C/002312/WS1424/0092
Odefsey-
EMEA/H/C/004156/WS1424/0032
Gilead Sciences Ireland UC, Lead Rapporteur: Robert James Hemmings

WS1425
Nuwiq-EMEA/H/C/002813/WS1425/0023
Vihuma-
EMEA/H/C/004459/WS1425/0005
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus

WS1440/G
Hirobriz Breezhaler-
EMEA/H/C/001211/WS1440/0050/G
Onbrez Breezhaler-
EMEA/H/C/001114/WS1440/0048/G
Oslif Breezhaler-
EMEA/H/C/001210/WS1440/0048/G
Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth

WS1443
Actos-EMEA/H/C/000285/WS1443/0080
Competact-
EMEA/H/C/000655/WS1443/0071
Glustin-EMEA/H/C/000286/WS1443/0079
Tandemact-
EMEA/H/C/000680/WS1443/0058
Takeda Pharma A/S, Lead Rapporteur: Peter Kiely, “To bring the annexes in line with QRD version 10 and the EC guideline of excipients on lactose. In addition the MAH took the opportunity to update the local representative in Estonia and Slovakia along with some editorial

changes throughout the annexes."

WS1448/G
Ultibro Breezhaler-
EMEA/H/C/002679/WS1448/0027/G
Ulunar Breezhaler-
EMEA/H/C/003875/WS1448/0026/G
Xoterna Breezhaler-
EMEA/H/C/003755/WS1448/0030/G
Novartis Europharm Limited, Lead Rapporteur:
Mark Ainsworth

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.

Qualification of Biomarkers:

HTA:

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 23-26 July 2018 CHMP plenary:

G.3.2. List of procedures starting in July 2018 for August 2018 CHMP adoption of outcomes

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