23 April 2018
EMA/CHMP/181307/2018
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Draft agenda for the meeting on 23-26 April 2018

Chair: Tomas Salmonson – Vice-Chair: Harald Enzmann

23 April 2018, 13:00 – 19:30, room 2A

24 April 2018, 08:30 – 19:30, room 2A

25 April 2018, 08:30 – 19:30, room 2A

26 April 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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
Send a question via our website www.ema.europa.eu/contact

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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 23-26 April 2018. See April 2018 CHMP minutes (to be published post May 2018 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 23-26 April 2018

1.3. Adoption of the minutes

CHMP minutes for 19-22 March 2018.

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. erenumab - EMEA/H/C/004447

indicated for prophylaxis of migraine in adults

Scope: Oral explanation

Action: Oral explanation to be held on 24 April 2018 at time 11.00

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

See 3.2

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

Oasmia Pharmaceutical AB; treatment of ovarian cancer

Scope: Oral explanation

Action: Oral explanation to be held on 24 April 2018 at time 09.00

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

See 3.2

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

AVI Biopharma International Ltd; treatment of Duchenne muscular dystrophy

Scope: Oral explanation

Action: Oral explanation to be held on 24 April 2018 at time 14.00

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

See 3.1

2.1.4. 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: Oral explanation

Action: Oral explanation to be held on 25 April 2018 at time 11.00

List of Outstanding Issues adopted on 22.02.2018.

See 3.2

2.1.5. 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: Oral explanation

Action: Oral explanation to be held on 25 April 2018 at time 11.00

List of Outstanding Issues adopted on 22.02.2018.

See 3.2

2.1.6. 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: Oral explanation

Action: Oral explanation to be held 25 April 2018 at time 11.00

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

See 3.2

2.1.7. 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: Oral explanation

Action: Oral explanation to be held on 24 April 2018 at time 16.00

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

See 3.2

2.1.8. nitisinone - EMEA/H/C/004582

treatment of hereditary tyrosinemia type 1

Scope: Oral explanation

Action: Oral explanation to be held on 25 April 2018 at time 09.00

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

See 3.2

2.1.9. ciclosporin - EMEA/H/C/004229

for the treatment of moderate dry eye disease in adults

Scope: Oral explanation, the draft list of experts for the ad hoc expert group meeting adopted by written procedure on 11 April 2018, report from ad-hoc expert group held on 13 April 2018.

Action: Oral explanation to be held on 25 April 2018 at time 14.00

List of Outstanding Issues adopted on 22.02.2018, 14.09.2017. List of Questions adopted on 23.03.2017.

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

No items

2.4. Referral procedure oral explanations

No items

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. masitinib - Orphan - EMEA/H/C/004398

AB Science; treatment of amyotrophic lateral sclerosis

Scope: Opinion adopted by written procedure on 18 April 2018.

Action: For information

List of Outstanding Issues adopted on 12.10.2017. List of Questions adopted on 26.01.2017.

3.1.2. bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449

treatment of adults infected with human immunodeficiency virus-1 (HIV-1)

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 22.02.2018. List of Questions adopted on 09.11.2017.

3.1.3. carmustine - EMEA/H/C/004326

treatment of brain tumors, multiple myeloma, Hodgkin's disease and non-Hodgkin's lymphomas

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 22.02.2018, 12.10.2017, 20.07.2017. List of Questions adopted on 13.10.2016.

3.1.4. sufentanil - EMEA/H/C/004335

management of acute moderate to severe pain

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 22.02.2018. List of Questions adopted on 20.07.2017.

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

3.2.1. erenumab - EMEA/H/C/004447

indicated for prophylaxis of migraine in adults

Scope: List of outstanding issue

Action: For adoption

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

See 2.1

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

Oasmia Pharmaceutical AB; treatment of ovarian cancer

Scope: List of outstanding issue

Action: For adoption

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

See 2.1

3.2.3. lesinurad / allopurinol - EMEA/H/C/004412

gout

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 09.11.2017.

3.2.4. 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: List of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 22.02.2018.

See 2.1

3.2.5. 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: List of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 22.02.2018.

See 2.1

3.2.6. adalimumab - EMEA/H/C/004429

treatment of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.09.2017.

3.2.7. 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: List of outstanding issue

Action: For adoption

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

See 2.1

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

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

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.12.2017.

3.2.9. 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: List of outstanding issue

Action: For adoption

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

See 2.1

3.2.10. nitisinone - EMEA/H/C/004582

treatment of hereditary tyrosinemia type 1

Scope: List of outstanding issue

Action: For adoption

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

See 2.1

3.2.11. naldemedine - EMEA/H/C/004256

treatment of opioid-induced constipation (OIC) in adult patients.

Scope: List of outstanding issue

Action: For adoption

List of Outstanding Issues adopted on 22.02.2018. List of Questions adopted on 20.07.2017.

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

Accelerated assessment

IONIS USA Ltd; treatment of transthyretin amyloidosis (hATTR)

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 20.02.2018.

3.2.13. trastuzumab - EMEA/H/C/004463

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

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 09.11.2017.

3.2.14. abemaciclib - EMEA/H/C/004302

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

Scope: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.12.2017.

3.2.15. 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 Questions adopted on 20.02.2018.

3.2.16. 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: List of outstanding issue

Action: For adoption

List of Questions adopted on 14.12.2017.

3.2.17. axicabtagene ciloleucel - Orphan - ATMP - EMEA/H/C/004480

Kite Pharma EU B.V.; treatment of diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL) and transformed follicular lymphoma (TFL)

Scope: List of outstanding issue

Action: For information

List of Questions adopted on 08.12.2017.

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

3.3.1. avacopan - Orphan - EMEA/H/C/004487

ChemoCentryx Ltd; induction of response in adult patients with granulomatosis with polyangiitis (Wegener's) (GPA) or microscopic polyangiitis (MPA)

Scope: List of questions

Action: For adoption

3.3.2. zanamivir - EMEA/H/C/004102

treatment of influenza A or B virus infection

Scope: List of questions

Action: For adoption

3.3.3. romosozumab - EMEA/H/C/004465

Treatment of osteoporosis

Scope: List of questions

Action: For adoption

3.3.4. fexinidazole - Article 58 - EMEA/H/W/002320

Accelerated assessment

treatment of human African trypanosomiasis (HAT)

Scope: List of questions

Action: For adoption

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

Accelerated assessment

Alnylam UK Limited; treatment of hereditary transthyretin-mediated amyloidosis

Scope: List of questions

Action: For adoption

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

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

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

Scope: SAG list of questions

Action: For adoption

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

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

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

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

Scope: Appointment of re-examination rapporteurs, draft timetable, SAG involvement

Action: For discussion

Opinion adopted on 22.03.2018.

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

Radius International Ltd; treatment of osteoporosis

Scope: Appointment of re-examination rapporteurs, draft timetable

Action: For discussion

Opinion adopted on 22.03.2018.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

3.7.1. sodium benzoate - Orphan - EMEA/H/C/004150

Lucane Pharma; treatment of non ketotic hyperglycinemia, urea cycle disorders including carbamoyl-phosphate synthase-1 deficiency, ornithine transcarbamylase deficiency, citrullinaemia type 1, argininosuccinic aciduria, hyperargininaemia, n-acetylglutamate synthase deficiency, ornithine translocase deficiency and lysinuric protein intolerance

Scope: Withdrawal of initial marketing authorisation application

Action: For information

List of Questions adopted on 22.02.2018, 22.06.2017.

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. Imbruvica - ibrutinib - Orphan - EMEA/H/C/003791/X/0037

Janssen-Cilag International NV

Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty

Scope: “Extension application to introduce a new pharmaceutical form (film-coated tablets) associated with new strengths (140 mg, 280 mg, 420 mg and 560 mg).”

Action: For adoption

List of Questions adopted on 22.02.2018.

4.1.2. Sprycel - dasatinib - EMEA/H/C/000709/X/0056/G

Bristol-Myers Squibb Pharma EEIG

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

Scope: “Extension application to introduce a new pharmaceutical form (powder for oral suspension) associated with a new strength (10 mg/ml)

C.I.6.a(type II) to include the treatment of children and adolescents aged 1 year to 18 years with Ph+ chronic phase CML for Sprycel. Sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, to add a warning on effects on growth and development in the paediatric population and to update the safety information. The Package Leaflet is updated in accordance.”

Action: For adoption

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

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. Bydureon - exenatide - EMEA/H/C/002020/X/0048/G

AstraZeneca AB

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

Scope: “Extension application to introduce new pharmaceutical form (prolonged-release suspension for injection) grouped with type II variation to align the PI for the approved Bydureon products (powder and solvent for prolonged-release suspension for injection, and powder and solvent for prolonged-release suspension for injection in pre-filled pen) with the PI proposed for the Bydureon new pharmaceutical form (prolonged-release suspension for injection in autoinjector). In addition, the MAH took the opportunity to make minor editorial changes through SmPC. Moreover, RMP version 28 has been submitted as part of this application.”

Action: For adoption

List of Questions adopted on 25.01.2018.

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

No items

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

No items

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

No items

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

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

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

Amgen Europe B.V.

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

Scope: “Extension of Indication to include the treatment of adults with minimal residual disease (MRD) positive B-cell precursor acute lymphoblastic leukaemia (ALL) for BLINCYTO; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, and to update the safety information. The Labelling is updated in accordance.
RMP version 4.0 is included in this submission.”

Action: For adoption

Request for Supplementary Information adopted on 14.12.2017, 22.06.2017.

5.1.2. Cimzia - certolizumab pegol - EMEA/H/C/001037/II/0065

UCB Pharma S.A.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: “Extension of Indication to include plaque psoriasis in adult patients for Cimzia; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 13 has also been submitted.”

Action: For adoption

Request for Supplementary Information adopted on 22.03.2018, 09.11.2017.

5.1.3. Dexdor - dexmedetomidine - EMEA/H/C/002268/II/0026

Orion Corporation

Rapporteur: Greg Markey, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Julie Williams

Scope: “Extension of Indication to include "For sedation of non-intubated adult patients

prior to and/or during diagnostic or surgical procedures requiring sedation, i.e. procedural/awake sedation" for Dexdor;
as a consequence, section 4.1, 4.2, 4.4, 4.6, 4.7, 4.8 and 5.1 of the SmPC. The Package Leaflet is updated in accordance.

RMP version 7 has been submitted"

Action: For adoption

5.1.4. Jinarc - tolvaptan - EMEA/H/C/002788/II/0009

Otsuka Pharmaceutical Europe Ltd

Rapporteur: Greg Markey, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Julie Williams

Scope: "Extension of Indications based on the results of a completed Post Authorisation Efficacy Study (PAES, Trial 156-13-210) as mandated by Annex II of the Product Information with tolvaptan (ANX 006). Trial 156-13-210 is a Phase 3b, Multi-centre, Randomized-withdrawal, Placebo-controlled, Double-blind, Parallel-group Trial to Compare the Efficacy and Safety of Tolvaptan (45 to 120 mg/day, Split-dose) in Subjects with Chronic Kidney Disease between Late Stage 2 to Early Stage 4 Due to Autosomal Dominant Polycystic Kidney Disease.

Updates to SmPC Sections 4.1, 4.8 (to add 'abdominal pain' to the table of adverse events and present the data in line with QRD recommendations) and 5.1 are being proposed. The Package Leaflet is updated in accordance. Minor additional editorial changes to the PI were also carried out.

Version 13.2 of the RMP was submitted, updated to reflect the study results."

Action: For adoption

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

Merck Sharp & Dohme Limited

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

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

Action: For adoption

5.1.6. Opdivo - nivolumab - EMEA/H/C/003985/II/0039

Bristol-Myers Squibb Pharma EEIG

Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: "Extension of Indication to include treatment of adult patients with advanced or recurrent gastric or gastroesophageal junction (GEJ) cancer after two or more prior systemic therapies, based on data from study ONO-4538-12. As a consequence, sections 4.1, 4.4, 4.8, and 5.1 of the SmPC are updated. The Annex II and Package Leaflet are updated in accordance. The RMP version version 11.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 14.12.2017.

5.1.7. Opdivo - nivolumab - EMEA/H/C/003985/II/0041

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of Indication to include adjuvant treatment of adults and adolescents 12 years of age and older with completely resected Stage III and IV melanoma for OPDIVO; 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 efficacy and safety information from the pivotal Study CA209238. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes to the PI.
The RMP version 12.0 has also been submitted. The MAH also took the opportunity to revise the due dates for two Category 4 studies (CA209172 and CA209171) to a later date."

Action: For adoption

Request for Supplementary Information adopted on 25.01.2018.

5.1.8. Perjeta - pertuzumab - EMEA/H/C/002547/II/0034

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Doris Stenver

Scope: "Extension of Indication for Perjeta in combination with trastuzumab and chemotherapy for the adjuvant treatment of adult patients with HER2-positive early breast cancer. The submission is based on the primary analysis of efficacy and safety data from the pivotal Phase III study BIG-4-11/BO25126/TOC4939g (APHINITY). With the submission of the APHINITY data, the MAH also aims to fulfil the Annex IID obligation from the approval of the neoadjuvant indication of Perjeta granted in 2015. Sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are. Annex II and the Package Leaflet have been updated accordingly.
The RMP version 10.0 has also been submitted." Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

Action: For adoption

Request for Supplementary Information adopted on 14.12.2017.

5.1.9. Prolia - denosumab - EMEA/H/C/001120/II/0068

Amgen Europe B.V.

Rapporteur: Kristina Dunder, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of Indication to include "Treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at increased risk of fracture. Prevention of osteoporosis in women and men at increased risk of fracture who are starting or have recently started long-term glucocorticoid therapy." for Prolia; as a consequence, sections 4.1 and 5.1 of the SmPC are updated to reflect the new indications or are consequential to the analysis of the data from the pivotal study. The Package Leaflet is updated in accordance.
The Risk Management Plan version 19.0 has also been updated to capture the new indications.
The variation proposed amendments to the Summary of Product Characteristics and Package Leaflet."

Action: For adoption

Request for Supplementary Information adopted on 09.11.2017, 22.06.2017.

5.1.10. Rapamune - sirolimus - EMEA/H/C/000273/II/0164

Pfizer Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include the treatment of patients with lymphangioleiomyomatosis. As a consequence section 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 6.0) are updated in accordance. In addition the MAH took the opportunity to make very minor formatting changes in the Labelling."

Action: For adoption

Request for Supplementary Information adopted on 25.01.2018, 20.07.2017.

5.1.11. Tagrisso - osimertinib - EMEA/H/C/004124/II/0019

AstraZeneca AB

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer whose tumours have epidermal growth factor receptor exon 19 deletions or exon 21 (L858R) substitution mutations, based on data from the FLAURA study (D5160C00007); a phase III, double-blind, randomised study to assess the efficacy and safety of AZD9291 versus a standard of care epidermal growth factor receptor-Tyrosine Kinase Inhibitor as first-line treatment in patients with epidermal growth factor receptor mutation-positive, locally-advanced or metastatic non-small-cell lung cancer.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC have been updated and

the Package Leaflet has been updated accordingly.
In addition, the MAH took the opportunity to implement editorial changes in the SmPC and Package Leaflet.
As part of this application the MAH is requesting an additional year of market protection.
An updated RMP version 8 was submitted as part of the application."

Action: For adoption

Request for Supplementary Information adopted on 22.02.2018.

5.1.12. 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 22.02.2018, 14.12.2017.

5.1.13. Venclyxto - venetoclax - Orphan - EMEA/H/C/004106/II/0008

AbbVie Limited

Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty

Scope: "Extension of Indication to include Venclyxto in combination with rituximab for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy.
As a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated.
The Package Leaflet is updated in accordance.
This submission also fulfils the Annex II condition to submit the results of the MURANO study comparing venetoclax plus rituximab to bendamustine plus rituximab in patients with relapsed/refractory CLL.
In addition, RMP version 3.0 is submitted."

Action: For adoption

5.1.14. Xeljanz - tofacitinib - EMEA/H/C/004214/II/0006

Pfizer Limited

Rapporteur: Robert James Hemmings, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus

Scope: "Extension of Indication to include treatment of adult patients with active psoriatic arthritis who have had an inadequate response or who have been intolerant to a prior disease-modifying anti-rheumatic drug (DMARD) therapy, based on data from studies A3921091, A3921092, A3921125. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the

Annex II with minor editorial changes. The RMP version 3.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 14.12.2017.

5.1.15. Xultophy - insulin degludec / liraglutide - EMEA/H/C/002647/II/0023

Novo Nordisk A/S

Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst

Scope: "Update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety information based on cardiovascular outcomes studies conducted a for each of the monocomponents
of Xultophy: LEADER (Liraglutide Cardiovascular Outcomes Trial) and DEVOTE (Insulin Degludec Cardiovascular Outcomes Trial).

The MAH is also proposing to reorganise parts of section 5.1 to improve the reader friendliness and to remove Xultophy from the list of medicines under additional monitoring.

The Package Leaflet is updated accordingly.

The RMP version 7.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 22.02.2018.

5.1.16. Yervoy - ipilimumab - EMEA/H/C/002213/II/0055

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of indication to include the treatment of advanced (unresectable or metastatic) melanoma in adults in combination with nivolumab for Yervoy. 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 and the RMP (version 20.0) are updated in accordance. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the contact details of the Irish local representative in the Package Leaflet."

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

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

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

Scope: Request by the applicant dated 10 April 2018 requesting an extension of clock stop to respond to the List of Questions adopted on 22 March 2018.

Action: For adoption

List of Questions adopted on 22.03.2018.

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)

8. Pre-submission issues

8.1. Pre-submission issue

No items

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. Flixabi - infliximab - EMEA/H/C/004020/MEA 007.1

Samsung Bioepis UK Limited (SBUK)

Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga

Scope: Revised PASS protocol in response to study nos.: SB2-G41-AS; SB2-G42-CD

Action: For adoption

9.1.2. Keytruda - pembrolizumab - EMEA/H/C/003820/ANX/018

Merck Sharp & Dohme Limited; treatment of urothelial cell cancer

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

Scope: "Update on Study KEYNOTE-361 – Annex II condition (PAES) – protocol amendment"

Action: For adoption

9.1.3. Xagrid - anagrelide - EMEA/H/C/00480/S/0081

Shire Pharmaceutical Contracts Limited;

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: Annual reassessment procedure with proposal to switch from MA under exceptional circumstances to a standard MA.

Action: For adoption

9.1.4. Zinbryta - daclizumab - EMEA/H/C/003862

Biogen Idec Ltd; treatment of multiple sclerosis (RMS)

Rapporteur: Bruno Sepodes, Co-Rapporteur: Greg Markey, PRAC Rapporteur: Eva A. Segovia

Scope: Letter from the applicant dated 1 March 2018 informing the withdrawal of marketing authorisation

Action: For information

10. Referral procedures

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

No items

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

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

MAHs: various

Rapporteur: TBA, Co-Rapporteur: TBA

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

Action: For adoption

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

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

No items

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

10.4.1. Diclofenac Sodium Spray Gel 4% cutaneous spray, solution and associated names– EMEA/H/A-29(4)/1467

MAHs: various

Rapporteur: TBA, Co-Rapporteur: TBA

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

Action: For adoption

Second wave of repeat use of MRP procedure

10.4.2. Paclitaxel Hetero - EMEA/H/A-29(4)/1256

Hetero Europe S.L.

Rapporteur: TBA, Co-Rapporteur: TBA

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

Action: For adoption

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

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

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

No items

11. Pharmacovigilance issue

11.1. Early Notification System

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

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

No items

13.2. Innovation Task Force briefing meetings

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

13.2.1. ITF briefing meeting

Meeting date: 30 March 2018

Action: For adoption

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. Enhanced early dialogue to facilitate accelerated assessment of priority medicines (PRIME) – revision 1

Action: For adoption

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on 9-12 April 2018

Action: For information

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

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

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

14.2.3. Committee for Herbal Medicinal Products (HMPC)

Report from the HMPC meeting held on 26-27 March 2018

Action: For information

14.2.4. Paediatric Committee (PDCO)

PIPs reaching D30 at April 2018 PDCO

Action: For information

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

Action: For information

Joint CHMP/PDCO session

Agenda for joint session

Action: For discussion

14.2.5. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 17-19 April 2018
Action: For information

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

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) on the meeting held on 23-25 April 2018

Action: For information

CMDh questions to PGWP on flecainide (PSUSA/00001396/201706)

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 9-12 April 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. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse,

Reports from BWP April 2018 meeting to CHMP for adoption:

- 09 reports on products in scientific advice and protocol assistance

- 07 reports on products in pre-authorisation procedures
- 02 reports on products in post-authorisation procedures
- 03 reports on products in plasma master file

Action: For adoption

14.3.3. Biostatistics Working Party (BSWP)

Chair: Anja Schiel/Jörg Zinserling

Nomination of additional assessor to BSWP

Action: For adoption

14.3.4. Blood Products Working Party (BPWP)

Chair: Jacqueline Kerr

Nomination of new alternate member to BPWP

Action: For adoption

Nomination of additional assessor to the BPWP

Action: For adoption

14.3.5. Cardiovascular Working Party (CVSWP)

Chair: Kristina Dunder

Election of a new vice-chair of Cardiovascular Working Party (CVSWP), the mandate of the previous vice-chair ended in December 2017 when Kristina Dunder was elected as Chair.

Action: For adoption

Nomination of additional assessor to the CVSWP

Action: For adoption

14.3.6. Rheumatology/Immunology Working Party (RIWP)

Chair: Jan Mueller-Berghaus

Nomination of additional assessor to the RIWP

Action: For adoption

14.3.7. Safety Working Party (SWP)

Chair: Jan Willem Van der Laan

Nomination of new alternate member to SWP

Action: For adoption

14.3.8. Modelling and Simulation Working Group (MSWG)

Chair (acting): Flora Musuamba Tshinanu

Conversion of MSWG to MSWP

In view of the current and anticipated impact of M&S approaches in drug development and regulatory review it is proposed to convert the EMA MSWG to a CHMP temporary working party.

Action: For adoption

Call for interest for Chair/Vice-Chair

Action: For adoption

14.3.9. Ad-hoc Influenza Working Group

Chair: Ton van der Stappen

Scope: Amended EU Strain selection for the Influenza Vaccines for the Season 2018/2019: Report from the Ad Hoc Influenza working group to the BWP

Action: For adoption

Scope: Amended EU Recommendation for the Seasonal Influenza Vaccine Composition for the Season 2018/2019

Action: For adoption

14.3.10. Pharmacogenomics Working Party (PGWP)

Chair: Krishna Prasad/Markus Paulmichl

Nomination of additional assessor to the PGWP

Action: For adoption

14.3.11. Temporary working parties and drafting groups composition

Action: For information

14.4. Cooperation within the EU regulatory network

No items

14.5. Cooperation with International Regulators

No items

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

No items

14.7. CHMP work plan

No items

14.8. Planning and reporting

No items

14.9. Others

No items

15. Any other business

15.1. AOB topic

15.1.1. Preparedness of the system and capacity increase

Action: For information

15.1.2. Article 58: Update from the March 2017 'Malta' CHMP meeting with African regulators

Action: For information

15.1.3. Information on the legislative proposal for HTA collaboration

Action: For information

16. Explanatory notes

The notes below give a brief explanation of the main sections and headings in the CHMP agenda and should be read in conjunction with the agenda or the minutes.

Oral explanations *(section 2)*

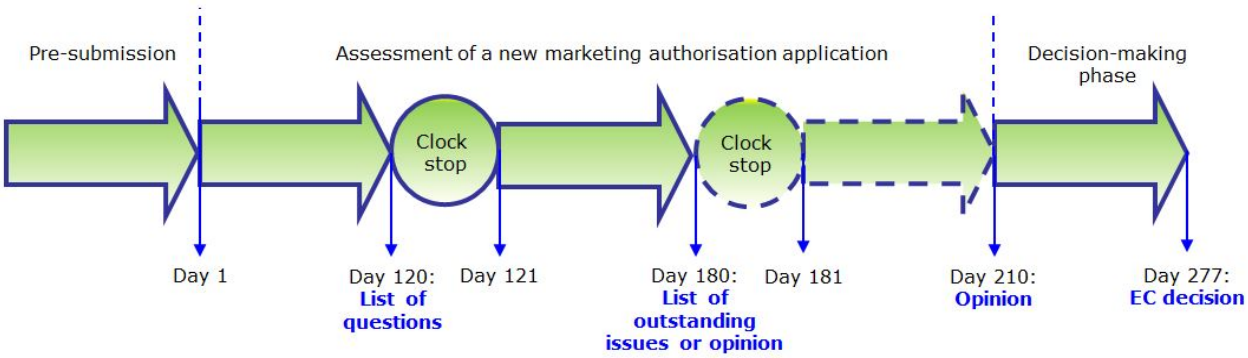
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures (section 10) but can relate to any other issue for which the CHMP would like to discuss with company representatives in person.

Initial applications *(section 3)*

This section lists applications for marketing authorisations of new medicines that are to be discussed by the Committee.

Section 3.1 is for medicinal products nearing the end of the evaluation and for which the CHMP is expected to adopt an **opinion** at this meeting on whether marketing authorisation should be granted. Once adopted, the CHMP opinion will be forwarded to the European Commission for a final legally binding decision valid throughout the EU.

The other items in the section are listed depending on the stage of the evaluation, which is shown graphically below:



The assessment of an application for a new medicine takes up to 210 'active' days. This active evaluation time is interrupted by at least one 'clock-stop' during which time the applicant prepares the answers to questions from the CHMP. The clock stop happens after day 120 and may also happen after day 180, when the CHMP has adopted a list of questions or outstanding issues to be addressed by the company. Related discussions are listed in the agenda under sections 3.2 (**Day 180 List of outstanding issues**) and 3.3 (**Day 120 list of questions**).

CHMP discussions may also occur at any other stage of the evaluation, and these are listed under section 3.4, **update on ongoing new applications for centralised procedures**.

The assessment leads to an opinion from the CHMP by day 210. Following a CHMP opinion the European Commission takes usually 67 days to issue a legally binding decision (i.e. by day 277 of the procedure). CHMP discussions on products that have received a CHMP opinion and are awaiting a decision are listed under section 3.6, **products in the decision making phase**.

Extension of marketing authorisations according to Annex I of Reg. 1234/2008 *(section 4)*

Extensions of marketing authorisations are applications for the change or addition of new strengths,

formulations or routes of administration to existing marketing authorisations. Extension applications follow a 210-day evaluation process, similarly to applications for new medicines (see figure above).

Type II variations - Extension of indication procedures *(section 5)*

Type II variations are applications for a change to the marketing authorisation which requires an update of the product information and which is not covered in section 4. Type II variations include applications for a new use of the medicine (extension of indication), for which the assessment takes up to 90 days. For the applications listed in this section, the CHMP may adopt an opinion or request supplementary information from the applicant.

Ancillary medicinal substances in medical devices *(section 6)*

Although the EMA does not regulate medical devices it can be asked by the relevant authorities (the so-called Notified Bodies) that are responsible for regulating these devices to give a scientific opinion on a medicinal substance contained in a medical device.

Re-examination procedures (new applications) under article 9(2) of regulation no 726/2004 *(section 3.5)*

This section lists applications for new marketing authorisation for which the applicant has requested a re-examination of the opinion previously issued by the CHMP.

Re-examination procedures *(section5.3)*

This section lists applications for type II variations (including extension of indication applications) for which the applicant has requested re-examination of the opinion previously issued by the CHMP.

Withdrawal of application *(section 3.7)*

Applicants may decide to withdraw applications at any stage during the assessment and a CHMP opinion will therefore not be issued. Withdrawals are included in the agenda for information or discussion, as necessary.

Procedure under article 83(1) of regulation (EC) 726/2004 (compassionate use) *(section 7)*

Compassionate use is a way of making available to patients with an unmet medical need a promising medicine which has not yet been authorised (licensed) for their condition. Upon request, the CHMP provides recommendations to all EU Member States on how to administer, distribute and use certain medicines for compassionate use.

Pre-submission issues *(section 8)*

In some cases the CHMP may discuss a medicine before a formal application for marketing authorisation is submitted. These cases generally refer to requests for an accelerated assessment for medicines that are of major interest for public health or can be considered a therapeutic innovation. In case of an accelerated assessment the assessment timetable is reduced from 210 to 150 days.

Post-authorisation issues *(section 9)*

This section lists other issues concerning authorised medicines that are not covered elsewhere in the agenda. Issues include supply shortages, quality defects, some annual reassessments or renewals or type II variations to marketing authorisations that would require specific discussion at the plenary.

Referral procedures *(section 10)*

This section lists referrals that are ongoing or due to be started at the plenary meeting. A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a

particular medicine or class of medicines on behalf of the EU. Further information on such procedures can be found here.

Pharmacovigilance issues *(section 11)*

This section lists issues that have been discussed at the previous meeting of the PRAC, the EMA's committee responsible for evaluating and monitoring safety issues for medicines. Feedback is provided by the PRAC. This section also refers to the early notification system, a system used to notify the European regulatory network on proposed EMA communication on safety of medicines.

Inspections Issues *(section 12)*

This section lists inspections that are undertaken for some medicinal products. Inspections are carried out by regulatory agencies to ensure that marketing authorisation holders comply with their obligations. Inspection can relate to good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP) or good pharmacovigilance practice (GVP).

Innovation task force *(section 13)*

The Innovation Task Force (ITF) is a body set up to encourage early dialogue with applicants developing innovative medicines. Minutes from the last ITF meeting as well as any related issue that requires discussion with the CHMP are listed in this section of the agenda. Further information on the ITF can be found here.

Scientific advice working party (SAWP) *(section 14.3.1)*

This section refers to the monthly report from the CHMP's Scientific Advice Working Party (SAWP) on scientific advice given to companies during the development of medicines. Further general information on SAWP can be found here.

Satellite groups / other committees *(section 14.2)*

This section refers to the reports from groups and committees making decisions relating to human medicines: the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), the Committee for Orphan Medicinal Products (COMP), the Committee for Herbal Medicinal Products (HMPC), Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT) and the Pharmamacovigilance Risk Assessment Committee (PRAC).

Invented name issues *(section 14.3)*

This section list issues related to invented names proposed by applicants for new medicines. The CHMP has established the Name Review Group (NRG) to perform reviews of the invented names. The group's main role is to consider whether the proposed names could create a public-health concern or potential safety risk. Further information can be found here.

More detailed information on the above terms can be found on the EMA website: www.ema.europa.eu/

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 April 2018
EMA/CHMP/248611/2018

Annex to 23-26 April 2018 CHMP Agenda

Pre submission and post authorisations issues

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
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
April 2018: **For adoption**

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

Final Outcome of Rapporteurship allocation for
April 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

SCENESSE - afamelanotide -
EMEA/H/C/002548/S/0019, Orphan
Clinuvel (UK) Limited, Rapporteur: Harald Enzmann, PRAC Rapporteur: Valerie Strassmann

Xagrid - anagrelide -
EMEA/H/C/000480/S/0081
Shire Pharmaceutical Contracts Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Defitelio - defibrotide -
EMEA/H/C/002393/R/0032, Orphan
Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Julie Williams

Imnovid - pomalidomide -
EMEA/H/C/002682/R/0028, Orphan
Celgene Europe Limited, Rapporteur: Robert

James Hemmings, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Patrick Batty
Request for Supplementary Information adopted on 22.02.2018.

Xofigo - radium-223 - EMEA/H/C/002653/R/0030
Bayer AG, Rapporteur: Harald Enzmann, Co-Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Patrick Batty

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Corbilta - levodopa / carbidopa / entacapone - EMEA/H/C/002785/R/0015
Orion Corporation, Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Bruno Sepodes, PRAC Rapporteur: Kirsti Villikka

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

Inflectra - infliximab - EMEA/H/C/002778/R/0056
Hospira UK Limited, Duplicate, Duplicate of Remsima, Rapporteur: Greg Markey, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Patrick Batty
Request for Supplementary Information adopted on 22.02.2018.

Lemtrada - alemtuzumab - EMEA/H/C/003718/R/0020
Genzyme Therapeutics Ltd, Duplicate, Duplicate of Lemtrada (WD), Rapporteur: Mark Ainsworth, Co-Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark
Request for Supplementary Information adopted on 22.03.2018.

Nexium Control - esomeprazole - EMEA/H/C/002618/R/0021
Pfizer Consumer Healthcare Limited, Rapporteur: Romaldas Mačiulaitis, Co-Rapporteur: Robert James Hemmings, PRAC Rapporteur: Simona Kudeliene
Request for Supplementary Information adopted

on 22.02.2018.

Remsima - infliximab - EMEA/H/C/002576/R/0047
Celltrion Healthcare Hungary Kft., Rapporteur: Greg Markey, Co-Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Patrick Batty
Request for Supplementary Information adopted on 22.02.2018.

B.2.3. Renewals of Conditional Marketing Authorisations

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

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

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

Signal detection

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

Signal of CMV reactivation
Aprycel - Dasatinib - EMEA/H/C/000709
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Fátima Ventura
PRAC recommendation on a variation: **For adoption**

Signal of pulmonary hypertension
Tyverb – Lapatinib - EMEA/H/C/000795
Novartis Europharm Limited, Rapporteur: Filip Josephson, Co-Rapporteur: Bruno Sepodes
PRAC recommendation on a variation: **For**

adoption

Signal of angioedema and urticaria
Brintellix – Vortioxetine -
EMEA/H/C/002717
H. Lundbeck A/S, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Martina Weise
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 April 2018 meeting:

EMEA/H/C/PSUSA/00000931/201709
(daptomycin)
CAPS:
Cubicin (EMEA/H/C/000637) (daptomycin), Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, "12 Sep 2016 to 11 Sep 2017"

EMEA/H/C/PSUSA/00001205/201709
(eltrombopag)
CAPS:
Revolade (EMEA/H/C/001110) (eltrombopag / eltrombopag olamine), Novartis Europharm Limited, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "01-Oct-2016 to 30-Sep-2017."

EMEA/H/C/PSUSA/00002285/201708
(pantoprazole)
CAPS:
CONTROLOC Control (EMEA/H/C/001097) (pantoprazole), Takeda GmbH, Rapporteur: Greg Markey
PANTOLOC Control (EMEA/H/C/001100) (pantoprazole), Takeda GmbH, Rapporteur: Greg Markey
PANTOZOL Control (EMEA/H/C/001013) (pantoprazole), Takeda GmbH, Rapporteur: Greg Markey
SOMAC Control (EMEA/H/C/001098) (pantoprazole), Takeda GmbH, Rapporteur: Greg Markey
NAPS:
ANAGASTRA - TAKEDA GMBH (KONSTANZ)
APTON - LABORATÓRIOS DELTA, S.A.
CONTROLOC - TAKEDA PHARMA SP.Z.O.O
CONTROLOC - MUNDIPHARMA PHARMACEUTICALS LTD
CONTROLOC - TAKEDA PHARMACEUTICALS

CROATIA D.O.O.
CONTROLOC I.V. - TAKEDA HELLAS S.A.
EUPANTOL - TAKEDA FRANCE S.A.S.
INIPOMP - TAKEDA FRANCE S.A.S.
KAIROL - FARMOZ - SOCIEDADE TÉCNICO MEDICINAL, S.A
PANTECTA - TAKEDA ITALIA S.P.A.
PANTECTA - TAKEDA GMBH (KONSTANZ)
PANTOC - TAKEDA FARMACEUTICOS PORTUGAL LDA.
PANTOC I.V. - TAKEDA FARMACEUTICOS PORTUGAL LDA.
PANTOLOC - TAKEDA PHARMA GES.M.B.H
PANTOLOC - TAKEDA PHARMA A/S
PANTOPAN - TAKEDA ITALIA S.P.A.
PANTOPRAZOL ALTAN - TAKEDA FARMACEUTICOS PORTUGAL LDA.
PANTOPRAZOL BYK - TAKEDA GMBH (KONSTANZ)
PANTOPRAZOL NYC - TAKEDA GMBH (KONSTANZ)
PANTOPRAZOL NYCOMED - TAKEDA GMBH (KONSTANZ)
PANTOPRAZOL SANDOZ - SANDOZ PHARMACEUTICALS D.D.
PANTOPRAZOL TEVA - TEVA PHARMACEUTICALS POLSKA SP. Z O.O.
PANTOPRAZOLE BRISTOL LABORATORIES - BRISTOL LABORATORIES LTD (BERKHAMSTED)
PANTOPRAZOLE TAKEDA UK - TAKEDA UK LTD
PANTORC - TAKEDA ITALIA S.P.A.
PANTOZOL - TAKEDA NEDERLAND BV
PANTOZOL - TAKEDA BELGIUM SCA/CVA
PANTOZOL I.V. - TAKEDA NEDERLAND BV, TAKEDA GMBH (KONSTANZ)
PEPTAZOL - RECORDATI INDUSTRIA CHIMICA E FARMACEUTICA S.P.A
PEPTAZOL - RECORDATI INDUSTRIA CHIMICA E FARMACEUTICA S.P.A.
PRAZOLACID - PHARMASWISS ČESKÁ REPUBLIKA S.R.O.
PROTIUM - TAKEDA UK LTD
PROTIUM I.V. - TAKEDA UK LTD
RIFUN - TAKEDA GMBH (KONSTANZ)
SOMAC - TAKEDA AS, TAKEDA GMBH (KONSTANZ)
TECTA - TAKEDA GMBH (KONSTANZ)
ULCOTENAL - TAKEDA GMBH (KONSTANZ)
ZURCAL - TAKEDA GMBH (KONSTANZ)
ZURCAL - TAKEDA FARMACEUTICOS PORTUGAL

LDA. TAKEDA AUSTRIA GMBH
ZURCAZOL - TAKEDA HELLAS S.A.
ZURCAZOL I.V. - TAKEDA HELLAS S.A.
КОНТРОЛОК - TAKEDA GMBH (KONSTANZ)
PRAC Rapporteur: Patrick Batty,
“24 August 2012 to 23 August 2017”

EMEA/H/C/PSUSA/00002653/201709
(rivaroxaban)
CAPS:
Xarelto (EMEA/H/C/000944) (rivaroxaban), Bayer AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, “16-Sep-2016 to 15-Sep-2017”

EMEA/H/C/PSUSA/00003001/201709
(trabectedin)
CAPS:
Yondelis (EMEA/H/C/000773) (trabectedin), Pharma Mar, S.A., Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, “18 September 2016 to 17 September 2017”

EMEA/H/C/PSUSA/00010133/201709
(regorafenib)
CAPS:
Stivarga (EMEA/H/C/002573) (regorafenib), Bayer AG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, “27-Sep-2016 to 26-Sep-2017”

EMEA/H/C/PSUSA/00010311/201709
(dulaglutide)
CAPS:
Trulicity (EMEA/H/C/002825) (dulaglutide), Eli Lilly Nederland B.V., Rapporteur: Greg Markey, PRAC Rapporteur: Carmela Macchiarulo, “19-March-2017 – 18-September-2017”

EMEA/H/C/PSUSA/00010366/201709
(naltrexone / bupropion)
CAPS:
Mysimba (EMEA/H/C/003687) (naltrexone hydrochloride / bupropion hydrochloride), Orexigen Therapeutics Ireland Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber, “10 March to 9 September 2017”

EMEA/H/C/PSUSA/00010368/201709
(oritavancin)
CAPS:
Orbactiv (EMEA/H/C/003785) (oritavancin), The Medicines Company UK Limited,

Rapporteur: Greg Markey, PRAC Rapporteur: Adam Przybylkowski, “from 20 March 2017 to 19 September 2017”	
EMEA/H/C/PSUSA/00010403/201709 (pembrolizumab) CAPS: **Keytruda** (EMEA/H/C/003820) (pembrolizumab), Merck Sharp & Dohme Limited, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Sabine Straus, “04/03/2017-03/09/2017”	
EMEA/H/C/PSUSA/00010499/201709 (eftrenonacog alfa) CAPS: **Alprolix** (EMEA/H/C/004142) (eftrenonacog alfa), Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski, “20 March 2017 to 19 September 2017”	
EMEA/H/C/PSUSA/00009119/201709 (denusomab) CAPS: **XGEVA** (EMEA/H/C/002173) (Denosumab), Amgen, Rapporteur:, PRAC Rapporteur: Kristina Dunder “01-Oct-2016 to 30-Sep-2017.”	

B.4. EPARs / WPARs

Aplidin - plitidepsin - EMEA/H/C/004354, Orphan Pharma Mar, S.A., treatment of multiple myeloma, 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.
Juluca - dolutegravir / rilpivirine - EMEA/H/C/004427 ViiV Healthcare UK Limited, treatement of HIV, Fixed combination application (Article 10b of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
KANJINTI - trastuzumab - EMEA/H/C/004361 Amgen Europe B.V., BREDA, treatment of metastatic breast cancer, early breast cancer, metastatic gastric cancer, Similar biological application (Article 10(4) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Pemetrexed Krka - pemetrexed - EMEA/H/C/003958	For information only. Comments can be sent to the EPL in case necessary.

KRKA d.d., Novo mesto, treatment of malignant pleural mesothelioma and non-small cell lung cancer, Generic, Generic of Alimta, Generic application (Article 10(1) of Directive No 2001/83/EC)	
Prasugrel Mylan - prasugrel - EMEA/H/C/004644 Mylan S.A.S, prevention of atherothrombotic events, Generic, Generic of Efient, Generic application (Article 10(1) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Rubraca - rucaparib - EMEA/H/C/004272, Orphan Clovis Oncology UK Ltd, treatment of ovarian cancer, New active substance (Article 8(3) of Directive No 2001/83/EC)	For information only. Comments can be sent to the EPL in case necessary.
Zessly - infliximab - EMEA/H/C/004647 Sandoz GmbH, treatment of rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, psoriasis and ulcerative colitis, Similar biological application (Article 10(4) 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

Benepali - etanercept - EMEA/H/C/004007/II/0031/G Samsung Bioepis UK Limited, Rapporteur: Andrea Laslop Request for Supplementary Information adopted on 22.02.2018.	
Dupixent - dupilumab - EMEA/H/C/004390/II/0002 sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 22.03.2018.	
Dupixent - dupilumab - EMEA/H/C/004390/II/0003/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 12.04.2018.	
Eptifibatide Accord - eptifibatide - EMEA/H/C/004104/II/0003 Accord Healthcare Limited, Generic, Generic of Integrilin, Rapporteur: Jayne Crowe	
Eylea - aflibercept - EMEA/H/C/002392/II/0040/G Bayer AG, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 22.02.2018.	
Eylea - aflibercept - EMEA/H/C/002392/II/0041/G Bayer AG, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 22.02.2018.	
Granupas - para-aminosalicylic acid - EMEA/H/C/002709/II/0024, Orphan Lucane Pharma, Rapporteur: Greg Markey	
Hemoblast - thrombin - EMEA/H/D/002769/II/0003/G BSI Group, Rapporteur: Daniela Melchiorri,	
Hizentra - human normal immunoglobulin - EMEA/H/C/002127/II/0093/G CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus	
Imraldi - adalimumab - EMEA/H/C/004279/II/0007/G Samsung Bioepis UK Limited (SBUK), Rapporteur: Outi Mäki-Ikola	
Maviret - glecaprevir / pibrentasvir - EMEA/H/C/004430/II/0006/G AbbVie Limited, Rapporteur: Joseph Emmerich	
Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0028 GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 12.04.2018.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Naglazyme - galsulfase - EMEA/H/C/000640/II/0070 BioMarin Europe Ltd, Rapporteur: Greg Markey Request for Supplementary Information adopted on 12.04.2018.	Request for supplementary information adopted with a specific timetable.
NexoBrid - concentrate of proteolytic	Request for supplementary information adopted

enzymes enriched in bromelain - EMEA/H/C/002246/II/0035, Orphan
MediWound Germany GmbH, Rapporteur: Harald Enzmann
Request for Supplementary Information adopted on 12.04.2018.
with a specific timetable.

NovoEight - turoctocog alfa - EMEA/H/C/002719/II/0021/G
Novo Nordisk A/S, Rapporteur: Jan Mueller-Berghaus
Request for Supplementary Information adopted on 15.03.2018, 14.12.2017.

Ongentys - opicapone - EMEA/H/C/002790/II/0009
Bial - Portela & Cª, S.A., Rapporteur: Greg Markey

Pegasys - peginterferon alfa-2a - EMEA/H/C/000395/II/0099/G
Roche Registration GmbH, Rapporteur: Filip Josephson
Request for Supplementary Information adopted on 22.02.2018.

Pioglitazone Accord - pioglitazone - EMEA/H/C/002277/II/0015/G
Accord Healthcare Limited, Generic, Generic of Actos, Rapporteur: Peter Kiely
Request for Supplementary Information adopted on 15.03.2018.

Taltz - ixekizumab - EMEA/H/C/003943/II/0014
Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder
Request for Supplementary Information adopted on 15.03.2018.

Trulicity - dulaglutide - EMEA/H/C/002825/II/0026
Eli Lilly Nederland B.V., Rapporteur: Greg Markey
Request for Supplementary Information adopted on 15.03.2018.

Vaniqa - eflornithine - EMEA/H/C/000325/II/0051
Almirall S.A, Rapporteur: Peter Kiely
Request for Supplementary Information adopted on 22.03.2018, 26.10.2017.

Zerbaxa - ceftolozane / tazobactam -

EMEA/H/C/003772/II/0015/G Merck Sharp & Dohme Limited, Rapporteur: Robert James Hemmings	
WS1177/G **Neulasta-** **EMEA/H/C/000420/WS1177/0097/G** **Ristempa (SRD)-** **EMEA/H/C/003910/WS1177/0012/G** Amgen Europe B.V., Lead Rapporteur: Robert James Hemmings Request for Supplementary Information adopted on 25.01.2018, 14.09.2017.	
WS1281/G **Hexacima-** **EMEA/H/C/002702/WS1281/0072/G** **Hexaxim-** **EMEA/H/W/002495/WS1281/0077/G** **Hexyon-** **EMEA/H/C/002796/WS1281/0076/G** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 12.04.2018. Request for Supplementary Information adopted on 25.01.2018.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

Abraxane - paclitaxel - **EMEA/H/C/000778/II/0087** Celgene Europe Limited, Rapporteur: Paula Boudewina van Hennik, “Update of section 4.8 of the SmPC in order to include the warning tumour lysis syndrome following a safety cumulative review of this signal. In addition, the marketing authorisation holder took the opportunity to update the wording on section 4.6 to introduce additional recommendation to perform a pregnancy test prior treatment with paclitaxel. The package leaflet has been updated accordingly.” Opinion adopted on 12.04.2018.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Bexsero - meningococcal group b vaccine (recombinant, component, adsorbed) - **EMEA/H/C/002333/II/0059** GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, “Update of section 4.2 of the SmPC to update the dosing schedule for infants (2 months to 5 months of age) to allow for 2 primary doses plus 1 booster dose in the second	

year of life based on the results from study V72_28 and its extension V72_28E1 and to update the intervals between primary doses for children (2 years to 10 years of age) to not less than 1 month based on the results from the extension study V72_28E1. Update of section 4.8 of the SmPC to include the number of subjects exposed to at least 1 dose based on the results from the studies V72_28 and V72_28E1. Update of section 5.1 of the SmPC to update the information about immunogenicity in infants and children based on the results from the studies V72_28 and V72_28E1. The Package leaflet is updated accordingly. In addition, the MAH took the opportunity to make some editorial changes in the SmPC and labelling." Request for Supplementary Information adopted on 22.02.2018, 12.10.2017.	
Celsentri - maraviroc - EMEA/H/C/000811/II/0054/G ViiV Healthcare UK Limited, Rapporteur: Filip Josephson, "Update of sections 4.5 and 5.2 of the SmPC in order to update the data regarding drug metabolising enzymes and drug transporters from several completed in vitro studies and to support the addition of pharmacogenomic information based on final results from study (A4001110), respectively. Furthermore, section 5.1 has been updated with information on genotypic resistance. Additionally, minor changes have been introduced in 4.2, 4.4, and 5.1 sections of the SmPC. The Package Leaflet section on How to measure the dose and take the medicine has been updated to further clarify the instructions." Opinion adopted on 12.04.2018.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Daklinza - daclatasvir - EMEA/H/C/003768/II/0028 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, "Submission of the final report from study AI444379. This is an interventional open-label phase 3 study evaluating daclatasvir and sofobuvir with ribavirin in cirrhotic subjects with genotype 3 chronic hepatitis C infection to demonstrate the sustained virologic response at follow-up Week 12 (SVR12) rate, defined as hepatitis C virus (HCV) ribonucleic acid (RNA) < lower limit of quantification (LLOQ) target	Request for supplementary information adopted with a specific timetable.

detected (TD) or target not detected (TND) at follow-up Week 12 in subjects treated with 24 weeks of daclatasvir (DCV) + sofosbuvir (SOF) + ribavirin (RBV) therapy was greater than the historical threshold sustained virologic response (SVR) rate." Request for Supplementary Information adopted on 12.04.2018.	
Humira - adalimumab - EMEA/H/C/000481/II/0172 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, "Update of sections 5.1 and 5.2 of the SmPC for 40mg/0.8ml and 40mg/0.4 ml Prefilled pen and prefilled syringe in order to add information on non-radiographic axial spondyloarthritis following final results from Humira remission-withdrawal-retreatment study (M13-375) listed in the RMP." Request for Supplementary Information adopted on 01.02.2018.	
Infanrix hexa - diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and Haemophilus influenzae type b (Hib) conjugate vaccine (adsorbed) - EMEA/H/C/000296/II/0235 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of section 4.5 of the SmPC in order to update the interactions section with additional data on the co-administration with Meningococcal serogroup B vaccine (MenB) in order to facilitate the administration of Infanrix hexa and Bexsero to infants and toddlers based on final results from clinical studies V72P12, V72P13 and V72P16." Opinion adopted on 12.04.2018. Request for Supplementary Information adopted on 08.02.2018.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Isentress - raltegravir - EMEA/H/C/000860/II/0073 Merck Sharp & Dohme Limited, Rapporteur: Greg Markey, "Update of sections 4.6 and 5.3 of the SmPC, upon request by PRAC following the assessment of the latest PSUR (PSUSA/00010373/201703), to include revised safety information about pregnancy and risk of malformative or foetal toxicity (LEG). The Package Leaflet has been updated accordingly."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 12.04.2018.	
Jinarc - tolvaptan - EMEA/H/C/002788/II/0010 Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey, “Submission of the final report from a completed PK study (156-14-216, a Phase 1, Single centre, Open-label, drug interaction trial to Investigate the Effect of Oral Flucomazole, a Moderate CYP3A4 Inhibitor, on Tolvaptan Pharmcokinetic in Healthy Adult Subjects - MEA 003).” Opinion adopted on 12.04.2018.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kyprolis - carfilzomib - EMEA/H/C/003790/II/0025, Orphan Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, “Update of sections 4.4, 4.8 and 5.1 of the SmPC to update information based on the final analysis of overall survival data from study PX-171-009 (ASPIRE): A Randomized, Multicenter, Phase 3 Study Comparing Carfilzomib, Lenalidomide, and Dexamethasone (CRd) vs Lenalidomide and Dexamethasone (Rd) in Subjects with Relapsed Multiple Myeloma. This variation aims to fulfil the recommendation resulting from the initial MAA. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.” Request for Supplementary Information adopted on 22.03.2018.	
Lumigan - bimatoprost - EMEA/H/C/000391/II/0055 Allergan Pharmaceuticals Ireland, Rapporteur: Mark Ainsworth, “Submission of the final report of the Phase 4 clinical safety study P-192024-054 listed as a category 3 study in the RMP.”	
MabThera - rituximab - EMEA/H/C/000165/II/0143 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, “Submission of the final CSR of the PRIMA study (MO18264), a stydy in Patients with Advanced Follicular Lymphoma Evaluating the Benefit of Maintenance Therapy with Rituximab after Induction of Response with Chemotherapy plus Rituximab in Comparison with No Maintenance Therapy.”	

Request for Supplementary Information adopted on 15.03.2018.

Mirvaso - brimonidine - EMEA/H/C/002642/II/0017

Galderma International, Rapporteur: Filip Josephson, “Update of section 4.8 of the SmPC in order to update the frequency of the adverse drug reaction (ADR) rosacea from “uncommon” to “common” following a re-examination of the frequency of ADRs in pertinent studies. The package leaflet is updated accordingly.”

NovoRapid - insulin aspart - EMEA/H/C/000258/II/0121

Novo Nordisk A/S, Rapporteur: Kristina Dunder, “Update of section 4.2 of the SmPC to include a passive discouragement of withdrawing insulin with a syringe from cartridges and pre-filled pens; update of section 6.6 of the SmPC to allow the withdrawal of insulin with a syringe from cartridges and pre-filled pens in emergency situations. This variation was submitted following a recommendation by the PRAC in November 2017, subsequent the evaluation of the signal on potential increased risk of medication error associated with withdrawing insulin from pre-filled pens and cartridges, leading to dysglycaemia. The PIL is updated accordingly. In addition, the MAH took the opportunity to reinsert and clarify information in the SmPC regarding mixing of NovoRapid with NPH insulin (sections 4.2 and 6.2), which has previously been deleted from the SmPC by mistake. Other editorial changes are also proposed within this variation.”

Pradaxa - dabigatran etexilate - EMEA/H/C/000829/II/0108

Boehringer Ingelheim International GmbH, Rapporteur: Mark Ainsworth, “Update of sections 4.2, 4.4. and 5.1 (Pradaxa 110 and 150 mg) for the SPAF - DVT/PE indication are proposed based on the results from study 1160.186 recomending that patients with non-valvular atrial fibrillation who undergo a PCI with stenting can be treated with PRADAXA® in combination with antiplatelets after haemostasis is achieved. The prescriber guide is also being updated.

Study 1160.186 is `A prospective Randomised, open label, blinded endpoint (PROBE) study to

Evaluate DUAL antithrombotic therapy with dabigatran etexilate (110 mg and 150 mg b.i.d.) plus clopidogrel or ticagrelor vs. triple therapy strategy with warfarin (INR 2.0-3.0) plus clopidogrel or ticagrelor and aspirin in patients with non-valvular atrial fibrillation that have undergone a percutaneous coronary intervention (PCI) with stenting (RE-DUAL PCI)'.

In addition, the MAH took the opportunity to correct in section 4.3 a contraindication that refers to concomitant treatment with heparin, based on the data assessed in the context of variation II/103 to reflect the fact that heparin is administered during ablation procedure at the same time as dabigatran."
Request for Supplementary Information adopted on 22.02.2018.

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."

Praluent - alirocumab - EMEA/H/C/003882/II/0036

sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, "Submission of the clinical study report of study LTS13463 (Open-Label Extension Study of EFC12492, R727-CL-1112, EFC12732, & LTS11717 Studies to Assess the Long-Term Safety and Efficacy of Alirocumab in Patients with Heterozygous Familial Hypercholesterolemia) as per MEA010."

Praluent - alirocumab -
EMEA/H/C/003882/II/0037
sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, “Submission of the second step analysis report of the clinical study EFC13786 (study title: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study Evaluating the Efficacy and Safety of Alirocumab in Patients with Primary Hypercholesterolemia not treated with a statin) as per MEA014.”

Remicade - infliximab -
EMEA/H/C/000240/II/0212
Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, “Update of section 4.4 to include a warning recommending adult patients to be brought up to date with all vaccinations if possible prior to initiating Remicade therapy (in line with the current warning for children) and to clarify that patients on infliximab may receive concurrent vaccinations, except for live vaccines. Relevant sections of the PL and the RMP (v 15.1) were updated accordingly.
The MAH took the opportunity the include minor editorial changes in the PI.”

Remicade - infliximab -
EMEA/H/C/000240/II/0213/G
Janssen Biologics B.V., Rapporteur: Kristina Dunder, “Update of section of 4.8 of the SmPC in order to add the following adverse reactions: ‘Hemophagocytic Lymphohistiocytosis (HLH)’ with a frequency ‘very rare’ and ‘Linear IgA Bullous Dermatosis (LABD)’ with a ‘rare’ frequency. In addition, the Marketing authorisation holder (MAH) took the opportunity to add additional instructions for obese Adult patients in section 6.6 of the SmPC; relevant sections of the PL have been updated accordingly. The MAH also took the opportunity to introduce some editorial changes in the Product Information.”

Revlimid - lenalidomide -
EMEA/H/C/000717/II/0097, Orphan
Celgene Europe Limited, Rapporteur: Alexandre Moreau, “Update of the SmPC section 4.8 to include solid organ transplant rejection as an adverse reaction (ADR) with the frequency not known in line with the Company Core Data Sheet (CCDS). The MAH also took the

opportunity to further align the SmPC section 4.8 with the CCDS by adding the following ADRs reported as serious in some clinical trials: cellulitis, hypercalcaemia, and musculoskeletal and connective tissue pain and discomfort (including back pain). Minor editorial changes have been introduced throughout the PI. The Package leaflet has been updated accordingly." Request for Supplementary Information adopted on 15.02.2018.	
SonoVue - sulphur hexafluoride - EMEA/H/C/000303/II/0037/G Bracco International B.V., Rapporteur: Alexandre Moreau, "Grouped variation application in order to align with Company Core Data Sheet (CCDS): • Update of section 4.4 of the SmPC in order to reword warning on hypersensitivity reactions. • Update of section 4.4 of the SmPC in order to reword warning for patients with unstable cardiopulmonary status • Update of section 4.4 of the SmPC in order to delete warning for patients on mechanical ventilation or with unstable neurological diseases • Update of section 4.4 of the SmPC in order to delete warning for patients with clinically significant pulmonary disease, including severe chronic obstructive pulmonary disease • Update of section 4.8 of the SmPC in order to revise table with Adverse Drug Reactions The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes/corrections in sections 4.8 and 4.9 of the SmPC." Request for Supplementary Information adopted on 22.02.2018.	
Spinraza - nusinersen - EMEA/H/C/004312/II/0004, Orphan Biogen Idec Ltd, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Qun-Ying Yue, "Update of section 4.8 of the SmPC to include new safety information related to hydrocephalus. The PIL and the RMP (new version 7.0) are proposed to be updated accordingly. In addition, the MAH took the opportunity to correct some	Request for supplementary information adopted with a specific timetable.

typographical errors in section 5.1 of the SmPC"
Request for Supplementary Information adopted on 12.04.2018, 08.02.2018.

Starlix - nateglinide - EMEA/H/C/000335/II/0033

Novartis Europharm Limited, Rapporteur: Greg Markey, "Update of section 5.2 of the SmPC to add information on the accumulation of M1 metabolite in diabetic patients with end-stage renal disease (ESRD), based on the review of the Core Data Sheet. This information is reflected in section 4.4 of the SmPC. The Package Leaflet and Labelling are updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with QRD template 10, combine the three SmPC into a single SmPC, align sections 1 and 2 of the package leaflet with the SmPC, and correct the name of the local representatives for Latvia and Bulgaria."
Request for Supplementary Information adopted on 22.03.2018, 07.12.2017.

Taltz - ixekizumab - EMEA/H/C/003943/II/0016

Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, "Update section 5.1 of the SmPC to include the results of study RHBS (a Phase 3b, multicenter, randomised, double blind, double dummy, active comparator, and parallel group study of the efficacy and safety of ixekizumab versus ustekinumab for the treatment of moderate to severe psoriasis). The MAH took the opportunity to introduce minor typographical amendments in the product information."

Trulicity - dulaglutide - EMEA/H/C/002825/II/0025

Eli Lilly Nederland B.V., Rapporteur: Greg Markey, "Update of sections 4.2 and 5.1 of the SmPC to reflect the use of dulaglutide in Type 2 Diabetes Mellitus patients as add-on to sodium-glucose co-transporter 2 inhibitors (SGLT2i) therapy following completion of a study that investigated the effect of once weekly dulaglutide 1.5 mg or 0.75 mg added to SGLT2is, with or without concomitant use of metformin, on glycemic control and safety over a 24-weeks in patients with inadequately controlled T2DM (Study H9X-MC-GBGE

(GBGE)). The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 22.02.2018.	
XALKORI - crizotinib - **EMEA/H/C/002489/II/0054** Pfizer Limited, Rapporteur: Alexandre Moreau, "Update of section 5.1 of the SmPC to reflect the final analysis of overall survival (OS), a secondary endpoint, in Study A8081014, a randomized phase 3 trial comparing oral crizotinib to first line chemotherapy in patients with ALK-positive advanced non-squamous non-small cell lung cancer (NSCLC)."	
Xeljanz - tofacitinib - **EMEA/H/C/004214/II/0008** Pfizer Limited, Rapporteur: Robert James Hemmings, "Submission of the final CSR for study A3921187 described in Part IV of the RMP. Study A3921187 is a phase 3b/4 randomized double-blind study of 5 mg of Tofacitinib with and without methotrexate in comparison to adalimumab with methotrexate in subjects with moderately to severely active rheumatoid arthritis."	
Xeljanz - tofacitinib - **EMEA/H/C/004214/II/0010** Pfizer Limited, Rapporteur: Robert James Hemmings, "To update sections 4.4 and 4.8 of the SmPC and PIL to add a warning on Hypersensitivity and to add drug hypersensitivity, angioedema, and urticaria as ADRs with frequency not known, following a PRAC signal recommendation. The Package Leaflet is updated accordingly."	
Xeljanz - tofacitinib - **EMEA/H/C/004214/II/0011** Pfizer Limited, Rapporteur: Robert James Hemmings, "To update section 4.4 of the SmPC to indicate that post-marketing cases of HB reactivation have been reported following routine pharmacovigilance review."	
Xydalba - dalbavancin - **EMEA/H/C/002840/II/0021** Allergan Pharmaceuticals International Ltd, Rapporteur: Filip Josephson, "Update to sections 4.4 and 4.8 of the product information in order	Request for supplementary information adopted with a specific timetable.

to include back-pain as a symptom of infusion-related reactions in alignment with the last version Company Core Data Sheet (CCDS). In addition, the MAH took the opportunity to add a precautionary statement to Section 6.6 to include flushing of the intravenous lines before and after dalbavancin infusion, to bring the PI in line with the latest QRD template version 10 and to update the local representatives in the PL" Request for Supplementary Information adopted on 12.04.2018.	
Zavicefta - ceftazidime / avibactam - EMEA/H/C/004027/II/0009 Pfizer Ireland Pharmaceuticals, Rapporteur: Robert James Hemmings, "Update of sections 4.2 and 4.8 of the SmPC in order to reflect the availability of final CSR for the paediatric study C3591004 (D4280C00015). Study D4280C00015 is a single blind, randomised, multi-centre, active controlled, trial to evaluate safety, tolerability, pharmacokinetics and efficacy of ceftazidime and avibactam when given in combination with metronidazole, compared with meropenem, in children from 3 months to less than 18 years of age with complicated intra-abdominal infections (cIAIs). In addition, the MAH has updated the sodium statements in the SmPC (section 4.4) and Package Leaflet to align with the Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. The legal status 'medicinal product subject to medical prescription' is proposed to be removed from Annex IIIA, as per the QRD template Moreover, the MAH is introducing a correction in the Polish annexes (from ZAVICEFTA 2 g + 0.5g to ZAVICEFTA 2 g/0.5g)."	
WS1298 **Enurev Breezhaler- EMEA/H/C/002691/WS1298/0024** **Seebri Breezhaler- EMEA/H/C/002430/WS1298/0024** **Tovanor Breezhaler- EMEA/H/C/002690/WS1298/0027** Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth, "Submission of the final study report of the Post-Authorisation Efficacy Study	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

(PAES) to compare the efficacy, safety and tolerability of glycopyrronium given at a dose of 44 µg QD and 22 µg BID in patients with stable COPD and moderate to severe airflow obstruction." Opinion adopted on 12.04.2018. Request for Supplementary Information adopted on 15.02.2018.	
WS1307 **OFEV-EMEA/H/C/003821/WS1307/0019** **Vargatef-** **EMEA/H/C/002569/WS1307/0019** Boehringer Ingelheim International GmbH, Lead Rapporteur: Sinan B. Sarac, "Update of section 4.4 of the SmPC for Ofev and Vargatef to amend the current warning on drug induced liver injury based one case of sever liver injury with fatal outcome reported for Ofev during the post-marketing phase. In addition section 4.4 of the Ofev SmPC is updated to include when the majority of the hepatic events occurred and on the need for hepatic transaminases and bilirubin levels to be measured at regular intervals during the first 3 months of treatment. Section 4.8 of the Vargatef SmPC is also updated to include in the summary of the safety profile that the safety data is also based on post-marketing data. The Package Leaflet is updated accordingly. The MAH is proposing to distribute a DHPC for Ofev. In addition, the Worksharing applicant (WSA) took the opportunity to make some corrections to the Bulgarian, Estonian, Icelandic, Latvian and Maltese translations for Ofev and Bulgarian, Estonian, Latvian and Maltese translations for Vargatef." Request for Supplementary Information adopted on 25.01.2018.	
WS1348 **Exviera-EMEA/H/C/003837/WS1348/0035** **Viekirax-** **EMEA/H/C/003839/WS1348/0042** AbbVie Limited, Lead Rapporteur: Filip Josephson, "Submission of the final report from study (M14-227) listed as a category 3 study in the RMP. This is a Phase 3b study designed to evaluate the safety and efficacy of ombitasvir/paritaprevir/ritonavir and dasabuvir in HCV infected patients with Child-Pugh B decompensated cirrhosis." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 12.04.2018.	
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, "C.I.4: Update of sections 4.2 and 6.6 of the SmPC of Humalog/Liprolog in cartridges following the signal PRAC recommendation (EPITT 18893); the Package Leaflet and Labelling are updated. 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. 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. Minor editorial changes have been included." Request for Supplementary Information adopted on 12.04.2018.	Request for supplementary information adopted with a specific timetable.

B.5.3. CHMP-PRAC assessed procedures

Advate - octocog alfa - **EMEA/H/C/000520/II/0091** Baxter AG, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 4.2 of the SmPC in order to remove a statement that the use of 2 ml presentations has not been documented for paediatric subjects below 2 years of age. This update follows final results from study 061101 listed as a category 3 study in the RMP; this was a prospective, non-interventional, post-marketing surveillance study that assessed the safety and efficacy of Advate reconstituted in 2 ml of sterile water for injection during routine clinical practice in the EU. The Package Leaflet is updated accordingly. The RMP version 15.1 has also been submitted." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 12.04.2018.

Alecensa - alectinib -
EMEA/H/C/004164/II/0010
Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Patrick Batty, "Update of sections 4.2 and 5.2 of the SmPC in order to update information on effect of hepatic impairment on PK of alectinib based on final results from study NP29783. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest EC guidance regarding warning statements on sodium."
Request for Supplementary Information adopted on 22.02.2018.

Caprelsa - vandetanib -
EMEA/H/C/002315/II/0028
Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of sections 4.1, 4.4 and 5.1 of the SmPC in order to delete the information regarding Rearranged during Transfection (RET) mutation. The application addresses SOB 001 and the MAH proposes to revert from conditional marketing authorisation to standard marketing authorisation. Annex II and Package Leaflet are updated accordingly. The RMP version 12.2 has also been submitted.

In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10."
Request for Supplementary Information adopted on 14.12.2017.

Cerdelga - eliglustat -
EMEA/H/C/003724/II/0015/G, Orphan
Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Dolores Montero Corominas, "Update of sections 4.2., 4.3., 4.4., 4.5. and 5.2. of the SmPC based on the final data from studies POP13777 "Pharmacokinetics of Oral Single-Dose eliglustat in Subjects with Hepatic Impairment" (MEA003.3) and POP13778 "Pharmacokinetics of Oral Single-Dose eliglustat in Subjects with Renal Impairment" (MEA004.3). Annex II D - Conditions Or Restrictions With Regard To The Safe And Effective Use Of The Medicinal Product

of the Product Information, additional risk minimisation measures has likewise been amended. The Package Leaflet is updated accordingly. The RMP version 5.0 has also been submitted." Request for Supplementary Information adopted on 22.02.2018, 14.12.2017.	
Defitelio - defibrotide - EMEA/H/C/002393/II/0026, Orphan Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, "Update of sections 4.8 and 5.1 of the SmPC in order to update the frequencies of adverse reactions included in the tabulated list of adverse reactions and to update the clinical efficacy and safety information based on the results from study 2006-05 listed as category 3 in the risk management plan (RMP). This is a phase 3, open-label expanded access study designed to provide access to defibrotide as an investigational new drug to patients with severe hepatic veno-occlusive disease. The final study report has been submitted. The RMP (version 3.4) and package leaflet are updated accordingly. In addition, the MAH took the opportunity to bring the SmPC in line with the latest QRD template (version 10), to update the list of local representatives in the package leaflet and to correct a translation error in the Polish, Finnish, Danish and Latvian languages." Opinion adopted on 12.04.2018. Request for Supplementary Information adopted on 08.02.2018, 30.11.2017, 28.09.2017.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Defitelio - defibrotide - EMEA/H/C/002393/II/0027, Orphan Gentium S.r.l., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, "Submission of an updated RMP version 4.0 in order to re-classify the imposed non-interventional PASS listed as a category 2 study in the RMP (specific obligation) to a study listed as a category 3 in the RMP (required additional pharmacovigilance activities). This study is an observational registry (DF-VOD2013-03-REG) which aims to record safety and outcome data in patients diagnosed with severe VOD following HSCT treated or not with defitelio. The Annex II of the product information is updated accordingly." Request for Supplementary Information adopted	

on 22.02.2018, 09.11.2017.	
Eliquis - apixaban - EMEA/H/C/002148/II/0050 Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, “Update of sections 4.2 and 5.1 of the SmPC in order to update the posology, method of administration and efficacy and safety information based on final results from study (EMANATE – b0661025/CV185267) listed as a PAES in the RMP; this is a phase 4 study to assess the effectiveness of apixaban compared with usual care anticoagulant in subjects with non-valvular atrial fibrillation (NVAF) undergoing cardioversion; the Package Leaflet is updated accordingly. The RMP version 19 has also been submitted. In addition, the Marketing authorisation holder took the opportunity to update the address of the MAH in the product information.” Request for Supplementary Information adopted on 25.01.2018.	
Keppra - levetiracetam - EMEA/H/C/000277/II/0169/G UCB Pharma S.A., Rapporteur: Koenraad Norga, PRAC Rapporteur: Laurence de Fays, “1) C.I.4 (type II): Update of section 4.8 of the SmPC to add the ADR Gait Disturbance, to address the CHMP recommendations from P46/085; 2) C.I.4 (type II): Update of section 4.2 of the SmPC to add Dysgeusia as a potential experience post administration and to section 4.5 of the SmPC to remove drug interaction with Methotrexate, in accordance with the latest Levetiracetam Company Core Data Sheet); 3) C.I.4 (type II): Update of Section 4.6 to add information on 'Women of childbearing potential' and to update the Pregnancy section, to address PRAC recommendations from LEG-084.1; The Package Leaflet is updated accordingly. An updated to the Risk Management Plan (version 8.1) is included to address PRAC recommendations from LEG 84.1.” Request for Supplementary Information adopted on 22.03.2018, 25.01.2018.	
Kuvan - sapropterin - EMEA/H/C/000943/II/0052, Orphan BioMarin International Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Almath Spooner,	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

"Based on a review of the post-marketing experience and in order to harmonise the safety information with the CCDS, update of section 4.8 of the Kuvan SmPC to add the following adverse events regarding gastrointestinal tract: dyspepsia, nausea and gastritis. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement the latest QRD template and bring up to date sections 17 and 18 of Annex IIIA." Opinion adopted on 12.04.2018. Request for Supplementary Information adopted on 30.11.2017.	
OPDIVO - nivolumab - EMEA/H/C/003985/II/0047 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning on the nivolumab use in patients who have previously undergone allogeneic HSCT and the increased risk of rapid onset and severe Graft versus Host Disease (GVHD) based on evidence from spontaneous case reports, literature case reports, and from 2 multicenter case series. Annex II.D and the Package Leaflet are updated accordingly. The RMP version 7.8 has also been submitted to include the "risk of GVHD with nivolumab after allogeneic HSCT" as an "Important Potential Risk" based on the RMP template (Revision 2). In addition, the Marketing authorisation holder (MAH) took the opportunity to make some minor editorial corrections to the PI." Request for Supplementary Information adopted on 22.03.2018.	
Prevenar 13 - pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - EMEA/H/C/001104/II/0161 Pfizer Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Qun-Ying Yue, "Submission of the final study report from study B1851041, a phase 4 post marketing study to determine ' National trends in Ambulatory Care Visits for Otitis Media in Children Under the Age of Five in the United States.' Consequently, the RMP version 12 has been updated." Request for Supplementary Information adopted	Request for supplementary information adopted with a specific timetable.

on 12.04.2018.	
Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0129 CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, “Update of section 4.3 of the SmPC to remove the hyperprolineamia contraindication. The package leaflet and RMP (version 6.0) are updated accordingly.”	
Revlimid - lenalidomide - EMEA/H/C/000717/II/0098, Orphan Celgene Europe Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, “Update 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. The section 4.4 of the SmPC has been updated accordingly. Furthermore, the RMP version 35 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.” Request for Supplementary Information adopted on 12.04.2018.	Request for supplementary information adopted with a specific timetable.
Rydapt - midostaurin - EMEA/H/C/004095/II/0002, Orphan Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Update of sections 4.5 and 5.2 of the SmPC in order to reflect the results from study R1600721 “Assessment of PKC412 and its metabolites (CGP052421 and CGP062221) as inhibitors of human bile salt export pump (BSEP) " and study R1701192 ‘In vitro assessment of cytochrome P450 3A4 and 3A5 enzyme inhibition by PKC412, CGP52421 and CGP62221’, in fulfilment of the post-authorisation measures MEA 011 and REC 014. In addition, the MAH took the opportunity to update section 5.2 to correct figures as per Study A2107-Amendment 02 already assessed and to make editorial changes in the SmPC. The RMP (v 2.0) has also been updated to reflect the study results. In addition, the search criteria for the important identified risk	

pulmonary toxicity (including pleural effusion and interstitial lung disease) was updated to include the PT-pleural effusion." Request for Supplementary Information adopted on 22.03.2018.	
Stribild - elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil - EMEA/H/C/002574/II/0087 Gilead Sciences International Limited, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Julie Williams, "Submission of the final study report for Study GS-EU-236-0141, listed as a category 3 study in the Risk Management Plan, in order to fulfil a post-authorisation measure (PAM) MEA 006 for Stribild; This study is an Observational Drug Utilization Study of Stribild in Adults with HIV-1 Infection With this application and as agreed with the EMA, Gilead is also taking this opportunity to address the outstanding questions from MEA 002.3." Request for Supplementary Information adopted on 12.04.2018, 11.01.2018.	Request for supplementary information adopted with a specific timetable.
SYLVANT - siltuximab - EMEA/H/C/003708/II/0026/G, Orphan Janssen-Cilag International NV, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to update the product information following final results from studies CNTO328MCD2001 and CNTO328MCD2002 listed as imposed obligation in the Annex II (ANX002 and ANX003). The Package Leaflet are updated accordingly. The RMP version 4.0 has also been submitted. In addition, the list of local representatives (Czech Republic, Lithuania and Portugal) in the PL is being revised" Opinion adopted on 12.04.2018. Request for Supplementary Information adopted on 30.11.2017.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Symtuza - darunavir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004391/II/0003/G Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Julie Williams, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect the week-48 results	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

from 2 studies (TMC114FD2HTX3001 and TMC114IFD3013) listed as category 3 studies in the RMP; these are phase 3 studies to evaluate the efficacy and safety of D/C/F/TAF once daily fixed-dose combination regimen versus a regimen consisting of DRV/COBI FDC co-administered with FTC/TDF FDC in ARV treatment-naïve HIV-1 infected subjects (study TMC114FD2HTX3001) and to evaluate switching to a D/C/F/TAF once-daily single-tablet regimen versus continuing the current regimen consisting of a boosted protease inhibitor combined with FTC/TDF in virologically-suppressed, HIV-1 infected subjects (study TMC114IFD3013). The RMP version 2.2 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to make minor editorial revision in the product information." Opinion adopted on 12.04.2018. Request for Supplementary Information adopted on 08.02.2018.	
Tecentriq - atezolizumab - EMEA/H/C/004143/II/0004 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of section 4.8 of the SmPC in order to update the safety information based on the primary results from study IMvigor211 in order to fulfil ANX 002 (the submission of the final CSR being listed as an imposed PAES in Annex II.D). This is a phase III, open-label, multicentre, randomized study to investigate the efficacy and safety of atezolizumab (anti- PD-L1 antibody) compared with chemotherapy in patients with locally advanced or metastatic urothelial bladder cancer after failure with platinum-containing chemotherapy. The Package Leaflet and the RMP (version 3.0, according to GVP module V revision 2) are updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to implement some editorial changes throughout the Product Information." Request for Supplementary Information adopted on 12.04.2018.	Request for supplementary information adopted with a specific timetable.
XGEVA - denosumab - EMEA/H/C/002173/II/0059 Amgen Europe B.V., Rapporteur: Kristina	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information and to revise the special warnings, precautions for use and undesirable effects based on cases of clinically significant hypercalcemia following discontinuation of denosumab in patients with growing skeletons (i.e., adolescent subject with giant-cell tumour of bone (GCTB) in Study 20062004) and in postmarketing reports of pediatric patients treated with denosumab for GCTB or for unapproved indications was previously determined to be an important identified risk ; the Package Leaflet are is updated accordingly. Consequently the RMP revised version 32 has also been submitted." Opinion adopted on 12.04.2018. Request for Supplementary Information adopted on 08.03.2018.	recommendation.
Yervoy - ipilimumab - EMEA/H/C/002213/II/0054 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Sabine Straus, "Update of section 5.1 of the SmPC to update the overall survival data of ipilimumab 3mg/kg monotherapy pooled across studies based on the final results of study CA184332 and CA184338 listed as category 3 studies in the RMP, in order to fulfil MEA 035 and MEA 030.1 respectively. Study CA184332 is a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab as first line therapy in a community practice setting and study CA184438 is a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab as first line therapy. The RMP version 18.4 has also been submitted." Request for Supplementary Information adopted on 12.04.2018.	Request for supplementary information adopted with a specific timetable.
WS1335 **Rixathon-** **EMEA/H/C/003903/WS1335/0010** **Riximyo-** **EMEA/H/C/004729/WS1335/0010** Sandoz GmbH, Lead Rapporteur: Jan Mueller-Berghaus, Lead PRAC Rapporteur: Doris Stenver, "Submission of final study reports for studies GP13-302 (a randomized, double-blind,	Request for supplementary information adopted with a specific timetable.

parallel-group safety study with the aim to specifically address a potential safety risk of a switch from treatment with originator rituximab (Mabthera/Rituxan) to treatment with GP2013) and GP13-201 (a 52-week multicenter, randomized, double-blind, parallel-arm, comparative study in patients with active Reumathoid Arthritis (RA) refractory or intolerant to standard DMARDs and one or up to three anti-TNFs therapies). The RMP (version 3.0) has been updated accordingly." Request for Supplementary Information adopted on 12.04.2018.	
WS1343 **Relvar Ellipta-** **EMEA/H/C/002673/WS1343/0036** **Revinty Ellipta-** **EMEA/H/C/002745/WS1343/0032** Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, "C.I.11.b) Submission of an updated RMP version 9.2 to reflect the addition of information with regards SLS-asthma completion (HZA115150- interventional post-authorisation safety Category 1 study to further investigate the risk of pneumonia-ANX005), to update the important identified risk of pneumonia with regards findings from the study, and to provide a justification for removal of the important potential risk of asthma related intubations and deaths and a justification for removal of missing information related to long term use in asthma (>1 year). Consequently Annex II condition of the product information is updated accordingly." Request for Supplementary Information adopted on 12.04.2018.	Request for supplementary information adopted with a specific timetable.

B.5.4. PRAC assessed procedures

PRAC Led **Bemfola - follitropin alfa -** **EMEA/H/C/002615/II/0016** Gedeon Richter Plc., Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Update of the RMP version 2 based on the phase-3 multicentre study conducted to compare the efficacy and safety of two r-hFSH formulations in normal ovulatory	Request for supplementary information adopted with a specific timetable.

women 35 to 42 years of age undergoing in vitro fertilisation (IVF) (CSR FIN3002)." Request for Supplementary Information adopted on 12.04.2018.	
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 listed as a category 3 study in the RMP. This is a final survey aimed to measure to the effectiveness of the educational materials at 6 months post-launch and 6 months post-redistribution of the revised healthcare professional leaflet. The RMP version 7.0 has also been submitted." Request for Supplementary Information adopted on 12.04.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Edarbi - azilsartan medoxomil - EMEA/H/C/002293/II/0021** Takeda Pharma A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the final report from the drug utilisation study listed as a category 3 study in the RMP. This post-authorisation safety study is a retrospective non-interventional cohort study using a patient level electronic medical records database in Germany aimed to describe the prescription of azilsartan medoxomil in patients with essential hypertension and those prescribed azilsartan medoxomil for other reasons." Request for Supplementary Information adopted on 12.04.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Eylea - aflibercept - EMEA/H/C/002392/II/0039** Bayer AG, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final report from the post authorisation safety study 16526, listed as a category 3 study in the RMP. This is an observational study to evaluate the physician and patient knowledge of safety	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

and safe use information for Aflibercept in Europe as stated in the EU Educational Material of Eylea." Opinion adopted on 12.04.2018. Request for Supplementary Information adopted on 08.02.2018, 30.11.2017.	
PRAC Led **Imraldi - adalimumab - EMEA/H/C/004279/II/0004** Samsung Bioepis UK Limited (SBUK), Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 2.1 in order to indicate changes in the distribution method for the Imraldi Patient Alert Card (PAC)from being included in the Annex IIIA of the Product Information to be provided to patients by healthcare professionals by including the PAC in the physician educational material. The Annexes I, II, IIIA and IIIB of the PI are updated accordingly." Opinion adopted on 12.04.2018.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Lucentis - ranibizumab - EMEA/H/C/000715/II/0070/G** Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "1. Type II- C.I.13: Submission of the final report from study LUMINOUS study (CRFB002A2406), an observational, multicenter study to assess the long term safety and effectiveness of ranibizumab in routine clinical practice, in fulfilment of the post-authorisation measures MEA 036, MEA 048 and MEA 054. Consequentially, the RMP has been updated to reflect these changes. 2. Type II-C.I.11: Submission of an updated RMP version 17.0 (RMP template Rev. 2) according to GVP Module V to include changes not consequential to LUMINOUS study. In addition, the MAH is proposing the removal of the use of educational materials and targeted follow-up checklists listed in Annex II-D of the Product Information." Request for Supplementary Information adopted on 12.04.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **MabThera - rituximab -**	Request for supplementary information adopted with a specific timetable.

EMEA/H/C/000165/II/0144 Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Update the RMP to remove the additional risk minimization measure of Educational Outreaches for the important identified risk of Infusion Related Reactions and Acute Infusion Related Reactions (IRR). Therefore, the RMP has been updated accordingly to version 16.0." Request for Supplementary Information adopted on 12.04.2018.	
PRAC Led **MULTAQ - dronedarone - EMEA/H/C/001043/II/0039/G** sanofi-aventis groupe, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "C.I.13: Submission of the final report from study DRONE_C_05917 listed as a category 3 study in the RMP. This is a non-interventional epidemiological study aimed for the surveillance of serious liver injuries/diseases (SLD) with the use of dronedarone using multiple databases in the US, including the addendum on surveillance of interstitial lung disease (ILD). The RMP version 11.0 has also been submitted. C.I.13: Submission of the final report from study DRONE_C_05911 listed as a category 3 study in the RMP. This is a non-interventional epidemiological study aimed to study the concomitant use of dronedarone and digoxin (or statins) and the risk of digitalis intoxication (or rhabdomyolysis and myopathy). The RMP version 11.0 has also been submitted." Opinion adopted on 12.04.2018. Request for Supplementary Information adopted on 11.01.2018, 26.10.2017.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Mycamine - micafungin - EMEA/H/C/000734/II/0035** Astellas Pharma Europe B.V., Rapporteur: Harald Enzmann, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Harald Enzmann, "Submission of the final survey report regarding Educational tools in the RMP and Educational tools as a LEG (39) and updated RMP version 18.0."	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 12.04.2018, 11.01.2018.	
PRAC Led **Nulojix - belatacept - EMEA/H/C/002098/II/0047/G** Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Filip Josephson, "Submission of the final report from studies IM103061 and IM103089, listed as a category 3 studies in the RMP. IM103061 is an epidemiological study on pregnancy outcome among belatacept users in the US. IM103089 evaluates data retrospectively to assess the association between belatacept and the risk of PTDL in renal transplant recipients in Europe. An updated RMP, reflecting completion of the two above studies is being submitted as part of this variation (Version 15)." Opinion adopted on 12.04.2018. Request for Supplementary Information adopted on 30.11.2017.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **NutropinAq - somatropin - EMEA/H/C/000315/II/0069/G** Ipsen Pharma, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "II: C.I.11: Submission of an updated RMP version 3.0 in order to include formatting in accordance with the new RMP template and to include updates from the post-approval safety study (PASS) International Cooperative Growth Study (iNCGS) Post Marketing Surveillance Program For NutropinAq. II: C.I.13: Submission of the final report from International Cooperative Growth Study (iNCGS) Post Marketing Surveillance Program For NutropinAq. This study collected long-term safety and effectiveness data on NutropinAq during treatment of paediatric growth disorders for which growth hormone is indicated." Opinion adopted on 12.04.2018.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Pergoveris - follitropin alfa / lutropin alfa - EMEA/H/C/000714/II/0055** Merck Serono Europe Limited, Rapporteur:	Request for supplementary information adopted with a specific timetable.

Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "The update Risk Management Plan version 5.1 for Pergoveris to · Align the RMP template with Good Pharmacovigilance Practice (GVP) Module V, revision 1. · Add the reference to Pergoveris solution for injection in pre-filled pen (300IU/150IU, 450IU/225IU and 900IU/450IU) following the approval in the European Union (EU) on the 8th of May 2017. · Revise the epidemiology section based on the recent literature data. · Revise non-clinical part of the safety specification section with the data available from r-hFSH (recombinant human follicle stimulating hormone), r-hLH (recombinant human luteinizing hormone) and Pergoveris. The clinical trial section has been updated for clinical studies for r-hFSH/r-hLH for Ovulation Induction (OI) and Assisted Reproductive Technologies (ART). · Update the patient exposure data and other sections based on the cases received up to the data lock point (DLP) of 31 July 2017 i.e. non-study post authorisation exposure section and additional EU requirements for the safety specification section and include other minor changes such as update of the reporting rates." Request for Supplementary Information adopted on 12.04.2018.	
PRAC Led **Resolor - prucalopride - EMEA/H/C/001012/II/0042** Shire Pharmaceuticals Ireland Limited, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "Submission of the final clinical study report for the post-authorization drug utilization study SHP555-804 in fulfilment of MEA 006.11 A drug utilisation study to examine characteristics of patients prescribed prucalopride (Resolor) and a pharmacoepidemiological study of the occurrence of major cardiovascular events, pregnancy, and pregnancy outcomes in the UK CPRD Database. The RMP (v 14.0) has also been updated to reflect the study results." Request for Supplementary Information adopted on 12.04.2018.	Request for supplementary information adopted with a specific timetable.

PRAC Led **Tasigna - nilotinib -** **EMEA/H/C/000798/II/0092, Orphan** Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, “Submission of an updated RMP version 21.0 in order to delete the important identified risk 'Myelosuppression', and to upgrade the risk 'Cardiac failure' from an important potential to an important identified risk. In addition, changes in the definition of the identified risks 'Hepatotoxicity' and 'Fluid retention' have been implemented.” Request for Supplementary Information adopted on 12.04.2018.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Xeljanz - tofacitinib -** **EMEA/H/C/004214/II/0009** Pfizer Limited, Rapporteur: Robert James Hemmings, PRAC Rapporteur: Sabine Straus, PRAC-CHMP liaison: Johann Lodewijk Hillege, “Submission of the final CSR for study A3921024 listed as a category 3 study in the RMP (MEA 003). Study A3921024 is a long term, open label follow-up study to evaluate the long-term safety of patients on 5 mg BID of XELJANZ with a secondary objective of evaluating sustained efficacy in patients with rheumatoid arthritis.” Opinion adopted on 12.04.2018.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Xofigo - radium-223 -** **EMEA/H/C/002653/II/0031** Bayer AG, Rapporteur: Harald Enzmann, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, “Submission of Clinical Study Report for study 17399. This is an observational post-authorisation safety study (PASS) listed as category 4 in the RMP to evaluate the use of radium-223 dichloride in patients in Sweden with a diagnosis of CRPC with bone metastases (mCRPC) and patients in whom radium-223 dichloride may have been potentially used off-label.” Opinion adopted on 12.04.2018.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Zavicefta - ceftazidime / avibactam -** **EMEA/H/C/004027/II/0008**	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP

Pfizer Ireland Pharmaceuticals, PRAC Rapporteur: Jolanta Gulbinovic, PRAC-CHMP liaison: Rugile Pilviniene, “To provide an updated Risk Management Risk (version 2.0) in order to incorporate data from the REPROVE study (already submitted in procedure II-02), align the RMP with the current EU template, and add current post-marketing experience relative to the RMP data lock point (24/8/17). The Phase 3 REPROVE study was a randomized, multicentre, double-blind, double-dummy, parallel group comparative study to determine the efficacy, safety and tolerability of CAZ-AVI (2000 mg ceftazidime and 500 mg avibactam) versus meropenem (1000 mg) in the treatment of NP, including VAP, in hospitalised adults 18 years of age or older.” Opinion adopted on 12.04.2018.	recommendation.
PRAC Led **WS1283** **Relvar Ellipta-** **EMEA/H/C/002673/WS1283/0035** **Revinty Ellipta-** **EMEA/H/C/002745/WS1283/0031** Glaxo Group Ltd, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, PRAC-CHMP liaison: Concepcion Prieto Yerro, “Submission of a final study report 205052 (PRJ2214) (drug utilization study of new users of fluticasone furoate/vilanterol (FF/VI) in the primary care setting: UK Clinical Practice Research Datalink (CPRD) study). The RMP version 9.1 has been updated accordingly.” Opinion adopted on 12.04.2018. Request for Supplementary Information adopted on 08.03.2018, 11.01.2018.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1299** **Enurev Breezhaler-** **EMEA/H/C/002691/WS1299/0025** **Seebri Breezhaler-** **EMEA/H/C/002430/WS1299/0025** **Tovanor Breezhaler-** **EMEA/H/C/002690/WS1299/0028** Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth, Lead PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, “Submission of the final study report of the Category 1 Post-Authorisation Safety Study	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

(PASS) on cardio and cerebrovascular outcomes (Multinational, multidatabase cohort study to assess adverse cardiovascular and cerebrovascular outcomes and mortality in association with inhaled NVA237 in Europe / CNVA237A2402T) with subsequent update of Annex II. Consequently the deletion from the list of additional monitoring led to the update of Annex I and IIIB. The MAH also took this oppotunity to update the local representatives. The RMP version 8 was submitted." Opinion adopted on 12.04.2018. Request for Supplementary Information adopted on 08.02.2018.	
PRAC Led **WS1340** **Ultibro Breezhaler-** **EMEA/H/C/002679/WS1340/0022** **Ulunar Breezhaler-** **EMEA/H/C/003875/WS1340/0022** **Xoterna Breezhaler-** **EMEA/H/C/003755/WS1340/0025** Novartis Europharm Limited, Lead Rapporteur: Mark Ainsworth, Lead PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final report of the multinational, multi-database drug utilization study of indacaterol/glycopyrronium bromide (QVA149) in Europe (CQVA149A2401) with the objective to estimate the use of QVA149 off-label and in the subpopulations with missing information mentioned in the risk management plan (RMP)." Opinion adopted on 12.04.2018. Request for Supplementary Information adopted on 08.02.2018.	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1342** **Exviera-EMEA/H/C/003837/WS1342/0034** **Viekirax-** **EMEA/H/C/003839/WS1342/0041** AbbVie Limited, Lead PRAC Rapporteur: Dolores Montero Corominas, PRAC-CHMP liaison: Concepcion Prieto Yerro, "To update the RMP to incorporate changes requested by PRAC during assessment of the 24 month PSUR applications (EMEA/H/C/PSUSA/00010363/201701 and EMEA/H/C/PSUSA/00010367/201701). These changes are as follows:	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

1. Addition of a new potential risk of depression and suicide in Module SVII.1 - Newly identified safety concerns. 2. Removal of off-label use and medication error as potential risks from Module SVII. 3. Renaming of the potential risk of development of resistance to Lack of Efficacy/Risk of Development of Resistance in Module SVII.3. In addition, the commitment dates for 4 ongoing studies listed in Part III.5.1 (Table of On-going and planned additional pharmacovigilance studies/activities in the pharmacovigilance plan) have been revised." Opinion adopted on 12.04.2018. Request for Supplementary Information adopted on 11.01.2018.	
PRAC Led **WS1357** **Efficib-EMEA/H/C/000896/WS1357/0089** **Janumet-EMEA/H/C/000861/WS1357/0089** **Januvia-EMEA/H/C/000722/WS1357/0063** **Ristaben-EMEA/H/C/001234/WS1357/0055** **Ristfor-EMEA/H/C/001235/WS1357/0076** **TESAVEL-EMEA/H/C/000910/WS1357/0063** **Velmetia-EMEA/H/C/000862/WS1357/0092** **Xelevia-EMEA/H/C/000762/WS1357/0067** Merck Sharp & Dohme Limited, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 10 in order to remove "theoretic carcinogenic potential" form the list of safety concerns, currently classified as "missing information"." Request for Supplementary Information adopted on 12.04.2018.	Request for supplementary information adopted with a specific timetable.

B.5.5. CHMP-CAT assessed procedures

Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0001, ATMP CO.DON AG, Rapporteur: Lisbeth Barkholt,	

Spherox - spheroids of human autologous matrix-associated chondrocytes - EMEA/H/C/002736/II/0002/G, ATMP

CO.DON AG, Rapporteur: Lisbeth Barkholt, , "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."

Zalmoxis - allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - EMEA/H/C/002801/II/0009/G, Orphan, ATMP

MolMed SpA, Rapporteur: Johannes Hendrikus Ovelgonne, CHMP Coordinator: Paula Boudewina van Hennik

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

WS1341/G
Tivicay-
EMEA/H/C/002753/WS1341/0033/G
Triumeq-
EMEA/H/C/002754/WS1341/0052/G

ViiV Healthcare UK Limited, Lead Rapporteur: Filip Josephson	
WS1345/G **Ebymect-** **EMEA/H/C/004162/WS1345/0030/G** **Edistride-** **EMEA/H/C/004161/WS1345/0024/G** **Forxiga-** **EMEA/H/C/002322/WS1345/0043/G** **Qtern-** **EMEA/H/C/004057/WS1345/0015/G** **Xigduo-** **EMEA/H/C/002672/WS1345/0041/G** AstraZeneca AB, Lead Rapporteur: Kristina Dunder	
WS1350 **Hexacima-** **EMEA/H/C/002702/WS1350/0078** **Hexaxim-** **EMEA/H/W/002495/WS1350/0083** **Hexyon-** **EMEA/H/C/002796/WS1350/0082** Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus,	
WS1358 **AMGEVITA-** **EMEA/H/C/004212/WS1358/0004** **SOLYMBIC-** **EMEA/H/C/004373/WS1358/0004** Amgen Europe B.V., Lead Rapporteur: Kristina Dunder,	Positive Opinion adopted by consensus on 12.04.2018. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1361 **AZILECT-** **EMEA/H/C/000574/WS1361/0079** **Rasagiline ratiopharm-** **EMEA/H/C/003957/WS1361/0012** Teva B.V., Lead Rapporteur: Bruno Sepodes, “To change the storage conditions for the finished product from "Do not store above 25 °C" to "Do not store above 30 °C". The applicant took the opportunity to introduce editorial changes in the product information by correcting minor spelling mistakes and to align with QRD template (EN, CS, DA, EL, ET, FI, HR, HU, IS, IT, LT, LV, NO, PT, SK, SL and SV).” Request for Supplementary Information adopted on 12.04.2018.	Request for supplementary information adopted with a specific timetable.

WS1367 **Abseamed-** **EMEA/H/C/000727/WS1367/0069** **Binocrit-** **EMEA/H/C/000725/WS1367/0069** **Epoetin alfa Hexal-** **EMEA/H/C/000726/WS1367/0068** Sandoz GmbH, Lead Rapporteur: Alexandre Moreau	
WS1373/G **AMGEVITA-** **EMEA/H/C/004212/WS1373/0005/G** **SOLYMBIC-** **EMEA/H/C/004373/WS1373/0005/G** Amgen Europe B.V., Lead Rapporteur: Kristina Dunder, “To update SmPC section 5.1 with the clinical interim data from OLE study M11-327. To update section 2 of the Package Leaflet to include a clarifying statement that allergic reactions to the product can in rare cases be life-threatening. In addition the MAH updated the PL and LT annexes to be in line with the originators annexes.”	
WS1375 **Actraphane-** **EMEA/H/C/000427/WS1375/0075** **Insulatard-** **EMEA/H/C/000441/WS1375/0072** **Mixtard-** **EMEA/H/C/000428/WS1375/0076** **Protaphane-** **EMEA/H/C/000442/WS1375/0071** Novo Nordisk A/S, Duplicate, Duplicate of Monotard (SRD), Ultratard (SRD), Lead Rapporteur: Sinan B. Sarac,	
Hexacima- **EMEA/H/C/002702/WS1304/0076** **Hexaxim-** **EMEA/H/W/002495/WS1304/0081** **Hexyon-** **EMEA/H/C/002796/WS1304/0080** Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus,	

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

Jinarc - tolvaptan - **EMEA/H/C/002788/II/0013**	The MAH withdrew the procedure on

Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey Withdrawal request submitted on 29.03.2018.	29.03.2018.
Pyramax - pyronaridine / artesunate - EMEA/H/W/002319/II/0018 Shin Poong Pharmaceutical Co., Ltd., Rapporteur: Joseph Emmerich, PRAC Rapporteur: Caroline Laborde Withdrawal request submitted on 06.04.2018.	The MAH withdrew the procedure on 06.04.2018.
Qtern - saxagliptin / dapagliflozin - EMEA/H/C/004057/II/0013 AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, Withdrawal request submitted on 03.04.2018.	The MAH withdrew the procedure on 03.04.2018.
Resolor - prucalopride - EMEA/H/C/001012/II/0044 Shire Pharmaceuticals Ireland Limited, Rapporteur: Greg Markey Withdrawal request submitted on 26.03.2018.	The MAH withdrew the procedure on 26.03.2018.
Samsca - tolvaptan - EMEA/H/C/000980/II/0029 Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey Withdrawal request submitted on 29.03.2018.	The MAH withdrew the procedure on 29.03.2018.

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

atazanavir - EMEA/H/C/004859 , treatment of HIV-1 infection
turoctocog alfa pegol - EMEA/H/C/004883, Orphan Novo Nordisk A/S, Treatment and prophylaxis of bleeding in patients with haemophilia A
cemiplimab - EMEA/H/C/004844 , as monotherapy, indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma
ciprofloxacin - EMEA/H/C/004394 , treatment of non-cystic fibrosis bronchiectasis (NCFBE) patients with chronic lung infection with Pseudomonas

aeruginosa (P. aeruginosa)	
miglustat - EMEA/H/C/004904 , treatment of adult patients with mild to moderate type 1 Gaucher disease and only in the treatment of patients for whom enzyme replacement therapy is unsuitable,	
pegvaliase - EMEA/H/C/004744, Orphan BioMarin International Limited, treatment of adults with phenylketonuria (PKU) who have inadequate blood phenylalanine control	
axalimogene filolisbac - EMEA/H/C/004473, ATMP , treatment of cervical cancer	
lanadelumab - EMEA/H/C/004806, Orphan Shire Pharmaceuticals Ireland Limited, treatment of angioedema attacks, prevention of angioedema attacks	**Accelerated review**
sotagliflozin - EMEA/H/C/004889 , indicated as an adjunct to insulin therapy to improve glycaemic control in adults with type 1 diabetes mellitus.	

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

Dupixent - dupilumab - EMEA/H/C/004390/X/0004/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Kimmo Jaakkola, “Extension application to add a new strength of 200 mg solution for injection in pre-filled syringe with safety system (PFS-S) and pre-filled pen (PFP), grouped with a type II variation (C.I.6.a) to add the following indications: - Add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older, who are inadequately controlled with medium-to-high dose inhaled corticosteroids (ICS) plus another medicinal product for maintenance treatment, including those with or without an eosinophilic phenotype; - Maintenance therapy to improve lung function; - Maintenance therapy to reduce oral steroid use and improve lung function in steroid-dependent asthma patients; Based on the pivotal studies DRI12544, QUEST and VENTURE.	

As a consequence, SmPC sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 have been updated and the Package Leaflet has been updated accordingly.
The RMP (version 2.0) is uppdated accordingly.
In addition, the MAH proposed to merge the SmPCs for the 200 mg and 300 mg strengths."

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

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka, "Extension application to add 2 new strengths of 50 mg and 87.5 mg for solution for injection in a pre-filled syringe with needle guard, for subcutaneous (SC) administration, grouped with a type II variation (C.I.6.a) to include paediatric use of polyarticular Juvenile Idiopathic Arthritis (2 years and above) for solution for injection (50 mg, 87.5 mg and 125 mg).
The above-described changes are grouped with variations:
The RMP (version 25.0) is updated in accordance.
In addition, the applicant took the opportunity to implement minor editorial changes in the product information."

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

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

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

viable t-cells - EMEA/H/C/002397, Orphan, ATMP

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

List of Questions adopted on 08.09.2017.

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)
List of Questions adopted on 09.11.2017.

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
List of Questions adopted on 14.12.2017.

deferiprone - EMEA/H/C/004710
, treatment of iron overload in thalassemia major,
List of Questions adopted on 09.11.2017.

gefitinib - EMEA/H/C/004826
, treatment of non-small cell lung cancer,
List of Questions adopted on 14.12.2017.

durvalumab - EMEA/H/C/004771
, treatment of locally advanced, unresectable non-small cell lung cancer (NSCLC)
List of Questions adopted on 25.01.2018.

Inhixa - enoxaparin sodium - EMEA/H/C/004264/X/0018
Techdow Europe AB, Duplicate, Duplicate of Thorinane, Rapporteur: Andrea Laslop, PRAC Rapporteur: Menno van der Elst, “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.”
List of Questions adopted on 14.12.2017.

lenalidomide - EMEA/H/C/004857
, treatment of multiple myeloma,
List of Questions adopted on 14.12.2017.

voretigene neparvovec - EMEA/H/C/004451, Orphan, ATMP
Spark Therapeutics Ireland Ltd, treatment of patients with vision loss due to Leber congenital amaurosis or retinitis pigmentosa inherited retinal dystrophy
List of Questions adopted on 08.12.2017.

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
List of Questions adopted on 14.12.2017.

melatonin - EMEA/H/C/004425, PUMA
, treatment of insomnia in children with Autism Spectrum Disorders and neurogenetic diseases
List of Questions adopted on 14.09.2017.

mexiletine hcl - EMEA/H/C/004584, Orphan
LUPIN (EUROPE) LIMITED, Treatment of myotonic disorders
List of Questions adopted on 14.12.2017.

pegfilgrastim - EMEA/H/C/003961
, treatment of neutropenia
List of Questions adopted on 14.09.2017.

inotersen - EMEA/H/C/004782, Orphan
IONIS USA Ltd, treatment of transthyretin amyloidosis (hATTR)
List of Questions adopted on 20.02.2018.

meropenem / vaborbactam - EMEA/H/C/004669
, treatment of infections
List of Questions adopted on 09.11.2017.

daunorubicin / cytarabine - EMEA/H/C/004282, Orphan
Jazz Pharmaceuticals Ireland Limited, treatment of adults with high-risk acute myeloid leukaemia (AML)
List of Questions adopted on 20.02.2018.

eravacycline - EMEA/H/C/004237
, treatment of complicated intra-abdominal infections (cIAI) in adults
List of Questions adopted on 14.12.2017.

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

Firdapse - amifampridine - EMEA/H/C/001032/S/0053, Orphan
BioMarin Europe Ltd, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams

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

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

Fluenz Tetra - influenza vaccine (live attenuated, nasal) -
EMEA/H/C/002617/R/0079
AstraZeneca AB, Rapporteur: Bart Van der Schueren, Co-Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Jean-Michel Dogné

Memantine Accord - memantine -
EMEA/H/C/002766/R/0010
Accord Healthcare Limited, Generic, Generic of Axura, Rapporteur: Milena Stain, PRAC Rapporteur: Dolores Montero Corominas

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

CABOMETYX - cabozantinib -
EMEA/H/C/004163/II/0005
Ipsen Pharma, Rapporteur: Robert James Hemmings, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Sabine Straus, “Extension of indication to include the treatment of advanced hepatocellular carcinoma in adults following prior systemic therapy for Cabometyx; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC are updated with safety and efficacy information. The package leaflet and the risk management plan (version 4.0) are also updated accordingly.”

Kalydeco - ivacaftor -
EMEA/H/C/002494/II/0069, Orphan
Vertex Pharmaceuticals (Europe) Ltd., Co-Rapporteur: Melinda Sobor, PRAC Rapporteur: Dolores Montero Corominas, “Extension of Indication to include treatment of cystic fibrosis in children age 12 to less than 24 months who have one of the currently approved gating mutations in the CFTR gene for Kalydeco 50 mg & 75 mg Granules; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. Relevant consequential changes are

made to the Kalydeco 150 mg film-coated tablet Product Information. The Package Leaflet is updated in accordance.
The RMP version 7.2 has also been submitted."

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

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

Lynparza - olaparib - EMEA/H/C/003726/II/0020

AstraZeneca AB, Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Carmela Macchiarulo, "Extension of indication to include the use of Lynparza tablets as a montherapy for the treatment of adult patients with BRCA1/2-mutated HER2 negative metastatic breast cancer who have previously been treated with chemotherapy. These patients could have received chemotherapy in the neoadjuvant, adjuvant or metastatic setting.

As a consequence, section 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC for Lynparza tablets have been updated. Section 4.8 of Lynparza capsules and relevant sections of the package leaflet have been updated accordingly.
Furthermore, RMP version 16 has also been provided."

MabThera - rituximab -
EMEA/H/C/000165/II/0149
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Extension of indication to include the maintenance of remission of polyangiitis (Wegener's) (GPA) and microscopic polyangiitis (MPA) for MabThera; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package leaflet is updated accordingly. In addition, the MAH took the opportunity to implement a terminology change in Annex II."

MabThera - rituximab -
EMEA/H/C/000165/II/0150
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Doris Stenver, "Extension of indication to include the treatment of patients with moderate to severe pemphigus vulgaris (PV) for MabThera; as a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package leaflet is updated accordingly."

Rapiscan - regadenoson -
EMEA/H/C/001176/II/0027
GE Healthcare AS, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, "Extension of Indication to include use in the measurement of fractional flow reserve (FFR) during invasive coronary angiography (ICA) in patients presenting a coronary artery stenosis for Rapiscan based on study 060912001: Comparison of Regadenoson (RAPISCAN) and Central Intravenous Adenosine for Measurement of Fractional Flow Reserve and data from published literature. 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. An updated RMP version 10.0 was provided as part of this extension of indication."

RoActemra - tocilizumab -
EMEA/H/C/000955/II/0076
Roche Registration GmbH, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, "To add the paediatric indication 'treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 1 year of age and older, who have responded inadequately to

previous therapy with NSAIDs and systemic corticosteroids' to the RoActemra 162 mg solution for injection in pre-filled syringe formulation, based on data from the Phase Ib pharmacokinetic/pharmacodynamic bridging study WA28118 (JIGSAW 118), designed to confirm the RoActemra subcutaneous dosing regimens in patients aged 1 to 17 years old with sJIA, as well as assess the safety of the RoActemra subcutaneous formulation. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet is updated accordingly.
In addition, sections 4.2, 4.8 and 5.2 of the SmPC of the RoActemra 20 mg/mL concentrate for solution for infusion formulation are updated to reflect data from the pivotal RoActemra intravenous study WA18221 (TENDER), a randomised, placebo-controlled study to evaluate the effect of tocilizumab on disease response in patients with active sJIA."

Trimbow - beclometasone dipropionate / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004257/II/0002

Chiesi Farmaceutici S.p.A., Rapporteur: Harald Enzmann, PRAC Rapporteur: Jan Neuhauser, "Extension of Indication for Trimbow to all adult patients with moderate or severe chronic obstructive pulmonary disease (COPD).

as a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated in order to add the results of two Phase III studies (Triple 7 and Triple 8);

Triple 7 (CCD-05993AA1-07) is a multinational, multicentre, randomised, open-label, active-controlled, 26-week, 2-arm, parallel group study to evaluate the non-inferiority of fixed combination of beclomethasone dipropionate plus formoterol fumarate plus glycopyrronium bromide administered via pressurised metered dose inhaler (pMDI) (CHF 5993) versus (vs.) fixed combination of
fluticasone furoate plus vilanterol administered via dry powder inhaler (DPI) (Relvar®) plus tiotropium bromide (Spiriva®) for the treatment of patients with Chronic Obstructive Pulmonary Disease (COPD).

Triple 8 (CCD-05993AA1-08) is a 52-week,

double blind, double dummy, randomized, multinational, multicentre, 2-arm parallel group, active controlled clinical trial of fixed combination of beclomethasone dipropionate plus formoterol fumarate plus glycopyrronium bromide administered via pMDI (CHF 5993) versus indacaterol/glycopyrronium (Ultibro®) via DPI in patients with Chronic Obstructive Pulmonary Disease (TRIBUTE) The Package Leaflet and the Risk Management Plan are updated in accordance."

B.6.8. 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
BiResp Spiromax - budesonide / formoterol - EMEA/H/C/003890/II/0024/G Teva Pharma B.V., Duplicate, Duplicate of DuoResp Spiromax, Rapporteur: Nithyanandan Nagercoil
DuoResp Spiromax - budesonide / formoterol - EMEA/H/C/002348/II/0024/G Teva Pharma B.V., Rapporteur: Nithyanandan Nagercoil
Eptifibatide Accord - eptifibatide - EMEA/H/C/004104/II/0004 Accord Healthcare Limited, Generic, Generic of Integrilin, Rapporteur: Jayne Crowe
Eylea - aflibercept - EMEA/H/C/002392/II/0046 Bayer AG, Rapporteur: Alexandre Moreau
Inhixa - enoxaparin sodium - EMEA/H/C/004264/II/0031 Techdow Europe AB, Duplicate, Duplicate of Thorinane, Rapporteur: Andrea Laslop
Insuman - insulin human - EMEA/H/C/000201/II/0124 Sanofi-Aventis Deutschland GmbH, Rapporteur: Bart Van der Schueren

Keytruda - pembrolizumab -
EMEA/H/C/003820/II/0046
Merck Sharp & Dohme Limited, Rapporteur:
Daniela Melchiorri

Lemtrada - alemtuzumab -
EMEA/H/C/003718/II/0021/G
Genzyme Therapeutics Ltd, Duplicate, Duplicate
of Lemtrada (WD), Rapporteur: Mark Ainsworth

MabThera - rituximab -
EMEA/H/C/000165/II/0151
Roche Registration GmbH, Rapporteur: Sinan B.
Sarac

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

Synflorix - pneumococcal polysaccharide
conjugate vaccine (adsorbed) -
EMEA/H/C/000973/II/0125
GlaxoSmithkline Biologicals SA, Rapporteur:
Kristina Dunder

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

WS1376/G
Blitzima-
EMEA/H/C/004723/WS1376/0013/G
Ritemvia-
EMEA/H/C/004725/WS1376/0013/G
Rituzena-
EMEA/H/C/004724/WS1376/0014/G
Truxima-
EMEA/H/C/004112/WS1376/0014/G
Celltrion Healthcare Hungary Kft., Lead
Rapporteur: Sol Ruiz

B.6.9. 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.”

Cyramza - ramucirumab -
EMEA/H/C/002829/II/0023/G
Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik, “Submission of the final report from study Study I4T-MC-JVCZ Randomized Phase 2 Trial Evaluating Alternative Ramucirumab Doses in Combination with Paclitaxel in Second-Line Metastatic or Locally Advanced, Unresectable Gastric or Gastroesophageal Junction Adenocarcinoma and Study I4T-MC-JVDB Randomized Phase 2 Trial Evaluating Pharmacokinetics and Safety of Four Ramucirumab Dosing Regimens in Second Line Gastric or Gastroesophageal Junction Adenocarcinoma in fulfilment with Annex II condition linked to Cyramza Marketing Authorisation. Annex II of the product information has been updated accordingly.”

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

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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."

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.”

Jinarc - tolvaptan - EMEA/H/C/002788/II/0015

Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey, “Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information on acute liver failure requiring liver transplantation, based post-marketing experience with tolvaptan in autosomal dominant polycystic kidney disease (ADPKD).
The Package Leaflet is updated accordingly.”

Keytruda - pembrolizumab - EMEA/H/C/003820/II/0044

Merck Sharp & Dohme Limited, 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).”

Kuvan - sapropterin - EMEA/H/C/000943/II/0059, Orphan

BioMarin International Limited, Rapporteur: Peter Kiely, “As requested following the Art 46 procedure assessment, update of section 5.1 of the SmPC to reflect the data of the final clinical study report for the long term extension phase of the SPARK study. Sections 4.2 and 4.4 are also updated.”

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."

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."

Samsca - tolvaptan - EMEA/H/C/000980/II/0030

Otsuka Pharmaceutical Europe Ltd, Rapporteur: Greg Markey, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information on acute liver failure requiring liver transplantation, based post-marketing experience with tolvaptan in autosomal dominant polycystic kidney disease (ADPKD). The Package Leaflet is updated accordingly."

Savene - dexrazoxane - EMEA/H/C/000682/II/0036

Clinigen Healthcare Ltd, Rapporteur: Alexandre Moreau, "Update of section 4.4 and 4.6 of the SmPC in order to add a warning on mutagenic activity of dexrazoxane and to update the contraception recommendations based on toxicological data and literature review, the Package Leaflet is updated accordingly. In addition the MAH took the opportunity to make an administrative amendment to the description of the pharmaceutical form for Savene in order to align with the relevant EDQM standard terms."

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."	
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 RMPI; 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."	
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."	
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.”	
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."

WS1381
Leganto-
EMEA/H/C/002380/WS1381/0027
Neupro-EMEA/H/C/000626/WS1381/0082
UCB Pharma S.A., Informed Consent of Neupro, Lead Rapporteur: Bruno Sepodes, "Update of section 4.8 of the SmPC in order to add an adverse drug reaction: Dropped Head Syndrome based on new pharmacovigilance data; The Package Leaflet is updated accordingly.
In addition, the Worksharing applicant (WSA) took the opportunity to correct some discrepancies found within the PIL of Greece, Cyrus and Romania and to update the Neupro Annex A in alignment with Leganto Annex A for the description of the multipack size."

WS1391
Epclusa-
EMEA/H/C/004210/WS1391/0026
Vosevi-EMEA/H/C/004350/WS1391/0014
Gilead Sciences International Limited, Lead Rapporteur: Filip Josephson, "Update of section 5.3 of the SmPC based on data from a 2-year rat carcinogenicity study TX-281-2030. In addition, the MAH took the opportunity to update the ATC code in line with the new classification of antivirals for treatment of HCV infections and to introduce minor linguistic amendments and typographical corrections throughout the Product Information."

B.6.10. CHMP-PRAC assessed procedures

Advate - octocog alfa -
EMEA/H/C/000520/II/0092
Baxter AG, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 5.1 of the SmPC in order to add new data on immune tolerance induction (ITI). This update follows final results from study PASS-INT-004; this was a prospective, multi-centre, uncontrolled, open-label, non-interventional postauthorization safety surveillance study conducted to evaluate Advate in ITI therapy in subjects with moderate or severe hemophilia A (baseline factor VIII ≤ 2%) and a high titer (> 5 BU) inhibitor to FVIII.

The RMP version 16.0 has also been submitted."

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."

Ovitrelle - choriogonadotropin alfa - EMEA/H/C/000320/II/0073/G

Merck Serono Europe Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, "Update of section 4.8 of the SmPC in order to indicate that thromboembolism can also occur without the presence of ovarian hyperstimulation syndrome (OHSS). The package leaflet and risk management plan (RMP) (version 5.1) are updated accordingly.
The RMP is also updated to extend the important potential risk of 'misuse' to 'weight loss and anabolic growth promoting effect'.
In addition, the marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the package leaflet, to make editorial changes in the product information and in the Annex A (list of authorised presentations). The MAH also took the opportunity to make some revisions in the RMP."

Ozempic - semaglutide -

EMEA/H/C/004174/II/0002/G
Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Qun-Ying Yue

Sivextro - tedizolid phosphate - EMEA/H/C/002846/II/0027
Merck Sharp & Dohme Limited, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Dolores Montero Corominas, "Update of section 4.8 of the SmPC in order to add safety information based on the final results from Bayer study 16099, listed as Post-Authorisation Efficacy Study (PAES) in the RMP; this is a prospective, randomized, open-label, active-controlled, multicenter study to evaluate the efficacy and safety of tedlizolid in Japanese patients with MRSA infections (skin and soft tissue infection [SSTI] and SSTI-related bacteremia).

The updated RMP version 4.0 is also being submitted, reflecting the new, second revision of the RMP template, issues by the EMA on 30 March 2017."

Stayveer - bosentan - EMEA/H/C/002644/II/0023
Marklas Nederlands BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Caroline Laborde, "Update of Annex II.D and the RMP following the submisison of the final (13th) study report for the DUO Registry (a Category 3 non-interventional post-approval safety study and additional risk minimisation measure in the bosentan European Risk Management Plan)."

Tasigna - nilotinib - EMEA/H/C/000798/II/0095, Orphan
Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Update of section 4.6 of the SmPC following a review of information on pregnancy, lactation, female and male infertility and embryo-foetal developmental toxicity from the published literature, the MAH's safety database and preclinical safety data from reproductive animal studies. The Package Leaflet has been updated accordingly.
In addition, upon request by EMA, the MAH is proposing a potential update of Annex II section D (Key Elements of the Educational Material) in order to align the wording in Annex II with the current safety concerns outlined in the Tasigna EU RMP Education Materials.

Further, the MAH took the opportunity to implement minor editorial changes, corrections and/or additions in the SmPC and Package Leaflet based on data already submitted and assessed previously, including the alignment of section 4 of the Package Leaflet with section 4.8 of the SmPC and completeness of the list of excipients in SmPC section 6.1 and changes to SmPC sections 4.4 and 4.5. Finally, the MAH also took the opportunity to update the contact details in the list of local representatives in the Package Leaflet."	
Tracleer - bosentan - EMEA/H/C/000401/II/0086 Actelion Registration Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Caroline Laborde, "Update of Annex II.D and the RMP following the submisison of the final (13th) study report for the DUO Registry (a Category 3 non-interventional post-approval safety study and additional risk minimisation measure in the bosentan European Risk Management Plan)."	
Volibris - ambrisentan - EMEA/H/C/000839/II/0054, Orphan Glaxo Group Ltd, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Dolores Montero Corominas, "Update of sections 4.2 and 5.2 of the SmPC based on results of a juvenile nonclinical toxicology study. The Risk Management Plan version 7.5 (in version 2 of the RMP template) has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct typographical errors including the rash frequency in section 4.8 of the SmPC and the date of renewal; and to introduce minor update in the braille section. Moreover, the MAH took the opportunity to propose combined version of the SmPCs for the different strengths."	
WS1390 **Levitra-EMEA/H/C/000475/WS1390/0062** **Vivanza-EMEA/H/C/000488/WS1390/0058** Bayer AG, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Dolores Montero Corominas, "Update of sections 4.4 and 4.8 of the SmPC to reflect data from two post-marketing observational studies indicating an	

increased risk of Non-arteritic Anterior Ischaemic Optic Neuropathy (NAION) when using phosphodiesterase 5 (PDE5) inhibitors. The MAH is also terminating the Bayer NAION study 12912 and the RMP is updated accordingly to version 5.0.
In addition, the PI is brought in line with version 10.0 of the QRD template and the contact details of the Bulgarian local representative are updated in the Package Leaflets. The Package Leaflets for the 5 mg, 10 mg and 20 mg film-coated tablets strengths are combined into a single Package Leaflet and the PI for the 10 mg orodispersible tablet is updated for aspartame and sorbitol, according to the annex to the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'. Some editorial amendments are also made to the PI."

B.6.11. PRAC assessed procedures

PRAC Led
Deltyba - delamanid - EMEA/H/C/002552/II/0030, Orphan
Otsuka Novel Products GmbH, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "Update of the RMP (verison 2.10), as requested by PRAC following the assessment of the Annual renewal to revise the risk re-categorisation justifications and lay language wording, as well as addition of clarifications to the described additional pharmacovigilance activities to assess the effectiveness of risk minimisation measures and set up date of EU network of laboratories."

PRAC Led
Soliris - eculizumab - EMEA/H/C/000791/II/0102, Orphan
Alexion Europe SAS, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Concepcion Prieto Yerro, "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."

PRAC Led

Thymanax - agomelatine - EMEA/H/C/000916/II/0038

Servier (Ireland) Industries Ltd., Duplicate, Duplicate of Valdoxan, Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Kristin Thorseng Kvande, PRAC-CHMP liaison: Svein Rune Andersen, "Submission of the final report from study CLE-20098-096 listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study: drug utilisation study (DUS) to assess effectiveness of risk-minimisation measures."

PRAC Led

Valdoxan - agomelatine - EMEA/H/C/000915/II/0039

Les Laboratoires Servier, Rapporteur: Svein Rune Andersen, PRAC Rapporteur: Kristin Thorseng Kvande, PRAC-CHMP liaison: Svein Rune Andersen, "Submission of the final report from study CLE-20098-096 listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study: drug utilisation study (DUS) to assess effectiveness of risk-minimisation measures."

PRAC Led

Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0186

Gilead Sciences International Limited, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Caroline Laborde, PRAC-CHMP liaison: Joseph Emmerich, "Submission of the final report from study GS-EU-174-1846, listed as a category 3 study in the RMP, in fulfilment of MEA 273. This is a 'Multicenter, Non-Interventional, Retrospective, Matched Cohort Study of Patients Monoinfected with Chronic Hepatitis B and with Moderate or Severe Renal Impairment Treated with Viread or Baraclude'."

B.6.12. CHMP-CAT assessed procedures

talimogene laherparepvec - EMEA/H/C/002771/II/0020, ATMP

, “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. In addition, the MAH took the opportunity to implement 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).”

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

WS1375
Actraphane-
EMEA/H/C/000427/WS1375/0075
Insulatard-
EMEA/H/C/000441/WS1375/0072
Mixtard-
EMEA/H/C/000428/WS1375/0076
Protaphane-
EMEA/H/C/000442/WS1375/0071
Novo Nordisk A/S, Duplicate, Duplicate of Monotard (SRD), Ultratard (SRD), Lead Rapporteur: Sinan B. Sarac

WS1383
Renagel-
EMEA/H/C/000254/WS1383/0110
Renvela-
EMEA/H/C/000993/WS1383/0044
Sevelamer carbonate Zentiva-
EMEA/H/C/003971/WS1383/0015
Genzyme Europe BV, Lead Rapporteur: Outi Mäki-Ikola

WS1384/G
PegIntron-
EMEA/H/C/000280/WS1384/0134/G
ViraferonPeg-
EMEA/H/C/000329/WS1384/0127/G
Merck Sharp & Dohme Limited, Lead Rapporteur: Filip Josephson

WS1385
Izba-EMEA/H/C/002738/WS1385/0009
Travatan-
EMEA/H/C/000390/WS1385/0058
Novartis Europharm Limited, Lead Rapporteur: Concepcion Prieto Yerro

WS1386
Competact-
EMEA/H/C/000655/WS1386/0070
Glubrava-
EMEA/H/C/000893/WS1386/0057
Takeda Pharma A/S, Lead Rapporteur: Peter Kiely

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.7. DOCUMENTS TABLED IN MMD AFTER THE CHMP PLENARY

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

B.7.2. Monthly Line listing for Type I variations

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

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

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

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

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

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

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

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

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

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

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

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

G. ANNEX G

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

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

Qualification of Biomarkers:

HTA:

G.2. Ongoing procedures

G.3. PRIME

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

G.3.1. List of procedures concluding at 23-26 April 2018 CHMP plenary:

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

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