28 May 2018
EMA/CHMP/352527/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 28-31 May 2018

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

28 May 2018, 13:00 – 19:30, room 2A

29 May 2018, 08:30 – 19:30, room 2A

30 May 2018, 08:30 – 19:30, room 2A

31 May 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.

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session to be held 28-31 May 2018. See (current) May 2018 CHMP minutes (to be published post June 2018 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 28-31 May 2018

1.3. Adoption of the minutes

CHMP minutes for 23-26 April 2018

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. caplacizumab - Orphan - EMEA/H/C/004426

Ablynx NV; indicated for the treatment of acquired thrombotic thrombocytopenic purpura (aTTP).

Scope: Oral explanation

Action: Oral explanation to be held on 30 May 2018 at time 15:00

List of Outstanding Issues adopted on 25.01.2018. List of Questions adopted on 22.06.2017.

See 3.1

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

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

Scope: Oral explanation

Action: Oral explanation to be held on 29 May 2018 at time 11:00

List of Outstanding Issues adopted on 22.03.2018. List of Questions adopted on 14.12.2017.

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

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

Vertex Pharmaceuticals (Europe) Ltd.

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

Scope: Oral explanation

Action: Oral explanation to be held on 29 May 2018 at time 11:00

Request for Supplementary Information adopted on 22.03.2018, 14.12.2017.

See 5.1

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. erenumab - EMEA/H/C/004447

indicated for prophylaxis of migraine in adults

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.04.2018, 22.02.2018. List of Questions adopted on 12.10.2017.

3.1.2. caplacizumab - Orphan - EMEA/H/C/004426

Ablynx NV; indicated for the treatment of acquired thrombotic thrombocytopenic purpura (aTTP).

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 25.01.2018. List of Questions adopted on 22.06.2017.

See 2.1

3.1.3. eteplirsen - Orphan - EMEA/H/C/004355

AVI Biopharma International Ltd; treatment of Duchenne muscular dystrophy

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 14.12.2017. List of Questions adopted on 21.04.2017.

3.1.4. adalimumab - EMEA/H/C/004866

treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, uveitis, paediatric uveitis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.04.2018, 22.02.2018.

3.1.5. adalimumab - EMEA/H/C/004865

treatment of juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa (HS), uveitis, paediatric uveitis

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.04.2018, 22.02.2018.

3.1.6. adalimumab - EMEA/H/C/004320

treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa (HS), Crohn's disease, paediatric Crohn's disease, ulcerative colitis, uveitis, paediatric uveitis.

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.04.2018, 22.02.2018. List of Questions adopted on 14.09.2017.

3.1.7. metreleptin - Orphan - EMEA/H/C/004218

Aegerion Pharmaceuticals Limited; treatment of leptin deficiency (lipodystrophy)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 22.02.2018, 14.12.2017. List of Questions adopted on 18.05.2017.

3.1.8. nitisinone - EMEA/H/C/004582

treatment of hereditary tyrosinemia type 1

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.04.2018, 22.02.2018. List of Questions adopted on 22.06.2017.

3.1.9. brexpiprazole - EMEA/H/C/003841

treatment of schizophrenia

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 22.03.2018. List of Questions adopted on 20.07.2017.

3.1.10. inotersen - Orphan - EMEA/H/C/004782

IONIS USA Ltd; treatment of transthyretin amyloidosis (hATTR)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 24.04.2018. List of Questions adopted on 20.02.2018.

3.1.11. trastuzumab - EMEA/H/C/004463

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 26.04.2018. List of Questions adopted on 09.11.2017.

3.1.12. vonicog alfa - Orphan - EMEA/H/C/004454

Baxalta Innovations GmbH; Treatment of von Willebrand Disease (VWD)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 22.03.2018. List of Questions adopted on 12.10.2017.

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

3.2.1. viable t-cells - Orphan - ATMP - EMEA/H/C/002397

Kiadis Pharma Netherlands B.V.; adjunctive treatment in haematopoietic stem cell transplantation (HSCT) for a malignant disease

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 08.09.2017.

3.2.2. glycopyrronium / formoterol fumarate dihydrate - EMEA/H/C/004245

indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD)

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 09.11.2017.

3.2.3. 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: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.12.2017.

3.2.4. deferiprone - EMEA/H/C/004710

treatment of iron overload in thalassemia major

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 09.11.2017.

3.2.5. dengue tetravalent vaccine (live, attenuated) - EMEA/H/C/004171

indicated for the prevention of dengue disease caused by dengue virus serotypes 1, 2, 3 and 4

Scope: List of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 23.03.2017. List of Questions adopted on 21.07.2016.

3.2.6. gefitinib - EMEA/H/C/004826

treatment of non-small cell lung cancer

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.12.2017.

3.2.7. tildrakizumab - EMEA/H/C/004514

treatment of adults with moderate-to-severe plaque psoriasis

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 20.07.2017.

3.2.8. durvalumab - EMEA/H/C/004771

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

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 25.01.2018.

3.2.9. tisagenlecleucel - Orphan - ATMP - EMEA/H/C/004090

Accelerated assessment

Novartis Europharm Limited; treatment of B cell acute lymphoblastic leukaemia (ALL) and diffuse large B cell lymphoma (DLBCL)

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 16.03.2018.

3.2.10. lenalidomide - EMEA/H/C/004857

treatment of multiple myeloma

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.12.2017.

3.2.11. 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: List of outstanding issue

Action: For adoption

List of Questions adopted on 08.12.2017.

3.2.12. 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: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.12.2017.

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

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

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.09.2017.

3.2.14. mexiletine hcl - Orphan - EMEA/H/C/004584

LUPIN (EUROPE) LIMITED; Treatment of myotonic disorders

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.12.2017.

3.2.15. paclitaxel - EMEA/H/C/004441

treatment of metastatic breast cancer

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.12.2017.

3.2.16. pegfilgrastim - EMEA/H/C/003961

treatment of neutropenia

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.09.2017.

3.2.17. meropenem / vaborbactam - EMEA/H/C/004669

treatment of urinary tract infection (cUTI), including pyelonephritis, intra-abdominal infection (cIAI), hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP), bacteraemia, infections due to bacterial organisms

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 09.11.2017.

3.2.18. daunorubicin / cytarabine - Orphan - EMEA/H/C/004282

Accelerated assessment

Jazz Pharmaceuticals Ireland Limited; treatment of adults with high-risk acute myeloid leukaemia (AML)

Scope: List of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 24.04.2018. List of Questions adopted on 20.02.2018.

3.2.19. eravacycline - EMEA/H/C/004237

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

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.12.2017.

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

3.3.1. fremanezumab - EMEA/H/C/004833

prevention of episodic and chronic migraine

Scope: List of questions

Action: For adoption

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

GW Research Ltd; Adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS)

Scope: List of questions

Action: For adoption

3.3.3. asparaginase - Orphan - EMEA/H/C/004736

ERYTECH Pharma S.A.; treatment of acute lymphoblastic leukaemia

Scope: List of questions

Action: For adoption

3.3.4. lorlatinib - EMEA/H/C/004646

treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC)

Scope: List of questions

Action: For adoption

3.3.5. lusutrombopag - EMEA/H/C/004720

treatment of thrombocytopenia

Scope: List of questions

Action: For adoption

3.3.6. treosulfan - Orphan - EMEA/H/C/004751

medac Gesellschaft fur klinische Spezialpraparate mbH; conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT)

Scope: List of questions

Action: For adoption

3.3.7. canakinumab - EMEA/H/C/004754

prevention of major cardiovascular events

Scope: List of questions

Action: For adoption

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

3.4.1. brigatinib - EMEA/H/C/004248

treatment of anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC)

Scope: Request for an additional extension of clock stop to respond to the List of Outstanding Issues adopted in January 2018.

Action: For adoption

List of Outstanding Issues adopted on 25.01.2018, 12.10.2017. List of Questions adopted on 22.06.2017.

3.4.2. vestronidase alfa - Orphan - EMEA/H/C/004438

Ultragenyx Germany GmbH; indicated for the treatment of Mucopolysaccharidosis VII (MPS VII; Sly syndrome) for patients of all ages

Scope: Draft list of experts for adoption for the ad hoc expert group meeting

Action: For adoption

List of Outstanding Issues adopted on 26.04.2018, 22.02.2018, List of Questions adopted on 14.09.2017.

3.4.1. volanesorsen - Orphan - EMEA/H/C/004538

Akcea Therapeutics UK Ltd.; indicated as an adjunct to diet for the treatment of patients with familial chylomicronemia syndrome (FCS).

Scope: Draft list of experts for adoption for the ad hoc expert group meeting

Action: For adoption

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

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

No items

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

No items

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

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

4.1.1. Xeljanz - tofacitinib - EMEA/H/C/004214/X/0005/G

Pfizer Limited

Rapporteur: Robert James Hemmings, PRAC Rapporteur: Sabine Straus

Scope: "Extension application to introduce a new strength (10 mg film coated tablets). In addition, the MAH proposed a type II variation (C.I.6.a) to extend the indication to include 'the induction and maintenance of treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent."

Action: For adoption

List of Questions adopted on 14.12.2017.

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. 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 Questions adopted on 14.12.2017.

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

Swedish Orphan Biovitrum AB (publ)

Rapporteur: Jan Mueller-Berghaus

Scope: "Extension application to introduce new strength of 4000 IU, 5000 IU and 6000 IU

primarily enabling phrophylactic dosing in adult patients."

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. Adcetris - brentuximab vedotin - Orphan - EMEA/H/C/002455/II/0055

Takeda Pharma A/S

Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Sabine Straus

Scope: "Extension of the existing Hodgkin lymphoma (HL) indication to include the frontline treatment of adult patients with CD30+ advanced HL in combination with chemotherapy, based on data from ECHELON-1 (C25003), a phase 3 multi-centre, randomised, open-label study comparing the modified progression-free survival (mPFS) obtained with brentuximab vedotin, doxorubicin, vinblastine and dacarbazine versus the mPFS obtained with doxorubicin, bleomycin, vinblastine and dacarbazine. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Furthermore, the PI is brought in line with the latest QRD template version 10. The MAH also submitted an updated RMP version 13."

Action: For adoption

5.1.2. Briviact - brivaracetam - EMEA/H/C/003898/II/0010/G

UCB Pharma S.A.

Rapporteur: Filip Josephson, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Adam Przybylkowski

Scope: "Extension of Indication to include adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in patients with epilepsy 4 years of

age and older for Briviact. As a consequence, sections 4.1, 4.2, 4.7, 5.1 and 5.2 of the SmPC are updated.
In addition, the Marketing authorisation holder (MAH) submitted a 5ml oral syringe and adaptor for the paediatric population.

The Package Leaflet and Labelling are updated in accordance.

Submission of the final Environmental Risk Assessment for the inclusion of the paediatric population in accordance with the new indication sought."

Action: For adoption

Request for Supplementary Information adopted on 22.03.2018, 12.10.2017.

5.1.3. Inovelon - rufinamide - Orphan - EMEA/H/C/000660/II/0045

Eisai Ltd

Rapporteur: Alexandre Moreau, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension of indication to include the treatment of seizures associated with Lennox Gastaut syndrome in patients 1 year of age and older as adjunctive therapy. As a consequence sections 4.1, 4.2, 4.5, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 10.0) are updated accordingly. In addition the Marketing Authorisation Holder (MAH) took the opportunity to make small corrections with the Product Information and to update the name and contact details of the local representative in Belgium and Luxembourg. Furthermore, the Product Information is brought in line with the latest QRD template version 10."

Action: For adoption

Request for Supplementary Information adopted on 14.12.2017.

5.1.4. 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, section 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 22.03.2018, 14.12.2017.

See 2.1

5.1.5. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0052

Merck Sharp & Dohme B.V.

Rapporteur: Daniela Melchiorri

Scope: “Restriction of the currently authorised indication in cisplatin-ineligible urothelial carcinoma patients to exclude patients whose tumors express PD-L1 CPS<10, as well as to exclude only the patients who have 1 or more risk factors predicting a worse outcome. Section 4.1 of the SmPC has been revised accordingly.”

Action: For adoption

5.1.6. Lenvima - lenvatinib - Orphan - EMEA/H/C/003727/II/0011/G

Eisai Europe Ltd.

Rapporteur: Bart Van der Schueren, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Ulla Wändel Liminga

Scope: “Extension of indication to include treatment of hepatocellular carcinoma (HCC) based on pivotal Study 304. Consequently, sections 4.1, 4.2, 4.4, 4.8, 5.1, and 5.2 of the SmPC are being updated and the package leaflet is updated accordingly. In addition, section 4.2 of the SmPC is being updated to add that the product can be administered as a suspension in water or apple juice. In addition, the labelling is updated to include the unique identifier. An updated RMP version 10 was provided as part of the application.”

Action: For adoption

Request for Supplementary Information adopted on 22.02.2018, 09.11.2017.

5.1.7. Mozobil - plerixafor - Orphan - EMEA/H/C/001030/II/0034

Genzyme Europe BV

Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus

Scope: “Extension of Indication to include paediatric patients aged 1 to 18 years for Mozobil, as a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance.”

Action: For adoption

5.1.8. Sprycel - dasatinib - EMEA/H/C/000709/II/0059

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Fátima Ventura, PRAC Rapporteur: Doris Stenver

Scope: “Extension of Indication to include a paediatric indication for Philadelphia chromosome positive acute lymphoblastic leukaemia for Sprycel; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, and 5.2 of the SmPC are updated.
The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to the product information.

The RMP version 16.0 has also been submitted."

Action: For adoption

5.1.9. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0007/G

Roche Registration GmbH

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

Scope: "Extension of indication to include in combination with bevacizumab, paclitaxel and carboplatin the first-line treatment of adult patients with metastatic non-squamous non small cell lung cancer (NSCLC), based on the interim results of study GO29436 (IMpower 150). As a consequence sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated.
In addition update of section 4.8 of the SmPC in order to update the monotherapy safety data and reflect the largest pooled monotherapy population available (now including also data from IMvigor211 and PCD4989g studies).
The Package Leaflet and the RMP (version 4.0) are updated in accordance. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to make small corrections and formatting changes throughout the SmPC.", Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

5.1.10. Tecentriq - atezolizumab - ANX 003 and EMEA/H/C/004143/II/0010

Roche Registration GmbH

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

Scope: "Restriction of the currently authorised indication in cisplatin-ineligible urothelial carcinoma patients to exclude patients whose tumors express PD-L1 CPS<10, as well as to exclude only the patients who have 1 or more risk factors predicting a worse outcome. Section 4.1 of the SmPC has been revised accordingly."

Action: For adoption

5.1.11. Translarna - ataluren - Orphan - EMEA/H/C/002720/II/0037

PTC Therapeutics International Limited

Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include a new population (children from 2 to less than 5 years of age) for Translarna; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and RMP (version 7.1) is updated in accordance."

Action: For adoption

Request for Supplementary Information adopted on 26.04.2018, 22.02.2018, 14.12.2017.

5.1.12. 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."

Action: For adoption

Request for Supplementary Information adopted on 22.02.2018.

5.1.13. 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

5.1.14. 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."

Action: For adoption

Request for Supplementary Information adopted on 22.02.2018.

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

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 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 22.02.2018.

5.1.16. WS1344
Edistride - dapagliflozin - EMEA/H/C/004161/WS1344/0025
Forxiga - dapagliflozin - EMEA/H/C/002322/WS1344/0044

AstraZeneca AB

Lead Rapporteur: Kristina Dunder, Lead Co-Rapporteur: Martina Weise, PRAC Rapporteur: Qun-Ying Yue

Scope: "Extension of Indication to include new indication for the treatment of insufficiently controlled type 1 diabetes mellitus as an adjunct to insulin, when insulin does not provide

adequate glycaemic control, for Forxiga and Edistride; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The updated RMP version 16 has also been submitted.
In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor editorial changes to SmPC and Package Leaflet."

Action: For adoption

5.1.17. WS1369
Elebrato Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004781/WS1369/0001
Trelegy Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/004363/WS1369/0001

GlaxoSmithKline Trading Services

Lead Rapporteur: Peter Kiely, Lead Co-Rapporteur: Harald Enzmann, PRAC Rapporteur: Qun-Ying Yue

Scope: "To modify the approved current COPD therapeutic indication to "maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD)".
As a consequence, the indication section (4.1), Undesirable effects section (4.8) and Pharmacodynamic Properties section (5.1), Pharmacokinetic properties section (5.2), Preclinical Safety data section (5.3) of the EU SmPC, and the Possible side effects section (4) of the package leaflet are updated accordingly. This is based on the result of study CTT116855 and study 200812 and the population PK report 208059.
The updated RMP (version 02) has also been submitted."

Action: For adoption

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

No items

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

No items

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. sodium salt of gamma-hydroxybutyric acid - H0004962

Support in the medium to long-term maintenance of alcohol abstinence in alcohol-dependent adult patients with a Very High Drinking Risk Level (consumption of more than 60 g alcohol/day for women and of more than 100 g alcohol/day for men) under careful medical supervision along with psychotherapy and social rehabilitation.
Treatment should be initiated only to patients whose duration of abstinence prior to treatment does not exceed 2 weeks.
Treatment of acute alcohol withdrawal syndrome in alcohol-dependent adult patients

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

Action: For adoption

8.1.2. angiotensin II - H0004930

For the treatment of hypotension in adults with distributive or vasodilatory shock who remain hypotensive despite fluid and vasopressor therapy

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. Ceplene - histamine dihydrochloride - EMEA/H/C/000796/II/0034, Orphan

Noventia Pharma Srl

Rapporteur: Jayne Crowe

Scope: "Submission of study report X-03064-3306- to fulfil SOB 002 - A cohort study to follow-up Minimal Residual Disease (MRD) in patients with Acute Myeloid Leukemia (AML) in First Complete Remission (CR1) - Comparison of patients who receive Ceplene/Interleukin-2 as remission maintenance therapy with matched controls."

Action: For adoption

Request for Supplementary Information adopted on 22.03.2018.

9.1.2. Daptomycin Hospira - daptomycin - EMEA/H/C/004310/II/0006/G

Hospira UK Limited

Rapporteur: Kolbeinn Gudmundsson

Scope: Request for an extension of clock stop to respond to the request for supplementary information.

Action: For adoption

Request for Supplementary Information adopted on 22.02.2018.

10. Referral procedures

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

10.1.1. Esmya - ulipristal acetate - EMEA/H/A-20/1460

Gedeon Richter Plc.

Rapporteurs for the Article 20 referral: PRAC Rapporteur: Ulla Wändel Liminga; PRAC Co-rapporteur: Menno van der Elst

Rapporteurs for Esmya: CHMP Rapporteur: Kristina Dunder, CHMP Co-rapporteur: Paula Boudewina van Hennik

PRAC Rapporteur: Ulla Wändel Liminga; PRAC Co-rapporteur: Menno van der Elst

Scope: Opinion

Action: For adoption

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

10.1.2. Zinbryta - daclizumab – EMEA/H/A-20/1456

Biogen Idec Ltd

Rapporteurs for the Article 20 referral: PRAC Rapporteur: Eva Segovia; PRAC Co-rapporteur: Marcia Sofia Sanches de Castro Lopes Silva,

Rapporteurs for Zinbryta: CHMP Rapporteur: Bruno Sepodes, CHMP Co-rapporteur: Greg MarkeyPRAC Rapporteur: Eva Segovia; PRAC Co-rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Opinion

Action: For adoption

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

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

10.2.1. Ethinylestradiol and norethisterone – EMEA/H/A-5(3)/1470

MAH various

Rapporteur: TBC, Co-rapporteur: TBC

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

Action: For adoption

Request from UK for a CHMP opinion on a recently published study using the zebrafish model for studying the developmental effect of norethisterone acetate and ethinylestradiol and any potential clinical implications on the human foetus.

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

No items

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

No items

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

10.5.1. Scandonest and associated names – mepivacaine - EMEA/H/A-30/1455

Septodont group of companies and associated companies

Rapporteur: Romaldas Maciulaitis, Co-rapporteur: Fatima Ventura

Scope: Opinion

Action: For adoption

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

List of Outstanding issues adopted at 22.02.2018, List of Questions adopted at 12.10.2017

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

10.6.1. Bacterial lysates-containing based medicinal products for respiratory condtions - EMEA/H/A-31/1465

MAH various

Rapporteur: TBC, Co-rapporteur: TBC

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

Action: For adoption

Review of the benefit-risk balance following notification by AIFA in Italy on 22 May 2018 of a referral under Article 31 of Directive 2001/83/EC.

10.6.2. Metamizole containing medicinal products – metamizole sodium - EMEA/H/A-31/1469

MAH various

Rapporteur: TBC, Co-rapporteur: TBC

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

Action: For adoption

The Polish National Competent Authority triggered a referral under Article 31 of Directive 2001/83 based on interest of the Union, requesting an opinion to CHMP on whether the

scientific data regarding the maximum daily dose and contraindications concerning pregnancy and breastfeeding are adequately presented in the product information of metamizole containing medicinal products.

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

May 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

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. PRAC and CHMP involvement in type II variations

A proposal for an initiative is brought to the Committee to create a working group of PRAC and CHMP members. The purpose of the group is to clarify the two committees' involvement in type II variations, in order to address issues encountered in the experience to date, most notably the lack of PRAC involvement in PRAC-requested variations (e.g. following signals, PSURs, other PRAC recommendations) or in the assessment of non-interventional PASS

results with implications for the PI.

Nomination of PRAC and CHMP representatives for the initiative.

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 14-17 May 2018

Action: For information

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

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 23-25 May 2018

Action: For information

14.2.3. Paediatric Committee (PDCO)

PIPs reaching D30 at May 2018 PDCO

Action: For information

Report from the PDCO meeting held on 29 May – 1 June 2018

Action: For information

Joint CHMP/PDCO session

Agenda for joint session

Action: For discussion

14.2.4. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 22-24 May 2018

Action: For information

14.2.5. 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 28-30 May 2018

Action: For information

CMDh questions to SAWP on multi-stakeholder scientific advice for OTC products (EMA/CMDh/296507/2018)

Action: For adoption

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 14-17 May 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.

14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 28-29 May 2018.

Action: For adoption

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP May 2018 meeting to CHMP for adoption:

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

Action: For adoption

14.3.4. Coordination with EMA Working Parties/Working Groups/Drafting Groups on ICH E9 (R1) addendum on estimands

BSWP Chair: Anja Schiel, CHMP: Robert James Hemmnings

Reflection of the potential impact of ICH E9 (R1) addendum on estimands and sensitivity analysis in clinical trials to the guideline on statistical principles for clinical trials on the CHMP scientific guidelines – feedback from WPs and DGs

Action: For information

14.3.5. Modelling and Simulation Working Party (MSWP)

Chair (acting): Flora Musuamba Tshinanu

Appointment of members

Action: For adoption

Call for interest for Chair/Vice-Chair

Action: For information

14.3.6. Blood Products Working Party (BPWP)

Chair: Jacqueline Kerr

BPWP final response on signal of lupus like syndrome for immunoglobulins to PRAC (EMA/CHMP/810262/2018)

Action: For adoption

14.3.7. Pharmacogenomics Working Party (PGWP)

Chair: Krishna Prasad/Markus Paulmichl

Programme of EMA multi-stakeholder workshop on predictive biomarker-based assay development in the context of drug development and lifecycle (EMA/136048/2018): CHMP members are invited to participate in workshop

Action: For information

14.3.8. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink/Henrike Potthast

Product-specific bioequivalence guidelines:

- Prasugrel hydrochloride film-coated tablets 5 mg and 10 mg product-specific bioequivalence guidance (batch 2)
  Rapporteur: Christina Thygesen
- Dabigatran etexilate hard capsules 75 mg, 110 mg and 150 mg product-specific bioequivalence guidance (batch 6)
  Rapporteur: Christina Thygesen
- Dimethyl fumarate gastro-resistant capsules 120 mg and 240 mg product-specific bioequivalence guidance (batch 7)
  Rapporteur: Henrike Potthast
- Ibuprofen 200 - 800 mg oral use, immediate release formulations product-specific bioequivalence guidance (batch 7)
  Rapporteur: Susan Cole
- Paliperidone prolonged-release tablet 1.5 mg, 3 mg, 6 mg, 9 mg and 12 mg product-

specific bioequivalence guidance revision 1 (batch 4)
Rapporteur: Eva Berglund/Malin Filler

- Pegylated liposomal doxorubicin hydrochloride 2 mg/ml product-specific bioequivalence guidance (batch 8)
  Rapporteur: Henrike Potthast

Action: For adoption

Product-specific bioequivalence guidelines, batch 9:

- Aliskiren film-coated tablet 150 mg and 300 mg product-specific bioequivalence guidance
  Rapporteur: Janet Mifsud
- Apixaban film-coated tablets 2.5 and 5 mg product-specific bioequivalence guidance
  Rapporteur: Carolien Versantvoort
- Gefitinib film-coated tablet 250 mg product-specific bioequivalence guidance
  Rapporteur: Eva Berglund/ Malin Filler
- Lapatinib film-coated tablet 250 mg product-specific bioequivalence guidance
  Rapporteur: Eva Berglund/ Malin Filler
- Octreotide acetate depot powder and solvent for suspension for injection 10 mg, 20 mg or 30 mg product-specific bioequivalence guidance
  Rapporteur: Susan Cole

Action: For adoption for public consultation

PKWP response to CMDh request for clarification on paliperidone PR tablets PSBGL (EMA/CHMP/277265/2018)
Rapporteur: Eva Gil-Berglund/Malin Filler

Action: For adoption

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Article 58: Update from the March 2017 ‘Malta’ CHMP meeting with African regulators

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)*

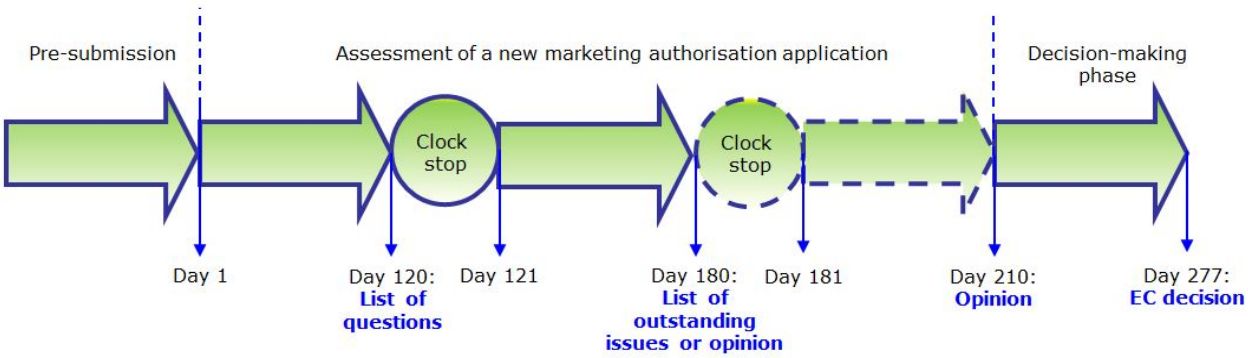
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

28 May 2018
EMA/CHMP/352514/2018

Annex to 28-31 May 2018 CHMP Agenda

Pre submission and post authorisations issues

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Send a question via our website www.ema.europa.eu/contact

A. PRE SUBMISSION ISSUES

A.1. ELIGIBILITY REQUESTS

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

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

Final Outcome of Rapporteurship allocation for
May 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

Ceplene - histamine dihydrochloride -
EMEA/H/C/000796/S/0035, Orphan
Noventia Pharma Srl, Rapporteur: Jayne Crowe,
PRAC Rapporteur: Almath Spooner

Vyndaqel - tafamidis -
EMEA/H/C/002294/S/0044, Orphan
Pfizer Limited, Rapporteur: Joseph Emmerich,
PRAC Rapporteur: Ghania Chamouni
Request for Supplementary Information adopted
on 22.03.2018.

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Abilify Maintena - aripiprazole -
EMEA/H/C/002755/R/0025
Otsuka Pharmaceutical Europe Ltd, Rapporteur:
Bruno Sepodes, Co-Rapporteur: Eleftheria
Nikolaidi, PRAC Rapporteur: Qun-Ying Yue

Ceplene - histamine dihydrochloride - EMEA/H/C/000796/R/0036, Orphan
Noventia Pharma Srl, Rapporteur: Jayne Crowe, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Almath Spooner

Evicel - human fibrinogen / human thrombin - EMEA/H/C/000898/R/0054
Omrix Biopharmaceuticals N. V., Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Brigitte Keller-Stanislawski
Request for Supplementary Information adopted on 26.04.2018.

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

INTELENCE - etravirine - EMEA/H/C/000900/R/0052
Janssen-Cilag International NV, Rapporteur: Joseph Emmerich, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Caroline Laborde

Invokana - canagliflozin - EMEA/H/C/002649/R/0037
Janssen-Cilag International NV, Rapporteur: Martina Weise, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Valerie Strassmann

Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/R/0039
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Doris Stenver

NovoEight - turoctocog alfa - EMEA/H/C/002719/R/0025
Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski

Opsumit - macitentan - EMEA/H/C/002697/R/0027, Orphan
Actelion Registration Limited, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Dolores Montero Corominas

Procysbi - mercaptamine - EMEA/H/C/002465/R/0019, Orphan

Chiesi Orphan B.V., Rapporteur: Kristina Dunder, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Qun-Ying Yue
Request for Supplementary Information adopted on 22.03.2018.

Rasilez HCT - aliskiren / hydrochlorothiazide - EMEA/H/C/000964/R/0087
Noden Pharma DAC, Rapporteur: Daniela Melchiorri, Co-Rapporteur: Melinda Sobor, PRAC Rapporteur: Carmela Macchiarulo

Relvar Ellipta - fluticasone furoate / vilanterol - EMEA/H/C/002673/R/0037
Glaxo Group Ltd, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Dolores Montero Corominas

Revinty Ellipta - fluticasone furoate / vilanterol - EMEA/H/C/002745/R/0033
Glaxo Group Ltd, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Dolores Montero Corominas

Tybost - cobicistat - EMEA/H/C/002572/R/0041
Gilead Sciences International Limited, Rapporteur: Robert James Hemmings, Co-Rapporteur: Joseph Emmerich, PRAC Rapporteur: Julie Williams
Request for Supplementary Information adopted on 22.03.2018.

B.2.3. Renewals of Conditional Marketing Authorisations

Bavencio - avelumab - EMEA/H/C/004338/R/0003, Orphan
Merck Serono Europe Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark

Translarna - ataluren - EMEA/H/C/002720/R/0041, Orphan
PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Sabine Straus
Request for Supplementary Information adopted on 26.04.2018.

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/R/0010, Orphan, ATMP

MolMed SpA, Rapporteur: Johannes Hendrikus Ovelgonne, CHMP Coordinator: Paula Boudewina van Hennik, PRAC Rapporteur: Brigitte Keller-Stanislawski

Request for Supplementary Information adopted on 20.04.2018.

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

PRAC recommendations on signals adopted at the PRAC meeting held on 14-17 May 2018

PRAC:

Signal of drug interaction between apixaban or edoxaban and selective serotonin reuptake inhibitors (SSRI) and/or serotonin and noradrenaline reuptake inhibitors (SNRI) leading to increased risk of bleeding.

Eliquis – apixaban – EMEA/H/C/002148
Bristol-Myers Squibb/Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Nithyanandan Nagercoil

Lixiana – edoxaban – EMEA/H/C/002629
Roteas – edoxaban – EMEA/H/C/004339
Daiichi Sankyo Europe GmbH, Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Martina Weise

Ariclaim – duloxetine – EMEA/H/C/000552
Eli Lilly Nederland B.V., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Kristina Dunder

Cymbalta – duloxetine – EMEA/H/C/000572
Duloxetine Lilly – duloxetine – EMEA/H/C/004000
Xeristar – duloxetine – EMEA/H/C/000573
Yentreve – duloxetine – EMEA/H/C/000545
Eli Lilly Nederland B.V., Rapporteur: Concepcion Prieto Yerro, Co-Rapporteur: Filip Josephson

Duloxetine Mylan – duloxetine – EMEA/H/C/003981
Generics UK Limited, Rapporteur: John Joseph Borg

Duloxetine Zentiva – duloxetine – EMEA/H/C/003935
Zentiva k.s., Rapporteur: Kristina Dunder

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

Signal of progressive multifocal leukoencephalopathy (PML)
Revlimid - lenalidomide – EMEA/H/C/000717
Celgene Europe Limited, Rapporteur: Alexandre Moreau, Co-Rapporteur: Filip Josephson
PRAC recommendation on a variation: **For adoption**

Signal of pulmonary haemorrhage
Lenograstim; lipegfilgrastim, pegfilgrastim

Lonquex – lipegfilgrastim – EMEA/H/C/002556
Sicor Biotech UAB., Rapporteur: Greg Markey, Co-Rapporteur: Johann Lodewijk Hillege

Neulasta - pegfilgrastim – EMEA/H/C/000420
Amgen Europe B.V., Rapporteur: Robert James Hemmings, Co-Rapporteur: Johann Lodewijk Hillege
PRAC recommendation on a variation**: For adoption**

Signal of aseptic meningitis
Keytruda – pembrolizumab – EMEA/H/C/003820
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, Co-Rapporteur: Jan Mueller-Berghaus
PRAC recommendation on a variation: **For adoption**

Signal on evaluation of preliminary data on congenital neurological disorders from an observational study.

Tivicay – dolutegravir - EMEA/H/C/003820

ViiV Healthcare B.V., Rapporteur: Filip Josephson, Co-Rapporteur: Joseph Emmerich
DHPC and communication plan have been circulated for written adoption
PRAC recommendation on a variation: **For adoption**

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

EMEA/H/C/PSUSA/00000235/201709
(arsenic trioxide)
CAPS:
Trisenox (EMEA/H/C/000388) (arsenic trioxide), Teva B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "01.10.2014 to 30.09.2017"

EMEA/H/C/PSUSA/00000939/201710
(deferasirox)
CAPS:

EXJADE (EMEA/H/C/000670) (deferasirox), Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "01 Nov 2016 – 31 Oct 2017"

EMEA/H/C/PSUSA/00002051/201710
(micafungin)
CAPS:
Mycamine (EMEA/H/C/000734) (micafungin), Astellas Pharma Europe B.V., Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, "09 Oct 2016- 08 Oct 2017"

EMEA/H/C/PSUSA/00002919/201710
(thalidomide)
CAPS:
Thalidomide Celgene (EMEA/H/C/000823) (thalidomide), Celgene Europe Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "10 October 2016 to 09 October 2017"

EMEA/H/C/PSUSA/00002999/201709
(toremifene)
CAPS:
Fareston (EMEA/H/C/000091) (toremifene), Orion Corporation, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "01/10/2014 - 30/09/2017"

EMEA/H/C/PSUSA/00010318/201710
(nintedanib (oncology indications))
CAPS:
Vargatef (EMEA/H/C/002569) (nintedanib), Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Agni Kapou, "22 Nov 2016 to 15 Oct 2017"

EMEA/H/C/PSUSA/00010319/201710
(nintedanib (respiratory indication))
CAPS:
OFEV (EMEA/H/C/003821) (nintedanib), Boehringer Ingelheim International GmbH, Rapporteur: Jayne Crowe, PRAC Rapporteur: Nikica Mirošević Skvrce, "16 Apr 2017 to 15 Oct 2017"

EMEA/H/C/PSUSA/00010387/201710
(edoxaban)
CAPS:
Lixiana (EMEA/H/C/002629) (edoxaban), Daiichi Sankyo Europe GmbH, Rapporteur: Concepcion Prieto Yerro

Roteas (EMEA/H/C/004339) (edoxaban), Daiichi Sankyo Europe GmbH, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Julie Williams, "22-APR-2017 – 21-OCT-2017"	
EMEA/H/C/PSUSA/00010449/201711 (cobicistat / elvitegravir / emtricitabine / tenofovir alafenamide) CAPS: **Genvoya** (EMEA/H/C/004042) (elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide), Gilead Sciences International Limited, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Amelia Cupelli, "05 May 2017 to 04 November 2017"	
EMEA/H/C/PSUSA/00010459/201710 (talimogene laherparepvec) CAPS: **Imlygic** (EMEA/H/C/002771) (talimogene laherparepvec), Amgen Europe B.V., Rapporteur: Olli Tenhunen, PRAC Rapporteur: Brigitte Keller-Stanislawski, "27 April 2017 to 26 October 2017"	
EMEA/H/C/PSUSA/00010612/201710 (sodium oxybate (oral use)) CAPS: **Xyrem** (EMEA/H/C/000593) (sodium oxybate), UCB Pharma Limited, Rapporteur: Bruno Sepodes NAPS: **ALCOVER** - LABORATORIO FARMACEUTICO C.T. S.R.L. PRAC Rapporteur: Ana Sofia Diniz Martins, "13-Oct-2016 to 12-Oct-2017"	

B.4. EPARs / WPARs

Biktarvy - bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449 Gilead Sciences International Limited, treatment of adults infected with human immunodeficiency virus-1 (HIV-1), 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.
Carmustine Obvius - carmustine - EMEA/H/C/004326 Obvius Investment B.V, treatment of brain tumors, multiple myeloma, Hodgkin's disease and non-Hodgkin's lymphomas, Generic, Generic application (Article 10(1) of Directive No	For information only. Comments can be sent to the EPL in case necessary.

2001/83/EC)	
Dzuveo - sufentanil - EMEA/H/C/004335 FGK Representative Service GmbH, management of acute moderate to severe pain, Hybrid application (Article 10(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

Adjupanrix - pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - EMEA/H/C/001206/II/0058/G GlaxoSmithkline Biologicals SA, Informed Consent of Pandemrix (EXP), Rapporteur: Greg Markey	
ATryn - antithrombin alfa - EMEA/H/C/000587/II/0033/G Laboratoire Francais du Fractionnement et des Biotechnologies, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 03.05.2018, 15.02.2018.	Request for supplementary information adopted with a specific timetable.
Benepali - etanercept - EMEA/H/C/004007/II/0035 Samsung Bioepis UK Limited, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
BYETTA - exenatide - EMEA/H/C/000698/II/0061/G AstraZeneca AB, Rapporteur: Kristina Dunder Opinion adopted on 17.05.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0094 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren Opinion adopted on 17.05.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cosentyx - secukinumab - EMEA/H/C/003729/II/0034 Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 17.05.2018.	
Cyramza - ramucirumab - EMEA/H/C/002829/II/0022 Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik Opinion adopted on 03.05.2018.	Positive Opinion adopted by consensus on 03.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Dupixent - dupilumab - EMEA/H/C/004390/II/0003/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 25.05.2018. Request for Supplementary Information adopted on 12.04.2018.	Positive Opinion adopted by consensus on 25.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Entyvio - vedolizumab - EMEA/H/C/002782/II/0029 Takeda Pharma A/S, Rapporteur: Greg Markey Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
Eptifibatide Accord - eptifibatide - EMEA/H/C/004104/II/0003 Accord Healthcare Limited, Generic, Generic of Integrilin, Rapporteur: Jayne Crowe Request for Supplementary Information adopted on 19.04.2018.	
Eylea - aflibercept - EMEA/H/C/002392/II/0046 Bayer AG, Rapporteur: Alexandre Moreau	
Flixabi - infliximab - EMEA/H/C/004020/II/0025 Samsung Bioepis UK Limited, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 17.05.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Fluenz Tetra - influenza vaccine (live attenuated, nasal) - EMEA/H/C/002617/II/0078/G AstraZeneca AB, Rapporteur: Bart Van der Schueren Opinion adopted on 17.05.2018.	Positive Opinion adopted by consensus on 17.05.2018. 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.	Request for supplementary information adopted with a specific timetable.

Imatinib Teva - imatinib - EMEA/H/C/002585/II/0033 Teva B.V., Generic, Generic of Glivec, Rapporteur: Jorge Camarero Jiménez Request for Supplementary Information adopted on 03.05.2018.	Request for supplementary information adopted with a specific timetable.
Imraldi - adalimumab - EMEA/H/C/004279/II/0005/G Samsung Bioepis UK Limited (SBUK), Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 15.03.2018.	
Insuman - insulin human - EMEA/H/C/000201/II/0124 Sanofi-Aventis Deutschland GmbH, Rapporteur: Bart Van der Schueren	
NovoSeven - eptacog alfa (activated) - EMEA/H/C/000074/II/0101/G Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik Opinion adopted on 17.05.2018. Request for Supplementary Information adopted on 15.02.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ontruzant - trastuzumab - EMEA/H/C/004323/II/0007 Samsung Bioepis UK Limited (SBUK), Rapporteur: Koenraad Norga Opinion adopted on 17.05.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
OPDIVO - nivolumab - EMEA/H/C/003985/II/0051/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez Opinion adopted on 17.05.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Prepandrix - A/Indonesia/05/2005 (H5N1) like strain used (PR8-IBCDC-RG2) - EMEA/H/C/000822/II/0075/G GlaxoSmithkline Biologicals SA, Rapporteur: Greg Markey	
Simponi - golimumab - EMEA/H/C/000992/II/0082/G Janssen Biologics B.V., Rapporteur: Kristina Dunder	
Strensiq - asfotase alfa - EMEA/H/C/003794/II/0027/G, Orphan Alexion Europe SAS, Rapporteur: Greg Markey	Positive Opinion adopted by consensus on 03.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Opinion adopted on 03.05.2018. Request for Supplementary Information adopted on 22.03.2018.	
Vaxelis - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and Haemophilus type B conjugate vaccine (adsorbed) - EMEA/H/C/003982/II/0030 MCM Vaccine B.V., Rapporteur: Bart Van der Schueren	
Vimizim - elosulfase alfa - EMEA/H/C/002779/II/0022/G, Orphan BioMarin Europe Ltd, Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 22.02.2018.	
Xolair - omalizumab - EMEA/H/C/000606/II/0084 Novartis Europharm Limited, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 03.05.2018.	Request for supplementary information adopted with a specific timetable.
WS1347 **Blitzima-** **EMEA/H/C/004723/WS1347/0008** **Ritemvia-** **EMEA/H/C/004725/WS1347/0008** **Rituzena-** **EMEA/H/C/004724/WS1347/0009** **Truxima-** **EMEA/H/C/004112/WS1347/0009** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz Request for Supplementary Information adopted on 22.03.2018.	

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

Afinitor - everolimus - EMEA/H/C/001038/II/0058 Novartis Europharm Limited, Rapporteur: Harald Enzmann, “Submission of the final report from study CRAD001Y2201, listed as a category 1 study in the RMP. This is a three arm randomised study investigating the combination of everolimus with exemestane versus everolimus alone versus capecitabine in patients with oestrogen receptor positive metastatic	

breast cancer after recurrence or progression on letrozole or anastrozole. Consequently, Annex II of the Product Information was updated to remove this study."	
Atripla - efavirenz / emtricitabine / tenofovir disoproxil - EMEA/H/C/000797/II/0129 Bristol-Myers Squibb and Gilead Sciences Ltd., Rapporteur: Martina Weise, "Update of sections 4.4 and 4.5 of the Atripla SmPC in order to add drug-drug interaction data based on the final results from study GS-US-342-1167 listed as category 3 study in the RMP; This is a Phase I Study to Evaluate the Pharmacokinetic Drug-Drug Interactions between Sofosbuvir/GS-5815 Fixed Dose Combination (FDC) Tablets and Antiretrovirals Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate (EFV/FTC/TDF; Atripla), Emtricitabine/Riplivirine/Tenofovir Disoproxil Fumarate (FTC/RPV/TDF; Complera), Dolutegravir (DTG; Tivicay) or Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Fumarate (EVG/COBI/FTC/TAF) in Healthy Subjects, Section 2 of the Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10 and minor linguistic amendments to the following languages: BG, CS, ET, HU, LT, LV, RO, SK." Opinion adopted on 17.05.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Brilique - ticagrelor - EMEA/H/C/001241/II/0038 AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.5 of the SmPC in order to include interaction information between morphine and ticagrelor based on the conclusion of the legally binding measure LEG 022; the Package Leaflet is updated accordingly." Opinion adopted on 17.05.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Caprelsa - vandetanib - EMEA/H/C/002315/II/0029 Genzyme Europe BV, Rapporteur: Alexandre Moreau, "Update of section 5.3 of the SmPC to reflect the results from pre-clinical study titled	

"ZD6474: A 104 Week Carcinogenicity Study by Oral Gavage in Rats", study number 521826." Request for Supplementary Information adopted on 22.02.2018.	
Ceplene - histamine dihydrochloride - EMEA/H/C/000796/II/0034, Orphan Noventia Pharma Srl, Rapporteur: Jayne Crowe, "Submission of study report X-03064-3306- to fulfil SOB 002 - A cohort study to follow-up Minimal Residual Disease (MRD) in patients with Acute Myeloid Leukemia (AML) in First Complete Remission (CR1) - Comparison of patients who receive Ceplene/Interleukin-2 as remission maintenance therapy with matched controls." Request for Supplementary Information adopted on 22.03.2018.	See 9.1 in main agenda
Darzalex - daratumumab - EMEA/H/C/004077/II/0013, Orphan Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, "Update of sections 4.4 and 4.8 of the SmPC in order to add the adverse reaction serious infusion-related reactions, including anaphylactic reactions with frequency unknown based on the cumulative review of clinical trial and post-marketing data. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to add a traceability statement to bring the product information in line with the guideline on good pharmacovigilance practices and to add specific text relating to the excipient sodium to align the product information with the updated published EMA EU excipient guideline." Opinion adopted on 03.05.2018. Request for Supplementary Information adopted on 15.03.2018.	Positive Opinion adopted by consensus on 03.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Deltyba - delamanid - EMEA/H/C/002552/II/0021, Orphan Otsuka Novel Products GmbH, Rapporteur: Greg Markey, "Update of sections 4.2, 4.4, 4.8, 4.9, 5.1 and 5.2 of the SmPC to reflect the results of the final study report of 242-09-213 (A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel Group Trial to Evaluate the Safety and Efficacy of Delamanid (OPC-67683) Administered Orally as 200 mg Total Daily Dose for Six Months in Patients With Pulmonary Sputum Culture-positive, Multidrug-resistant	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Tuberculosis), submitted to fulfill SOB-01. The Package leaflet is updated accordingly." Opinion adopted on 17.05.2018. Request for Supplementary Information adopted on 25.01.2018, 14.09.2017.	
Dynastat - parecoxib - EMEA/H/C/000381/II/0072 Pfizer Limited, Rapporteur: Jayne Crowe, "Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to update the information on the use of parecoxib beyond 3 days based on a recent publication on the 'Safety of parecoxib when used for more than 3 days for the management of postoperative pain'; this is an observatory study of the Pfizer clinical trial database to identify randomized, double-blind, placebo controlled trials in which patients could have, potentially, received parecoxib for longer than 3 days for the management of postoperative pain. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the Package Leaflet in line with the SmPC with the inclusion of diazepam and omeprazole in section 2 of the Package Leaflet." Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
Eliquis - apixaban - EMEA/H/C/002148/II/0051 Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.8 of the SmPC in order to reflect all adverse drug reactions for all indications with the correct calculated frequency based on clinical trials data. The package leaflet is updated accordingly." Opinion adopted on 17.05.2018. Request for Supplementary Information adopted on 15.02.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
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."	
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 are updated accordingly"	
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."	
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	Request for supplementary information adopted with a specific timetable.

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.	
Iclusig - ponatinib - EMEA/H/C/002695/II/0045/G, Orphan Incyte Biosciences UK Ltd, Rapporteur: Greg Markey, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to reflect updated safety and efficacy information based on data from final study AP24534-10-201 (PACE) " A Pivotal Phase 2 Trial of Ponatinib (AP24534) in Patients with Refractory Chronic Myeloid Leukemia and Ph+ Acute Lymphoblastic Leukemia" , as well as data from final study AP24534-07-101 "A Phase 1 Dose Escalation Trial to Determine the Safety, Tolerability and Maximum Tolerated Dose of Oral AP24534 in Patients with Refractory or Advanced Chronic Myelogenous Leukemia and other Hematologic Malignancies". The Package Leaflet is updated accordingly."	
Imbruvica - ibrutinib - EMEA/H/C/003791/II/0042, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, "Update of section 5.3 of the SmPC in order to update preclinical safety data information based on final results from a non-clinical carcinogenicity study in mouse (MEA011.1). In addition, the Marketing authorisation holder (MAH) took the opportunity to align the Package leaflet to information already included in the SmPC and to update the list of local representatives for Lithuania, Czech Republic, Netherlands and Portugal in the Package Leaflet."	
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." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 17.05.2018.

Jinarc - tolvaptan -
EMEA/H/C/002788/II/0016
Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey, “Update of sections 4.3 and 4.4 of the SmPC in order to add a contraindication and a warning on hypersensitivity to benzazepine derivatives, thus aligning the product information to the patient population studied in clinical trials and the RMP for Jinarc; the Package Leaflet is updated accordingly.”

Keytruda - pembrolizumab -
EMEA/H/C/003820/II/0044
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, “Update of section 5.1 of the SmPC in order to reflect the final overall survival efficacy data from study Keynote-024; a randomized, open-label phase III trial of pembrolizumab versus platinum based chemotherapy in 1L subjects with PD-L1 strong metastatic non-small cell lung cancer (NSCLC).”

NovoEight - turoctocog alfa -
EMEA/H/C/002719/II/0023
Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus, “Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to reflect data on untreated patients resulting from final results of the Guardian 2 (NN7008-3568) study and the Guardian 4 (NN7008-3809) study for Novoeight. The Package Leaflet was updated accordingly.” Request for Supplementary Information adopted on 22.03.2018.

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.”

Pradaxa - dabigatran etexilate -
EMEA/H/C/000829/II/0111
Boehringer Ingelheim International GmbH, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Doris Stenver, “Update of section 5.1 of the SmPC to reflect the phase II outcome results

from the Global Registry on Long-Term Oral Antithrombotic TReatment In PAtients with Atrial Fibrillation (GLORIA-AF) including the main objective "to collect real-world data on important outcome events of antithrombotic treatments for the prevention of stroke" for patients taking pradaxa. In addition, the results of the Medicare study (P14-15648) are proposed to be included also in section 5.1 with further information on the effectiveness and safety of pradaxa in patients with NVAF (non-valvular atrial fibrillation) in a real-world setting. The RMP (version 35.0) has also been updated to reflect the study results." Request for Supplementary Information adopted on 26.04.2018.	
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." Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
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."	
Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0046 Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, "Update of the PI to align with the company's Core Safety Data Sheet:	Request for supplementary information adopted with a specific timetable.

Update of information related to liver function tests, thrombotic and thromboembolic complications, MDS in the section 4.4; Update of DDI and food interaction information in the sections 4.5 and 5.2; Update of the section 4.8 by: inclusion and removal of ADRs, changes in some ADRs frequencies following pooling of safety data; Reorganisation of the section 5.1 in relation to severe aplastic anaemia; Update of the section 5.3 with information related to Juvenile animal studies. The MAH took the opportunity to make some editorial changes throughout the PI. The Package leaflet is updated accordingly." Request for Supplementary Information adopted on 03.05.2018.	
Samsca - tolvaptan - EMEA/H/C/000980/II/0031 Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey, "Update of sections 4.3 and 4.4 of the SmPC in order to add a contraindication and a warning on hypersensitivity to benzazepine derivatives, thus aligning the product information to the patient population studied in clinical trials and the RMP for Samsca; the Package Leaflet is updated accordingly."	
Simponi - golimumab - EMEA/H/C/000992/II/0079 Janssen Biologics B.V., Rapporteur: Kristina Dunder, "Update of sections 4.2 and 5.1 of the SmPC in order to update the information on maintenance regimen for patients weighing <80 kg based on analyses of PK, efficacy and safety from the pivotal C0524T18 study. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 22.02.2018.	
Stelara - ustekinumab - EMEA/H/C/000958/II/0063 Janssen-Cilag International NV, Rapporteur: Greg MarkeyMargot Martin, "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 22.03.2018.	
Taltz - ixekizumab - EMEA/H/C/003943/II/0018 Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, "Update of section 5.1 of the SmPC, providing a short summary of the results of study RHBQ A Multicenter, Randomized, Double-Blind Study Comparing the Efficacy and Safety of Ixekizumab Versus Placebo in Patients with Moderate-to-Severe Genital Psoriasis."	
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0051/G Biogen Idec Ltd, Rapporteur: Martina Weise, "Submission of the final report from study 109HV114. This is a randomised, open-label, single-dose, crossover study in healthy volunteers to assess the pharmacokinetics of 4 new formulations compared to Tecfidera 240mg capsules. Submission of the final report from study 109MS201 listed as a category 3 study in the RMP. This is an open-label, multicentre study in patients with Relapsing-Remitting Multiple Sclerosis to evaluate the safety and tolerability of 240 mg Tecfidera three times daily administered as add-on therapy to beta interferons (IFNβ) or Glatiramer Acetate (GA). Submission of the synopsis report from study 109MS308. This is a randomised, multicentre, double-blind, placebo-controlled study of the efficacy and safety of Tecfidera in delaying disability progression in patients with secondary progressive multiple sclerosis. Submission of the final report (abbreviated) from study 109MS416. This is a randomised, multicentre, treatment-blinded, parallel group Phase IIIb study aimed to evaluate the effect of 6-week up-titration of Tecfidera treatment on	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

the severity of gastrointestinal adverse effects in patients with multiple sclerosis." Opinion adopted on 17.05.2018.	
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 ADRs 'acute hepatic failure' and 'weight increased' based on post-marketing and clinical trial data. The Package Leaflet has been updated accordingly." Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
Triumeq - dolutegravir / abacavir / 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 ADRs 'acute hepatic failure' and 'weight increased' based on post-marketing and clinical trial data. The Package Leaflet has been updated accordingly." Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
Truvada - emtricitabine / tenofovir disoproxil - EMEA/H/C/000594/II/0147 Gilead Sciences International Limited, 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."	
Zebinix - eslicarbazepine acetate - EMEA/H/C/000988/II/0064 Bial - Portela & Cª, S.A., Rapporteur: Martina Weise, "Update of section 4.8 of the SmPC to add urticaria, angioedema and Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TEN) as adverse drug reactions with unknown frequency, based on recent safety signal evaluation information. The Package Leaflet is updated accordingly. In addition, revision of section 4.4 of the SmPC to align the information on the adverse event angioedema with the information already present in the Package	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Leaflet." Opinion adopted on 17.05.2018. Request for Supplementary Information adopted on 15.03.2018.	
Zykadia - ceritinib - **EMEA/H/C/003819/II/0016** Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.2, 4.4, 4.8 and 5.2 of the SmPC in order to include amendments to the posology in hepatically impaired patients and update the safety information, respectively. The updates are based on the results from the hepatic function Study CLDK378A2110 which evaluated the PK, safety and tolerability of a single oral dose of ceritinib in subjects with varying degrees of impaired hepatic function and results from physiology-based pharmacokinetic (PBPK) modeling at steady-state. Submission of the Report for Study A2110 fulfils MEA 001 for Zykadia." Request for Supplementary Information adopted on 22.03.2018, 14.12.2017, 09.11.2017, 14.09.2017.	
WS1273/G **Effentora-** **EMEA/H/C/000833/WS1273/0047/G** Teva B.V., Lead Rapporteur: Martina Weise, "Update of sections 4.2 and 4.4 of the SmPC in order to add a warning on Hyperalgesia following an internal cumulative review. The Package Leaflet is updated accordingly. Update of sections 4.4 and 4.45 of the SmPC in order to add a warning on the interaction of fentanyl with benzodiazepines or other CNS depressants including alcohol following an internal cumulative review. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce editorial and format changes in the SmPC and PL." Request for Supplementary Information adopted on 22.03.2018, 01.02.2018.	
WS1295 **Advagraf-** **EMEA/H/C/000712/WS1295/0048** **Modigraf-** **EMEA/H/C/000954/WS1295/0026**	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Astellas Pharma Europe B.V., Lead Rapporteur: Jayne Crowe, “Update of section 4.8 of the SmPC in order to add new information on pain in extremity reported as part of calcineurin-inhibitor induced pain syndrome (CIPS). In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor updates throughout the Product Information. The Package Leaflet was updated accordingly.” Opinion adopted on 17.05.2018. Request for Supplementary Information adopted on 15.03.2018.	
WS1316 **Glyxambi-** **EMEA/H/C/003833/WS1316/0011** **Jardiance-** **EMEA/H/C/002677/WS1316/0037** **Synjardy-** **EMEA/H/C/003770/WS1316/0032** Boehringer Ingelheim International GmbH, Lead Rapporteur: Johann Lodewijk Hillege, “Update of section 5.1 of the SmPC for Jardiance, Synjardy and Glyxambi in order to add clinically relevant information on hear failure and microvascular endpoints based on the results from trial 1245.25 (EMPA-REG OUTCOME study). The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to update section 4.4 of the SmPC to align the statement regarding diabetic ketoacidosis for all SGLT-2 Inhibitors.” Request for Supplementary Information adopted on 22.02.2018.	
WS1322 **Genvoya-** **EMEA/H/C/004042/WS1322/0042** **Stribild-EMEA/H/C/002574/WS1322/0090** **Tybost-EMEA/H/C/002572/WS1322/0042** Gilead Sciences International Limited, Lead Rapporteur: Robert James Hemmings, “Update of Section 4.5 of the SmPC for Genvoya, Tybost and Stribild based on data on Drug-drug Interaction between cobicistat containing products and Direct Oral Anticoagulants (DOACs). The Patient Leaflet (PIL) has been updated for all three products as a consequence. The Worksharing MAH has taken this	Request for supplementary information adopted with a specific timetable.

opportunity to introduce some minor administrative amendments throughout the product information for all three products respectively, as needed (i.e., correction of abbreviations, correction of formatting errors and correction of spelling mistakes). Minor administrative update is also made to Annex III for all three products.

The MAH has also taken this opportunity to implement some minor linguistic amendments (MLAs) to the translations of the respective product information annexes:

- Genvoya: CS, DA, DE, FI, HR, HU, IS, NO, PT and RO languages
- Tybost: DA, ES and HU languages
- Stribild: DA, DE, ES, FI, FR, IS, LV, MT, NO and RO languages"

Request for Supplementary Information adopted on 17.05.2018, 22.02.2018.

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."

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.” Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
WS1356/G **Humalog-** **EMEA/H/C/000088/WS1356/0163/G** **Liprolog-** **EMEA/H/C/000393/WS1356/0125/G** Eli Lilly Nederland B.V., Lead Rapporteur: Robert James Hemmings, “B.II.e.5.b: To delete the BASAL presentations: EU/1/96/007/010, 029, 037 and 038 for Humalog Basal and EU/1/01/195/022, 023, 026 and 027 for Liprolog Basal. C.I.4: Update of sections 4.2 and 6.6 of the SmPC of Humalog/Liprolog in pre-filled pens and cartridges to address the PRAC recommendation regarding the potential increased risk of medication error associated with withdrawing insulin from pre-filled pens and cartridges, leading to dysglycaemia.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

In addition, the Worksharing applicant (WSA) took the opportunity to combine all SmPCs resulting in four SmPCs: 100 units/ml presentations, Mix 25 100 units/ml presentations, Mix50 100 units/ml presentations and 200 units/ml presentations. The MAH also brought the product information in line with the latest QRD template version 10, 02/2016, and included the recommendation to only use Lilly insulin cartridges with Lilly reusable pens. Minor editorial changes have been included.
The Package Leaflet and Labelling are updated accordingly."
Opinion adopted on 17.05.2018.
Request for Supplementary Information adopted on 12.04.2018.

WS1359
Invega-EMEA/H/C/000746/WS1359/0059
Trevicta-EMEA/H/C/004066/WS1359/0012
Xeplion-EMEA/H/C/002105/WS1359/0038
Janssen-Cilag International NV, Lead Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC in order to include somnambulism and sleep-related eating disorder under a rare and not know frequency respectively after post marketing reports analysis. The Package Leaflet is updated accordingly.
In addition, for INVEGA/XEPLION/TREVICTA the details of the local representatives in Portugal, Belgium and Luxembourg are updated in the Package Leaflet.
An update is also proposed to the INVEGA Package Leaflet at section 2 to add a standard statement concerning sodium content according to "Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use". Updated wording to align to the Excipients Guideline is also proposed for Risperdal Oral, together with removing the brand name (West Medimop) for the vial adaptors for Risperdal Consta."

WS1362
Enbrel-EMEA/H/C/000262/WS1362/0217
LIFMIOR-EMEA/H/C/004167/WS1362/0014
Pfizer Limited, Lead Rapporteur: Robert James Hemmings, "Submission of the final report from

the study 20050111 listed as category 3 study in the RMP, in order to fulfil Enbrel P46 0134.2. This is a multicentre, open-label extension study to evaluate the long-term safety and efficacy of etanercept in paediatric subjects with moderate to severe plaque psoriasis for up to 264 weeks (or until the quarterly visit after the subject's 18th birthday, whichever comes last) who participated in controlled study 20030211."	
WS1363 **Kisplyx-EMEA/H/C/004224/WS1363/0010** **Lenvima-EMEA/H/C/003727/WS1363/0013** Eisai Europe Ltd., Lead Rapporteur: Bart Van der Schueren, "Update of sections 4.4 and 4.8 of the SmPC to add wound healing and aortic dissection. The PIL is updated accordingly." Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
WS1371 **Rasilez-EMEA/H/C/000780/WS1371/0119** **Rasilez HCT-EMEA/H/C/000964/WS1371/0086** Noden Pharma DAC, Lead Rapporteur: Daniela Melchiorri, "Update of section 4.8 and 5.1 of the Rasilez SmPC and section 4.8 of the Rasilez/HCTZ SmPC in order to reflect the results from paediatric study CSPP100A2365E2 (a multicenter, 52 to 104 week extension study to evaluate the long term growth and development of pediatric hypertensive patients 6–17 years of age treated previously with aliskiren) provided as per the requirement of article 46."	

B.5.3. CHMP-PRAC assessed procedures

Adenuric - febuxostat - EMEA/H/C/000777/II/0047 Menarini International Operations Luxembourg S.A., Rapporteur: Andrea Laslop, PRAC Rapporteur: Jan Neuhauser, "Update of sections 4.4 and 4.5 of the SmPC in order to reflect the results of preclinical study MRPO-2015-PKM-005 "Pharmacokinetic of azathioprine in the rat after one-week daily oral treatment at three different dosages and with the concomitant oral administration of febuxostat or allopurinol" and clinical study REP-POPPK-MRP-2015-PKM-005	

"Population Pharmacokinetic analysis from study titled Pharmacokinetic of azathioprine in the rat after one-week daily oral treatment at three different dosages and with the concomitant oral administration of febuxostat or allopurinol", investigating the drug-drug interaction with azathioprine when co-administered with febuxostat. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to correct the typing errors and to bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 25.01.2018, 14.09.2017.	
Amyvid - florbetapir (18F) - EMEA/H/C/002422/II/0029 Eli Lilly Nederland B.V., Rapporteur: Harald Enzmann, PRAC Rapporteur: Valerie Strassmann, "Submission of the final report from study I6E-MC-AVBF listed as a category 3 study in the RMP. This is a non-interventional category 3 PASS: European Drug Usage Survey for Amyvid to assess the usage pattern of Amyvid in the EU. Section 4.4 of SmPC has been reformatted as result of this study. The RMP version 3.1 has also been submitted." Opinion adopted on 17.05.2018. Request for Supplementary Information adopted on 08.02.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cosentyx - secukinumab - EMEA/H/C/003729/II/0033/G Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, PRAC Rapporteur: Eva A. Segovia, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to include information on dose up-titration for Psoriatic Arthritis (PsA) and update of the radiographic sub-section for Psoriatic Arthritis (PsA) based on results from the 24-week data from study CAIN457F2342, the pooled data from PsA Phase 3 studies, the pooled data from patients who up-titrated their secukinumab dose in studies CAIN457F2306E1, CAIN457F2312 and CAIN457F2318, and long-term study observations which demonstrate higher rates of discontinuation for patients on secukinumab 150 mg compared to patients on secukinumab 300 mg. 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 and to bring the Package leaflet in line with the latest approved SmPC as per procedure (EMEA/H/C/003729/IB/0028). The RMP (v.3.0) has also been updated including suicidal ideation and behavior as an important potential risk in the RMP and including minor administrative/editorial changes (LEG 005.2)."	
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."	
Dificlir - fidaxomicin - EMEA/H/C/002087/II/0032/G Astellas Pharma Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Qun-Ying Yue, "C.I.11.b) Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to update the safety information following final results from the drug utilisation study ANEMONE listed as an additional pharmacovigilance activity in the RMP. 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.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

C.I.3 Update of sections 4.4 and 5.2 of the SmPC in order to update the safety information based on results from the PROFILE study, an open label study designed to evaluate the pharmacokinetics of fidaxomicin in IBD subjects with CD. The Package Leaflet is updated accordingly. The RMP version 9.0 has also been submitted." Opinion adopted on 17.05.2018. Request for Supplementary Information adopted on 30.11.2017.	
Eylea - aflibercept - EMEA/H/C/002392/II/0045 Bayer AG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of sections 4.2 and 5.1 of the SmPC in order to add information for the Health Care Professional related to earlier treatment extension and related increments intervals based on final results from phase 4 study ALTAIR. This is an interventional study evaluating the efficacy and safety of repeated doses of intravitreal (IVT) aflibercept with variable treatment intervals in Japanese subjects with neovascular AMD. The Package Leaflet is updated accordingly. The RMP version 24.1 has also been submitted." Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
Gazyvaro - obinutuzumab - EMEA/H/C/002799/II/0023, Orphan Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Patrick Batty, "Update of section 4.8 and 5.1 of the SmPC in order to update the overall survival data based on final results from study BO21004/CLL11 listed as a category 3 study in the RMP; this is the pivotal study that evaluated the efficacy and safety of obinutuzumab as therapy for patients with previously untreated CLL with comorbidities; The RMP version 4.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity format the listing of "other side effects" and correct the term heart attack to heart failure in section 4 of the Package Leaflet." Opinion adopted on 17.05.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Gilenya - fingolimod - EMEA/H/C/002202/II/0047	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP

Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, “Submission of the CSR for Study D2399, a long-term safety and tolerability study of fingolimod 0.5 mg/day in approximately 5000 patients with relapsing multiple sclerosis.” Opinion adopted on 17.05.2018. Request for Supplementary Information adopted on 08.03.2018.	Members were in agreement with the CHMP recommendation.
Harvoni - ledipasvir / sofosbuvir - EMEA/H/C/003850/II/0064 Gilead Sciences International Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, “Update of section 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to update the safety and efficacy information based on interim results from study GS-US-334-0154 listed as a category 3 study in the RMP; this is a study to evaluate the safety, efficacy and pharmacokinetics of treatment with Ledipasvir/Sofosbuvir Fixed-Dose Combination for 12 weeks in Genotype 1 or 4 HCV-Infected Subjects with Renal Insufficiency; the Package Leaflet is updated accordingly. The RMP version 3.2 has also been submitted.” Request for Supplementary Information adopted on 22.02.2018.	
Invokana - canagliflozin - EMEA/H/C/002649/II/0034 Janssen-Cilag International NV, Rapporteur: Martina Weise, PRAC Rapporteur: Valerie Strassmann, “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 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 17.05.2018.	Request for supplementary information adopted with a specific timetable.
OFEV - nintedanib - EMEA/H/C/003821/II/0018/G, Orphan Boehringer Ingelheim International GmbH, Rapporteur: Jayne Crowe, PRAC Rapporteur: Nikica Mirošević Skvrce, "Update of section 4.4 in order to amend the current warning on co-administration with pirfenidone and update of section 5.1 to include the results of study 1199.222, a phase IV, 12 week, open label, randomised, parallel group study to evaluate the safety, tolerability and pharmacokinetics of oral nintedanib in combination with oral pirfenidone in comparison with nintedanib alone in patients with idiopathic pulmonary disease (IPF). The Package Leaflet is updated accordingly. Update of section 5.2 of the SmPC in order to include the results of study 1199.229, a phase IV, open label, multi-dose, 2 groups study to investigate the drug-drug interaction between nintedanib anfd pirfenidone in patients with IPF, a category 3 study in the RMP. The RMP version 5.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement some corrections to the French and Swedish translations." Opinion adopted on 17.05.2018. Request for Supplementary Information adopted on 08.03.2018, 11.01.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Oncaspar - pegaspargase - EMEA/H/C/003789/II/0016/G	Request for supplementary information adopted with a specific timetable.

Baxalta Innovations GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Patrick Batty, “Update of sections 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.1 5.2 and 5.3 of the SmPC with the final results from studies DFCI 11-001 and AALL07P4 listed as category 3 studies in the RMP; Study DFCI 11-001 is a Phase 2, open-label, randomized, multicenter study to determine the safety and feasibility of administering an investigational asparaginase product (asparaginase formulation) compared with Oncaspar in subjects aged 1 to <22 years with newly diagnosed ALL and lymphoblastic lymphoma. Study AALL07P4 is a multicenter, open label, randomized, active-controlled, parallel design clinical pilot study conducted to evaluate the PK, pharmacodynamics, safety, immunogenicity and efficacy of an investigational asparaginase product in comparison with Oncaspar in patients aged 1 to <31 years newly diagnosed with high risk B-precursor ALL. The Package Leaflet is proposed to be updated accordingly. The RMP version 3.0 has also been submitted.” Request for Supplementary Information adopted on 17.05.2018.	
Ozempic - semaglutide - EMEA/H/C/004174/II/0002/G Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Qun-Ying Yue	
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 editorial changes in line with the QRD	Request for supplementary information adopted with a specific timetable.

template." Request for Supplementary Information adopted on 17.05.2018, 11.01.2018.	
Revlimid - lenalidomide - EMEA/H/C/000717/II/0098, Orphan Celgene Europe Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of section 4.4 of the SmPC and of the Annex II key elements of the risk minimisation programme with information on prescription duration and to revise due dates of the PASS CC-5013-MDS-10 and 12; furthermore, the RMP version 35.1 has been revised in line with the updated Guideline on Good Pharmacovigilance Practices (GVP) Module V to propose the reclassification and/or renaming of known safety concerns associated with the use of lenalidomide. Consequently, Annex IID has been updated accordingly also to remove activities deemed not to belong to the risk minimisation measures. In addition, the labelling information related to the pregnancy prevention has been updated in line with other products in the class. Minor editorial changes have also been introduced throughout the PI." Opinion adopted on 17.05.2018. Request for Supplementary Information adopted on 12.04.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
TAGRISSO - osimertinib - EMEA/H/C/004124/II/0021 AstraZeneca AB, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Sabine Straus, "Update of SmPC sections 4.5, 4.6 and 5.2 to reflect the results of Study D5160C00036, undertaken to assess the effect of single and multiple oral doses of osimertinib on the pharmacokinetics of a P-glycoprotein probe drug (Fexofenadine) in patients with advanced EGFRm NSCLC that have progressed on a prior EGFR-TKI regimen. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make a minor correction in Annex II and to implement minor editorial and/or QRD-template related changes in the SmPC and Package Leaflet. A revised RMP version 9 was provided as part of the application." Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.

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 9 was provided as part of the application." Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
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. 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 17.05.2018, 08.03.2018.	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 25.01.2018.	
Zelboraf - vemurafenib - EMEA/H/C/002409/II/0048/G Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of the SmPC section 5.2 with the information on mean bioavailability of vemurafenib at steady state together with information on renal elimination based on the phase I study GO28395. Submission of the CSR from the study GO27826: A Phase III, Randomised, Double-Blind, Placebo-Controlled Study of Vemurafenib (RO5185426) Adjuvant Therapy in Patients with Surgically Resected, Cutaneous BRAF-Mutant Melanoma at High Risk for Recurrence. Minor editorial changes have been included in the PI. The RMP version 11.0 has also been updated." Opinion adopted on 17.05.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1312 **Prezista-** **EMEA/H/C/000707/WS1312/0093** **Rezolsta-** **EMEA/H/C/002819/WS1312/0023** **Symtuza-** **EMEA/H/C/004391/WS1312/0005** Janssen-Cilag International NV, Lead	

Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, “Update of sections 4.2, 4.4, 4.6, 5.1 and 5.2 of the SmPCs for Prezista, Rezolsta and Symtuza to reflect the data of the category 3 study TMC114HIV3015 in HIV-1 infected pregnant women. The PL of Symtuza is also updated. Updated RMPs (version 25.3 for Prezista, 4.3 for Rezolsta and 2.1 for Symtuza) are proposed accordingly. In addition, the MAH took the opportunity to implement the template version 2 for the Prezista and Rezolsta RMPs, removal of the fulfilled category 4 DAD study from the Prezista and Rezolsta RMPs, removal of observational study on growth in children and ‘growth abnormalities in the paediatric population’ as important potential risk in the Prezista RMP and addition of the missing information ‘Safety in patients with cardiac conduction disorders’ in the Rezolsta RMP (alignement with Tybost RMP).” Request for Supplementary Information adopted on 22.03.2018.	
WS1333 **Blitzima-** **EMEA/H/C/004723/WS1333/0007** **Ritemvia-** **EMEA/H/C/004725/WS1333/0007** **Rituzena-** **EMEA/H/C/004724/WS1333/0008** **Truxima-** **EMEA/H/C/004112/WS1333/0008** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz, Lead PRAC Rapporteur: Doris Stenver, “Submission of the clinical study report (CSR) of final results (up to 76 weeks) of Study CT-P10 3.2. In addition, results up to Week 24 of Study CT-P10 3.3 (corresponding CSR submitted in D180 update [SN0004] are updated in this variation.” Request for Supplementary Information adopted on 08.03.2018.	
WS1349/G **Gardasil-** **EMEA/H/C/000703/WS1349/0076/G** **Silgard-** **EMEA/H/C/000732/WS1349/0064/G** MSD Vaccins, Lead Rapporteur: Kristina Dunder, Lead PRAC Rapporteur: Qun-Ying Yue, “Update	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

of section 5.1 of the SmPC in order to update the information following final results from two Long-term follow-up (LTFU) studies: - Protocol V501-020-21, a category 3 study part of the pharmacovigilance activities foreseen in the Risk Management Plan (RMP) of the qHPV vaccine. It is an extension of study V501-020 (the pivotal efficacy study of qHPV vaccine in young men 16 to 26 years of age) to assess effectiveness and immunogenicity of the qHPV vaccine for up to 10 years of follow-up. Submission of this final report fulfils Gardasil MEA 070.3 and Silgard MEA 069.3. - Extension of Protocol V501-16. The base study was an MSD-sponsored randomized clinical trial that assessed the immunogenicity of a 2 dose Schedule of the qHPV in adolescents 9 to 13 years of age compared to a 3-dose schedule in young women16 to 26 years of age. The study provides additional immunogenicity follow-up through 5 years post-vaccination. Submission of this study fulfils Gardasil REC 083 and Silgard REC 080. RMP version 12 has also been submitted, updated to to reflect completion of the above-mentioned category 3 study. In addition, the Worksharing applicant (WSA) took the opportunity to bring the PI in line with the latest QRD template version 10 and to amend the details of one local representative in the package leaflet." Opinion adopted on 17.05.2018.	

B.5.4. PRAC assessed procedures

PRAC Led **Bronchitol - mannitol - EMEA/H/C/001252/II/0031, Orphan** Pharmaxis Pharmaceuticals Limited, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Robert James Hemmings, "Submission of the final report of a survey of healthcare professionals to measure to the effectiveness of the communication of risk minimisation messages in the educational materials at 6 months post-launch and 6 months post-redistribution of the revised healthcare	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

professional leaflet. The RMP version 7.0 has also been approved." Opinion adopted on 17.05.2018. Request for Supplementary Information adopted on 12.04.2018.	
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." Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **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." Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Renvela - sevelamer carbonate - EMEA/H/C/000993/II/0043** Genzyme Europe BV, PRAC Rapporteur: Laurence de Fays, PRAC-CHMP liaison: Bart Van der Schueren, "Submission of the final report from study SEVELC08371. This was a historical cohort study of adult patients with severe chronic kidney disease assessing the risk of bladder cancer by sevelamer exposure." Opinion adopted on 17.05.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Suboxone - buprenorphine / naloxone - EMEA/H/C/000697/II/0037** Indivior UK Limited, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "C.I.13: Submission of	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

the final report for study PEUS005" SUBOXONE mortality study in the UK with The Health Improvement Network Database (THIN)". This is a PASS to estimate the all-cause mortality among patients exposed to SUBOXONE in comparison to buprenorphine and methadone. RMP version 13.0 has been submitted." Opinion adopted on 17.05.2018.	
PRAC Led **Sycrest - asenapine - EMEA/H/C/001177/II/0031/G** N.V. Organon, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "Submission of the final reports from studies P08307 (EP04026.001), P08308 (EP04026.003), P08309 (EP04026.002) and P08310 (EP04026.004) listed as a category 3 studies in the RMP. They are observational studies with the aim to assess safety and utilisation of asenapine in different contexts. No changes in the PI are proposed. The RMP (version 5.1) is updated accordingly." Opinion adopted on 17.05.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **TAGRISSO - osimertinib - EMEA/H/C/004124/II/0022** 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 D5165C00001 (CAURAL) from the Pharmacovigilance Plan." Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
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." Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.

PRAC Led **WS1270** **Enbrel-EMEA/H/C/000262/WS1270/0216** **LIFMIOR-** **EMEA/H/C/004167/WS1270/0013** Pfizer Limited, Lead Rapporteur: Robert James Hemmings, Lead PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Robert James Hemmings, "Submission of the final report from study B1801396, a non-interventional PASS listed as a category 3 study in the RMP. This is a non-interventional, population-based, multi-country, observational cohort register study to evaluate the risk of adverse pregnancy outcomes in patients with rheumatoid arthritis and related inflammatory diseases, who were treated with etanercept compared to patients with the same diseases of interest who were treated with non-biologic systemic drugs, but without etanercept or other biologics during pregnancy, using merged data from Sweden, Denmark and Finland." Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **WS1326** **Truvada-** **EMEA/H/C/000594/WS1326/0145** **Viread-EMEA/H/C/000419/WS1326/0184** Gilead Sciences International Limited, Lead Rapporteur: Joseph Emmerich, Lead PRAC Rapporteur: Caroline Laborde, PRAC-CHMP liaison: Joseph Emmerich, "Submission of the final report from study GS-EU-104-0433, listed as a category 3 study in the RMP. This is an observational, drug utilisation study of Viread in children and adolescents with HIV-1 infection, in fulfilment of a post-authorisation measure (PAM) for Viread (MEA 46) and Truvada (MEA 276)." Opinion adopted on 17.05.2018. Request for Supplementary Information adopted on 08.03.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1364** **Lyrica-EMEA/H/C/000546/WS1364/0092** **Pregabalin Pfizer-** **EMEA/H/C/003880/WS1364/0021** Pfizer Limited, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Sabine	Request for supplementary information adopted with a specific timetable.

Straus, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of an updated RMP version 12.0 in order to include the changes proposed by EMEA/H/C/PSUSA/00002511/201701, updating the safety specifications and risk minimisation measures. The pharmacovigilance plan has also been updated. The draft protocol for non-interventional non-imposed PASS (A0081359) titled “A population-based cohort study of Pregabalin to characterize pregnancy outcomes” has been submitted. The MAH has taken the opportunity to include minor updates and to align the RMP to template revision 2.” Request for Supplementary Information adopted on 17.05.2018.	

B.5.5. CHMP-CAT assessed procedures

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0020, ATMP Amgen Europe B.V., Rapporteur: Olli Tenhunen, “Update of section 4.8 of the SmPC in order to add the new ADR ‘hypersensitivity’ with a frequency allocation of ‘unknown’. The Package Leaflet is updated accordingly. Further, the MAH is implementing a minor editorial change in section 3 of the SmPC in order to clarify that the current description of the liquid applies to both strengths, and minor changes in section 4.4 of the SmPC and the Package Leaflet regarding sorbitol and sodium subsequent to the revised Annex to the EC guideline on excipients in the labelling (EMA/CHMP/302620/2017). In addition, the MAH took the opportunity to update the contact details of the local representative in Slovenia in the Package Leaflet.”	
Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0002/G, ATMP CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder, , “Update of sections 4.2, 4.7, 4.8 and 5.1, of the SmPC in order to revise the wording and to update the safety and efficacy information based on the interim results from studies 16 HS 13 (24-month follow-up data) and 16 HS 14 (48-month follow-up data); the Package leaflet is updated	

accordingly. Study 16 HS 13 is listed as a specific obligation post-authorisation efficacy study (PAES) in Annex II. It is a phase III, randomised, open label study aimed to evaluate the long-term efficacy and safety of Spherox vs. microfracture in patients with cartilage defects of the knee with a defect size between 1 and 4 cm2. Study 16 HS 14 is listed as a category 3 study in the RMP. It is a phase II, randomised, open label study, aimed to evaluate the efficacy and safety of the treatment of large defects (4-10 cm^2) with 3 different doses of Spherox (ACT3D-CS) in subjects with cartilage defects of the knee." 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

WS1320/G **Tivicay-** **EMEA/H/C/002753/WS1320/0035/G** **Triumeq-** **EMEA/H/C/002754/WS1320/0054/G** ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson Opinion adopted on 17.05.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1324/G **Afinitor-** **EMEA/H/C/001038/WS1324/0056/G** **Votubia-** **EMEA/H/C/002311/WS1324/0050/G** Novartis Europharm Limited, Lead Rapporteur: Harald Enzmann Request for Supplementary Information adopted on 03.05.2018.	Request for supplementary information adopted with a specific timetable.
WS1352/G **Corlentor-** **EMEA/H/C/000598/WS1352/0049/G** **Ivabradine Anpharm-** **EMEA/H/C/004187/WS1352/0008/G** **Procoralan-**	Positive Opinion adopted by consensus on 03.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

EMEA/H/C/000597/WS1352/0048/G Les Laboratoires Servier, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 03.05.2018.	
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 Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
WS1360 **Zutectra-** **EMEA/H/C/001089/WS1360/0035** Biotest Pharma GmbH, Lead Rapporteur: Jan Mueller-Berghaus, “To harmonise section 4.8 of the SmPC following the PRAC Rapporteur's recommendation provided during the PSUSA PRAC Assessment Report (EMEA/H/C/PSUSA/00001631/201611). In addition, the MAH took the opportunity to update Annex II and Annex IIIA according to latest QRD template v 10.0. Finally, the contact details of the MAH in section 7 and of the SmPC and in the PL and the contact details for the HR local representative in the PL were updated.” Opinion adopted on 17.05.2018. Request for Supplementary Information adopted on 15.03.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1368/G **Aflunov-** **EMEA/H/C/002094/WS1368/0043/G** **Foclivia-** **EMEA/H/C/001208/WS1368/0037/G** Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 17.05.2018.	Request for supplementary information adopted with a specific timetable.
WS1378 **Blitzima-** **EMEA/H/C/004723/WS1378/0011** **Ritemvia-** **EMEA/H/C/004725/WS1378/0011** **Rituzena-** **EMEA/H/C/004724/WS1378/0012**	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Truxima- **EMEA/H/C/004112/WS1378/0012** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz, “B.II.f.1.b.5 - Extension of the shelf life of the finished product of Truxima, Blitzima, Rituzena and Ritemvia for 100 mg presentation from 24 months to 30 months and 500 mg presentation from 36 months to 48 months.” Opinion adopted on 17.05.2018.	
WS1379 **Blitzima-** **EMEA/H/C/004723/WS1379/0012** **Ritemvia-** **EMEA/H/C/004725/WS1379/0012** **Rituzena-** **EMEA/H/C/004724/WS1379/0013** **Truxima-** **EMEA/H/C/004112/WS1379/0013** Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz Opinion adopted on 17.05.2018.	Positive Opinion adopted by consensus on 17.05.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1386 **Competact-** **EMEA/H/C/000655/WS1386/0070** **Glubrava-** **EMEA/H/C/000893/WS1386/0057** Takeda Pharma A/S, Lead Rapporteur: Peter Kiely Specification.”	
WS1388/G **Actos-** **EMEA/H/C/000285/WS1388/0079/G** **Competact-** **EMEA/H/C/000655/WS1388/0069/G** **Glubrava-** **EMEA/H/C/000893/WS1388/0056/G** **Glustin-** **EMEA/H/C/000286/WS1388/0078/G** **Tandemact-** **EMEA/H/C/000680/WS1388/0057/G** Takeda Pharma A/S, Lead Rapporteur: Peter Kiely,	

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

Zinplava - bezlotoxumab - **EMEA/H/C/004136/II/0010** Merck Sharp & Dohme Limited, Rapporteur: Jan Mueller-Berghaus	The MAH withdrew the procedure on 09.05.2018.

Withdrawal request submitted on 09.05.2018.

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

febuxostat - EMEA/H/C/004773
, treatment of hyperuricaemia,

silodosin - EMEA/H/C/004964
, treatment of prostatic hyperplasia (BPH),

crisaborole - EMEA/H/C/004863
, treatment of mild to moderate atopic dermatitis

talazoparib - EMEA/H/C/004674
, for the treatment of adult patients with germline breast cancer susceptibility gene (BRCA) mutated human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer.

treprostinil - EMEA/H/C/004847, Orphan
SciPharm Sarl, Treatment of chronic thromboembolic pulmonary hypertension

ulipristal acetate - EMEA/H/C/005017
, treatment of uterine fibroids,

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

Trisenox - arsenic trioxide - EMEA/H/C/000388/X/0068
Teva B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, “Extension application to add a new strength of 2 mg/ml (concentrate for solution for solution for infusion) in vials.
The RMP (version 2.0) is updated accordingly.”

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

buprenorphine - EMEA/H/C/004651
, treatment of opioid dependence within a framework of medical, social and psychological treatment

List of Questions adopted on 25.01.2018.

doravirine - EMEA/H/C/004747
, treatment of adults infected with HIV-1 without past or present evidence of viral resistance to treatment of adults infected with HIV-1 without past or present evidence of viral resistance to doravirine
List of Questions adopted on 22.03.2018.

doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746
, treatment of adults infected with HIV-1 without past or present evidence of viral resistance to doravirine, lamivudine, or tenofovir
List of Questions adopted on 22.03.2018.

galcanezumab - EMEA/H/C/004648
, prophylaxis of migraine
List of Questions adopted on 22.03.2018.

damoctocog alfa pegol - EMEA/H/C/004054, Orphan
Bayer AG, Treatment and prophylaxis of haemophilia A
List of Questions adopted on 25.01.2018.

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)
List of Questions adopted on 16.03.2018.

pegfilgrastim - EMEA/H/C/004700
, treatment of neutropenia
List of Questions adopted on 25.01.2018.

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

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,

Qarziba - dinutuximab beta -

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

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

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

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

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

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

Sovaldi - sofosbuvir -
EMEA/H/C/002798/R/0050
Gilead Sciences International Limited, 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

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

Venclyxto - venetoclax -
EMEA/H/C/004106/R/0013, Orphan
AbbVie Limited, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty

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

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

Coagadex - human coagulation factor X -
EMEA/H/C/003855/II/0007, Orphan
Bio Products Laboratory Limited, Rapporteur: Andrea Laslop, PRAC Rapporteur: Julie Williams, "Update of section 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."

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

Roche Registration GmbH, Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Amelia Cupelli, "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)

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, "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."	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0052 Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Restriction of the currently authorised indication in cisplatin-ineligible urothelial carcinoma patients to exclude patients whose tumors express PD-L1 CPS<10, as well as to exclude only the patients who have 1 or more risk factors predicting a worse outcome. Section 4.1 of the SmPC has been revised accordingly."	See 5.1 main agenda
NovoSeven - eptacog alfa (activated) - EMEA/H/C/000074/II/0104 Novo Nordisk A/S, Rapporteur: Paula Boudewina van Hennik, Co-Rapporteur: Nithyanandan Nagercoil, "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."	
Revolade - eltrombopag / eltrombopag olamine - EMEA/H/C/001110/II/0049 Novartis Europharm Limited, Rapporteur:	

Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, “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.”

WS1372
OPDIVO-
EMEA/H/C/003985/WS1372/0053
Yervoy-EMEA/H/C/002213/WS1372/0057
Bristol-Myers Squibb Pharma EEIG, Lead Rapporteur: Jorge Camarero Jiménez, Lead Co-Rapporteur: Paula Boudewina van Hennik, Lead PRAC Rapporteur: Brigitte Keller-Stanislawski, “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.”

B.6.8. 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

Circadin - melatonin -
EMEA/H/C/000695/II/0053/G
RAD Neurim Pharmaceuticals EEC Ltd., Rapporteur: Bruno Sepodes

Cyramza - ramucirumab -
EMEA/H/C/002829/II/0025
Eli Lilly Nederland B.V., Rapporteur: Paula

Boudewina van Hennik

Dacogen - decitabine -
EMEA/H/C/002221/II/0034/G, Orphan
Janssen-Cilag International N.V., Rapporteur:
Alexandre Moreau

Dupixent - dupilumab -
EMEA/H/C/004390/II/0006/G
sanofi-aventis groupe, Rapporteur: Jan Mueller-
Berghaus

Episalvan - birch bark extract -
EMEA/H/C/003938/II/0010
Amryt AG, Rapporteur: Kristina Dunder

Evicel - human fibrinogen / human
thrombin - EMEA/H/C/000898/II/0059
Omrix Biopharmaceuticals N. V., Rapporteur:
Jan Mueller-Berghaus

Gazyvaro - obinutuzumab -
EMEA/H/C/002799/II/0028, Orphan
Roche Registration GmbH, Rapporteur: Sinan B.
Sarac

Gliolan - aminolevulinic acid -
EMEA/H/C/000744/II/0015
medac Gesellschaft fur klinische
Spezialpraparate mbH, Rapporteur: Bruno
Sepodes

Herzuma - trastuzumab -
EMEA/H/C/002575/II/0006
Celltrion Healthcare Hungary Kft., Rapporteur:
Jan Mueller-Berghaus, PRAC Rapporteur:
Brigitte Keller-Stanislawski

Keytruda - pembrolizumab -
EMEA/H/C/003820/II/0051/G
Merck Sharp & Dohme B.V., Rapporteur:
Daniela Melchiorri

Kineret - anakinra -
EMEA/H/C/000363/II/0060
Swedish Orphan Biovitrum AB (publ),
Rapporteur: Mark Ainsworth

Litak - cladribine -
EMEA/H/C/000504/II/0015
Lipomed GmbH, Rapporteur: Robert James
Hemmings

NovoEight - turoctocog alfa -
EMEA/H/C/002719/II/0026/G
Novo Nordisk A/S, Rapporteur: Jan Mueller-

Berghaus

Olanzapine Apotex - olanzapine - EMEA/H/C/001178/II/0034
Apotex Europe BV, Generic, Generic of Zyprexa, Rapporteur: John Joseph Borg

Rekovelle - follitropin delta - EMEA/H/C/003994/II/0008/G
Ferring Pharmaceuticals A/S, Rapporteur: Joseph Emmerich

Repatha - evolocumab - EMEA/H/C/003766/II/0026/G
Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege

Respreeza - human alpha1-proteinase inhibitor - EMEA/H/C/002739/II/0023/G
CSL Behring GmbH, Rapporteur: Kristina Dunder

Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0001
GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren

Strensiq - asfotase alfa - EMEA/H/C/003794/II/0030/G, Orphan
Alexion Europe SAS, Rapporteur: Greg Markey

Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0126
GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder

Synflorix - pneumococcal polysaccharide conjugate vaccine (adsorbed) - EMEA/H/C/000973/II/0127/G
GlaxoSmithkline Biologicals SA, Rapporteur: Kristina Dunder

Trumenba - meningococcal group B vaccine (recombinant, adsorbed) - EMEA/H/C/004051/II/0008
Pfizer Limited, Rapporteur: Johann Lodewijk Hillege

Yervoy - ipilimumab - EMEA/H/C/002213/II/0058/G
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik

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

WS1404
Nuwiq-EMEA/H/C/002813/WS1404/0022
Vihuma-
EMEA/H/C/004459/WS1404/0004
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus

B.6.9. 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 in order to introduce pre-clinical safety information regarding the excretion of paclitaxel metabolites into the milk of lactating rats as well as an effect on male and female fertility of rats based on a review of the available literature.”

Cayston - aztreonam -
EMEA/H/C/000996/II/0073, Orphan
Gilead Sciences International Limited, 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 Product Information to reduce the risk of medication errors. 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."

Genvoya - elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004042/II/0046

Gilead Sciences International Limited, Rapporteur: Robert James Hemmings, "Update of sections 4.8 and 5.1of the SmPC for Genvoya in order to amend the safety and pharmacodynamic information based on the final results from study Study GS-US-292-1515, listed as a category 3 study in the RMP; this is A Phase 2/3, Open-Label Study to Evaluate the Safety and Efficacy of E/C/F/TAF in HIV-1 Infected Virologically Suppressed Adolescents.

The MAH also took the opportunity to make administrative updates to Section 4.5 and 5.1 of the SmPC."

Giotrif - afatinib - EMEA/H/C/002280/II/0028

Boehringer Ingelheim International GmbH, Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to update the efficacy section with data in EGFR TKI-naïve NSCLC patients whose tumours harbour uncommon EGFR mutations based on a meta-analysis across three trials (1200.22, 1200.32 and 1200.34). In addition, the Marketing authorisation holder (MAH) took the opportunity to implement minor linguistic amendments to the translations of the product information annexes: BG, CZ, DE, DK, FI, IS, IT, NO, PT, SE and SK."

Jinarc - tolvaptan - EMEA/H/C/002788/II/0016

Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey, "Update of sections 4.3 and 4.4 of the SmPC in order to add a contraindication and a warning on hypersensitivity to benzazepine derivatives, thus aligning the product information to the patient population studied in clinical trials and the RMP for Jinarc; the Package Leaflet is updated accordingly."

Keytruda - pembrolizumab - EMEA/H/C/003820/II/0048

Merck Sharp & Dohme B.V., Rapporteur:

Daniela Melchiorri, “Update of sections 4.2, 5.1 and 5.3 of the SmPC in order to align the posology of Keytruda for the melanoma -and 2nd line NSCLC indications to a 200 mg Q3W fixed dose regimen already approved for more recent indications (1st line NSCLC, classical Hodgkin lymphoma and urothelial carcinoma) based on the available overall PK and exposure data. The Package Leaflet has 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.”

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.”

Lokelma - sodium zirconium cyclosilicate - EMEA/H/C/004029/II/0003/G

AstraZeneca AB, Rapporteur: Romaldas Mačiulaitis, “1) type II (C.I.4): Update of sections 4.8 and 5.1 of the SmPC in order to update the information based on final results from study ZS-005 (category 3 PASS study in the RMP). This is an open-label, multicentre, multi-dose, prospective maintenance study to investigate the long-term safety and efficacy of Lokelma (sodium zirconium cyclosilicate) in subjects with hyperkalaemia.
2) type II (C.I.4): Update of section 4.5 of the SmPC in order to add information regarding the use with drugs that have the potential for drug-drug interaction based on an increase in gastric PH.
The Package Leaflet has been updated accordingly.”

Orgalutran - ganirelix - EMEA/H/C/000274/II/0041

Merck Sharp & Dohme Limited, 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."

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."

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 MEA012."

Samsca - tolvaptan - EMEA/H/C/000980/II/0031

Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey, "Update of sections 4.3 and 4.4 of

the SmPC in order to add a contraindication and a warning on hypersensitivity to benzazepine derivatives, thus aligning the product information to the patient population studied in clinical trials and the RMP for Samsca; the Package Leaflet is updated accordingly."

Saxenda - liraglutide - EMEA/H/C/003780/II/0018

Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.8 and 5.2 of the SmPC in order to update the safety information based on the conclusions of the assessment of Clinical trial reports NN8022-3967 and NN8022-4181, previously submitted in accordance with Article 46 of Regulation (EC) No1901/2006, as amended, and assessed by the CHMP (P46 016)."

Soliris - eculizumab - EMEA/H/C/000791/II/0103, Orphan

Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez, "To update SmPC section 4.4 describing reports of serious infections with Neisseria species (other than Neisseria meningitidis), including disseminated gonococcal infections, SmPC section 4.5 describing the theoretical potential for drug-drug interaction between eculizumab and intravenous human immunoglobulin (IVIg), SmpC section 4.6 clarifying that there is currently insufficient data to adequately characterize the safety of eculizumab in pregnant women with refractory gMG and SmPC section 4.8, clarifying sepsis as the most common presentation of Neisseria meningococcal infections. The annex II and the package leaflet are updated accordingly. The MAH took the opportunity to align the Product information with the QRD template."

Somavert - pegvisomant - 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."

Stocrin - efavirenz - EMEA/H/C/000250/II/0114

Merck Sharp & Dohme Limited, Duplicate, Duplicate of Sustiva, Rapporteur: Bruno Sepodes, "Update of sections 4.3 and 4.5 of the SmPC in order to add contraindication with elbasvir/grazoprevir and to update information on interactions between efavirenz and elbasvir/grazoprevir, sofosbuvir/velpatasvir, sofosbuvir/velpatasvir/voxilaprevir, and etonogestrel implant; based on the post-approval and literature data. The Package Leaflet is updated accordingly."

Strensiq - asfotase alfa - EMEA/H/C/003794/II/0029, Orphan

Alexion Europe SAS, Rapporteur: Greg Markey, "Update of annex II after submission of the final report from study AA-HPP-208 listed as a category 1 study in the RMP (ANX001.2). This is a multicentre, randomized, open-label, Phase 2a study of Strensiq in patients with hypophosphatasia."

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."

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."

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.”

Venclyxto - venetoclax - EMEA/H/C/004106/II/0011, Orphan

AbbVie Limited, Rapporteur: Filip Josephson, “Submission of the interim report from study M14-032 a phase II open-label study investigating efficacy and safety of venetoclax in patients with CLL with relapse or refractory to B-cell receptor signalling pathway inhibitor therapy, listed as a category 2 study in the RMP.

Consequently, the remaining SOB is fulfilled and Annex II E is updated accordingly.”

Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/II/0047

AbbVie Limited, 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.”

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.”

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.”

WS1400
Exviera-EMEA/H/C/003837/WS1400/0039
Viekirax-
EMEA/H/C/003839/WS1400/0046
AbbVie Limited, 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 Hepatitis C Virus (HCV) Infection, listed as a category 3 study in the RMP."

WS1401
Genvoya-
EMEA/H/C/004042/WS1401/0047
Stribild-EMEA/H/C/002574/WS1401/0094
Tybost-EMEA/H/C/002572/WS1401/0044
Gilead Sciences International Limited, 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."

B.6.10. CHMP-PRAC assessed procedures

Bydureon - exenatide -
EMEA/H/C/002020/II/0050
AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "Update of sections 4.1, 4.2, 4.4 and 5.1 of the SmPC based on the final CSR of study EXSCEL (EXenatide Study of Cardiovascular Event Lowering; 'A randomized, placebo controlled clinical trial to evaluate cardiovascular outcomes after treatment with exanatide once weekly in patients with type 2 diabetes mellitus ') in fulfilment of PAM (LEG 009). The Package Leaflet is updated accordingly. In addition, RMP version 31 has been submitted as part of this application."

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."

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."

Soliris - eculizumab - EMEA/H/C/000791/II/0102, Orphan
Alexion Europe SAS, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Eva A. Segovia, "Submission of the Clinical Study Report of the study C11-003 listed as Cat 3 study in the RMP. This is an observational, multi-center, multinational long term follow up study of atypical hemolytic uremic syndrome (aHUS) patients treated with eculizumab in a prior clinical study. The Risk Management Plan is updated to version 18 with: The new EU format, the proposal to remove the missing information "Long term safety in aHUS patients", the proposal to align the frequency of the submission of the reports on the HCP survey, the controlled distribution and the aHUS registry to the PSUR submission every 2 years."

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."

Tremfya - guselkumab -
EMEA/H/C/004271/II/0002/G
Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski

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."

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, 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)"

B.6.11. PRAC assessed procedures

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."

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 8.0). 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, Change in meningococcal epidemiology/serogroup replacement, Lack of efficacy, 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 pregnancy and lactation."

PRAC Led

Volibris - ambrisentan -

EMEA/H/C/000839/II/0055, Orphan

Glaxo Group Ltd, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Dolores Montero Corominas, PRAC-CHMP liaison: Concepcion 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."

PRAC Led

Zavesca - miglustat -

EMEA/H/C/000435/II/0062/G, Orphan

Actelion Registration Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, 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)"

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.”

B.6.12. CHMP-CAT assessed procedures

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

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

WS1377/G
Infanrix hexa-
EMEA/H/C/000296/WS1377/0241/G
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

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

WS1395
Fluenz Tetra-
EMEA/H/C/002617/WS1395/0081
Pandemic influenza vaccine H5N1
AstraZeneca-
EMEA/H/C/003963/WS1395/0014
AstraZeneca AB, 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

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 28-31 May 2018 CHMP plenary:

G.3.2. List of procedures starting in May 2018 for June 2018 CHMP adoption of outcomes

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