25 February 2019
EMA/CHMP/134786/2019 Corr.1[1]
Inspections, Human Medicines Pharmacovigilance and Committees Division

Committee for medicinal products for human use (CHMP)

Final agenda for the meeting on 25-28 February 2019

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

25 February 2019, 13:00 – 19:30, room 2A

26 February 2019, 08:30 – 19:30, room 2A

27 February 2019, 08:30 – 19:30, room 2A

28 February 2019, 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).

[1] Correction in sections 2.4.1 and 10.6.1

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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 25-28 February 2019. See (current) February 2019 CHMP minutes (to be published post March 2019 CHMP meeting).

1.2. Adoption of agenda

CHMP agenda for 25-28 February 2019

1.3. Adoption of the minutes

CHMP minutes for 28-31 January 2019

ORGAM minutes for 18 February 2019

2. Oral Explanations

2.1. Pre-authorisation procedure oral explanations

2.1.1. andexanet alfa - EMEA/H/C/004108

treatment of direct or indirect factor Xa(FXa) inhibitor when reversal of anticoagulation is needed

Scope: Oral explanation/Opinion

Action: Oral explanation to be held on 27 February 2019 at time 11:00

List of Outstanding Issues adopted on 13.12.2018, 22.02.2018, 09.11.2017. List of Questions adopted on 15.12.2016.

See 3.1

2.1.2. buprenorphine - EMEA/H/C/004743

Substitution treatment for opioid drug dependence

Scope: Oral explanation

Action: Oral explanation to be held on 26 February 2019 at time 11:00

List of Outstanding Issues adopted on 15.11.2018. List of Questions adopted on 22.03.2018.

2.1.3. 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: Possible oral explanation/Opinion

Action: Oral explanation to be held on 27 February 2019 at time 14:00

List of Outstanding Issues adopted on 15.11.2018, 20.09.2018, 28.06.2018, 26.04.2018. List of Questions adopted on 14.12.2017.

See 3.1

2.2. Re-examination procedure oral explanations

No items

2.3. Post-authorisation procedure oral explanations

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

sanofi-aventis groupe

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

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

Oral explanation

Action: Oral explanation to be held on 26 February 2019 at time 09:00

List of Outstanding Issues adopted on 15.11.2018. List of Questions adopted on 26.07.2018.

See 4.1

2.4. Referral procedure oral explanations

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

MAH various

Rapporteur: Jan Mueller-Berghaus, Co-rapporteur: Daniela Melchiorri

Scope: Oral Explanations, Report from SAG anti-infectives held on 12 February 2019

Action: Oral explanations to be held on 26 February 2019 at time 16:00 and 17:00

See 10.6

3. Initial applications

3.1. Initial applications; Opinions

3.1.1. zanamivir - EMEA/H/C/004102

treatment of influenza A or B virus infection

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 31.01.2019, 13.12.2018, 18.10.2018. List of Questions adopted on 26.04.2018.

3.1.2. lorlatinib - EMEA/H/C/004646

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 18.10.2018. List of Questions adopted on 31.05.2018.

3.1.3. andexanet alfa - EMEA/H/C/004108

treatment of direct or indirect factor Xa(FXa) inhibitor when reversal of anticoagulation is needed

Scope: Oral explanation/Opinion

Action: For adoption

List of Outstanding Issues adopted on 13.12.2018, 22.02.2018, 09.11.2017. List of Questions adopted on 15.12.2016.

See 2.1

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

BioMarin International Limited; treatment of adults with phenylketonuria (PKU) who have inadequate blood phenylalanine control

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 13.12.2018. List of Questions adopted on 26.07.2018.

3.1.5. paclitaxel - EMEA/H/C/004441

treatment of metastatic breast cancer

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 31.01.2019, 26.07.2018, 31.05.2018. List of Questions adopted on 14.12.2017.

3.1.6. risankizumab - EMEA/H/C/004759

treatment of psoriasis in adults

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 31.01.2019. List of Questions adopted on 20.09.2018.

3.1.7. 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: Possible Oral Explanation/Opinion

Action: For adoption

List of Outstanding Issues adopted on 15.11.2018, 20.09.2018, 28.06.2018, 26.04.2018. List of Questions adopted on 14.12.2017.

See 2.1

3.1.8. sotagliflozin - EMEA/H/C/004889

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

Scope: Opinion

Action: For adoption

List of Outstanding Issues adopted on 31.01.2019, 15.11.2018. List of Questions adopted on 26.07.2018.

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

3.2.1. ambrisentan - EMEA/H/C/004985

treatment of pulmonary arterial hypertension (PAH)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.09.2018.

3.2.2. cabazitaxel - EMEA/H/C/004951

treatment of prostate cancer

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.09.2018.

3.2.3. avatrombopag - EMEA/H/C/004722

treatment of thrombocytopenia

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.09.2018.

3.2.4. romosozumab - EMEA/H/C/004465

Treatment of osteoporosis

Scope: Possible oral explanation, List of outstanding issues, Ad Hoc Expert Group Report

Action: For adoption

List of Outstanding Issues adopted on 15.11.2018, 20.09.2018. List of Questions adopted on 26.04.2018.

See 2.1

3.2.5. hydroxycarbamide - EMEA/H/C/004837

prevention of complications of Sickle Cell disease

Scope: List of outstanding issues

Action: For adoption

List of Outstanding Issues adopted on 15.11.2018. List of Questions adopted on 28.06.2018.

3.2.6. posaconazole - EMEA/H/C/005005

treatment of fungal infections

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.09.2018.

3.2.7. edaravone - Orphan - EMEA/H/C/004938

Mitsubishi Tanabe Pharma Europe Ltd; treatment of amyotrophic lateral sclerosis (ALS)

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.09.2018.

3.2.8. crisaborole - EMEA/H/C/004863

treatment of mild to moderate atopic dermatitis

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.09.2018.

3.2.9. ioflupane (123i) - EMEA/H/C/004745

indicated for detecting loss of functional dopaminergic neuron terminals in the striatum

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.09.2018.

3.2.10. talazoparib - EMEA/H/C/004674

for the treatment of adult patients with germline breast cancer susceptibility gene (BRCA) mutated human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 20.09.2018.

3.2.11. ibalizumab - EMEA/H/C/004961

Accelerated assessment

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 11.12.2018.

3.2.12. ravulizumab - Orphan - EMEA/H/C/004954

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

Scope: List of outstanding issues

Action: For adoption

List of Questions adopted on 15.11.2018.

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

3.3.1. esketamine - EMEA/H/C/004535

treatment-resistant depression

Scope: List of questions

Action: For adoption

3.3.2. plazomicin - EMEA/H/C/004457

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

Scope: List of questions

Action: For adoption

3.3.3. onasemnogene abeparvovec - Orphan - ATMP - EMEA/H/C/004750

Accelerated assessment

AveXis Netherlands B.V.; treatment of spinal muscular atrophy (SMA)

Scope: List of questions

Action: For information

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

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

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

Scope: Report from the SAG meeting held on 03 December 2018

Action: For adoption

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

3.4.2. deferasirox - EMEA/H/C/005014

treatment of chronic iron overload

Scope: Letter from applicant dated 15 February 2019 requesting an extension of clock stop to respond to the list of questions adopted on 15.11.2018.

Action: For adoption

List of Questions adopted on 15.11.2018.

3.4.3. etanercept - EMEA/H/C/004711

Rheumatoid arthritis, Juvenile idiopathic arthritis, Psoriatic arthritis, Axial spondyloarthritis, Ankylosing spondylitis, Non-radiographic axial spondyloarthritis, Plaque psoriasis, Paediatric

plaque psoriasis

Scope: Letter from applicant dated 05 February 2019 requesting an extension of clock stop to respond to the list of questions adopted on 20.09.2018.

Action: For adoption

List of Questions adopted on 20.09.2018.

3.4.4. emapalumab - Orphan - EMEA/H/C/004386

Novimmune B.V.; treatment of paediatric patients with primary haemophagocytic lymphohistiocytosis (HLH).

Scope: Letter from applicant dated 21 February 2019 requesting an extension of clock stop to respond to the list of questions adopted on 13.12.2018

Action: For adoption

List of Questions adopted on 13.12.2018.

3.4.5. pegfilgrastim - EMEA/H/C/004556

reduction in the duration of neutropenia and the incidence of febrile neutropenia

Scope: Letter from applicant dated 21 February 2019 requesting an extension of clock stop to respond to the list of outstanding issues adopted on 13.12.2018

Action: For adoption

List of Outstanding Issues adopted on 13.12.2018. List of Questions adopted on 22.03.2018.

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

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

Scope: List of questions to the SAG-Oncology

Action: For adoption

Day 90 List of Questions adopted on 11.12.2018.

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

3.5.1. Doxolipad - doxorubicin hydrochloride - EMEA/H/C/004110

TLC Biopharmaceuticals B.V.; treatment of breast and ovarian cancer

Scope: Appointment of re-examination rapporteur, timetable

Action: For adoption

Hybrid application (Article 10(3) of Directive No 2001/83/EC)

Opinion adopted on 31.01.2019. List of Outstanding Issues adopted on 26.07.2018. List of Questions adopted on 14.09.2017.

3.6. Initial applications in the decision-making phase

No items

3.7. Withdrawals of initial marketing authorisation application

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

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

Scope: Withdrawal of initial marketing authorisation application

Action: For information

List of Outstanding Issues adopted on 15.11.2018, 26.07.2018. List of Questions adopted on 09.11.2017.

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. Aimovig - erenumab - EMEA/H/C/004447/X/0001

Novartis Europharm Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Kirsti Villikka

Scope: “Extension application to add a new strength of 140 mg.”

Action: For adoption

List of Questions adopted on 13.12.2018.

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

sanofi-aventis groupe

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

Scope: “Extension application to add a new strength of 200 mg solution for injection in pre-filled syringe with safety system (PFS-S) and pre-filled pen (PFP), grouped with a type II variation (C.I.6.a) to add the following indications:
- Add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older, who are inadequately controlled with medium-to-high dose inhaled corticosteroids (ICS) plus another medicinal product for maintenance treatment, including those with or without an eosinophilic phenotype;
- Maintenance therapy to improve lung function;
- Maintenance therapy to reduce oral steroid use and improve lung function in steroid-dependent asthma patients;

Based on the pivotal studies DRI12544, QUEST and VENTURE.
As a consequence, SmPC sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 have been updated and the Package Leaflet has been updated accordingly.
The RMP (version 2.0) is updated accordingly.
In addition, the MAH proposed to merge the SmPCs for the 200 mg and 300 mg strengths."

Action: For information

List of Outstanding Issues adopted on 15.11.2018. List of Questions adopted on 26.07.2018.

See 2.3

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

No items

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

No items

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

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

Pfizer Europe MA EEIG

Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Letter from applicant dated 20 February 2019 requesting an extension of clock stop to respond to the list of outstanding issues adopted on 31.01.2019

Action: For adoption

List of Outstanding Issues adopted on 31.01.2019. List of Questions adopted on 26.07.2018.

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. Benlysta - belimumab - EMEA/H/C/002015/II/0062

GlaxoSmithKline (Ireland) Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include patients aged 5 years and older in the current approved indication for Benlysta (belimumab powder for solution for infusion 120 mg/ml and 400 mg/ml) based on the results of the safety, efficacy and pharmacokinetics study in patients aged 5 years to 17 years (BEL114055). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated with safety and efficacy information.
Update of sections 4.2, 5.1 and 5.2 of the SmPC for Benlysta (belimumab, solution for injection in pre-filled pen and pre-filled syringe, 200 mg) to reflect the paediatric data available for the intravenous formulation. The Package Leaflet is updated accordingly.
The RMP version 28.0 is submitted to reflect the results of the study and to bring it in line with the GVP Module V RMP template version 2.0. In addition, the MAH took the opportunity to make some editorial changes in the product information and bring it in line with the latest QRD template version 10.0."

Action: For adoption

5.1.2. Imbruvica - ibrutinib - Orphan - EMEA/H/C/003791/II/0046

Janssen-Cilag International NV

Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Extension of Indication to include new indication for Imbruvica; to broaden the current indication and apply for an extension of indication with respect to include treatment of adult patients with Waldenström's macroglobulinaemia (WM) in combination with rituximab. This proposed broaden indication is supported by the final clinical study report results of phase 3 study PCYC-1127-CA. As a consequence, sections 4.1 and 4.8 of the SmPC are updated. No changes were required to the broaden indication for the Package Leaflet. In addition, the Marketing authorisation holder (MAH) took the opportunity to update in the SmPC and Package Leaflet with minor editorial/administrative changes.
An updated version of the Imbruvica EU Risk Management Plan (RMP) (version 12) is also included in this submission."

Action: For adoption

5.1.3. Imbruvica - ibrutinib - Orphan - EMEA/H/C/003791/II/0047

Janssen-Cilag International NV

Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: “Extension of Indication to include new indication for Imbruvica (ibrutinib); to extend the existing chronic lymphocytic leukaemia (CLL) indication to include combination use with obinutuzumab for the treatment of adult patients with previously untreated CLL. This proposed indication is supported by the data from the phase 3 study PCYC-1130-CA. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated, in 4.1 to include the extended indication, in 4.8 to update the safety information to include long term safety (supported by results of study 3038-1) and section 5.1 to update the existing CLL label studies with long term efficacy data for CLL (supported by long term efficacy results of study PCYC-1112-CA and PCYC-1116-CA).
The Package Leaflet is updated in accordance. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the SmPC and Package Leaflet with minor editorial/administrative changes.
An updated version of the Imbruvica EU Risk Management Plan (RMP) (version 12) is also included in this submission.”

Action: For adoption

5.1.4. Imnovid - pomalidomide - Orphan - EMEA/H/C/002682/II/0031/G

Celgene Europe BV

Rapporteur: Greg Markey, Co-Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Patrick Batty

Scope: “Extension of indication to include treatment with Imnovid in combination with bortezomib and dexamethasone of adult patients with multiple myeloma who have received at least one prior treatment regimen including lenalidomide; as a result, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. As a consequence the MAH submitted a request to add 14-capsule pack sizes for the 1 mg, 2 mg, 3 mg and 4 mg Imnovid strengths to support the proposed posology and pomalidomide dose modification. The SmPC, Labelling and Package leaflet are updated in accordance. Update of section 5.1 of the SmPC in order to update the information on pomalidomide mechanism of action based on literature data.”

Action: For adoption

Request for Supplementary Information adopted on 18.10.2018.

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

Amgen Europe B.V.

Rapporteur: Jorge Camarero Jiménez,

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

Action: For adoption

Request for Supplementary Information adopted on 15.11.2018.

5.1.6. Lucentis - ranibizumab - EMEA/H/C/000715/II/0076

Novartis Europharm Limited

Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

Scope: "Extension of indication to include treatment of moderately severe to severe non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) in adults for Lucentis; as a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated with the safety information. The Package Leaflet is updated in accordance. RMP version 19.0 is also being submitted."

Action: For adoption

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

AstraZeneca AB

Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to include the use of Lynparza tablets as a monotherapy 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, sections 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."

Action: For adoption

Request for Supplementary Information adopted on 13.12.2018, 20.09.2018, 28.06.2018.

5.1.8. Lynparza - olaparib - EMEA/H/C/003726/II/0023

AstraZeneca AB

Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to include the use of Lynparza as a monotherapy for the maintenance treatment of adult patients with newly diagnosed advanced BRCA-mutated high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete response or partial response) to first-line platinum-based chemotherapy.
As a consequence, sections 4.1 (indication and posology) and 4.8 of the SmPC (summary profile and tabulated list of adverse reactions) are updated in order to include information on a single pivotal Phase 3 study (D0818C00001, referred to as SOLO 1). The Package Leaflet is updated in accordance.
The updated pooled safety information for this submission has also been incorporated and aligned in the capsule SmPC and PL.", 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 13.12.2018.

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

Genzyme Europe BV

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

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

Action: For adoption

Request for Supplementary Information adopted on 13.12.2018, 31.05.2018.

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

Novartis Europharm Limited

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

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

Action: For adoption

Request for Supplementary Information adopted on 15.11.2018, 26.07.2018.

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

PTC Therapeutics International Limited

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

Scope: "Extension of Indication to include non-ambulatory patients with Duchenne muscular dystrophy; this variation additionally presents, as supportive data, the final results of the long term clinical study PTC-124-GD-019-DMD (an Open-Label Study for Previously Treated Ataluren (PTC124) Patients with Nonsense Mutation Dystrophinopathy), submitted in line with the requirements of the Article 46 of the Paediatric Regulation.
As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance.
The RMP version 8.0 has also been submitted."

Action: For adoption

Request for Supplementary Information adopted on 13.12.2018.

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

Pfizer Europe MA EEIG

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

Scope: "Extension of Indication for Trumenba to include active immunisation of children 1-9 years old. Sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated in parallel based on the

results from the two pivotal studies B1971017 and B1971035. The Package Leaflet is updated in accordance. The RMP version 2.0 has also been submitted.
In addition, the Marketing Authorisation Holder (MAH) took the opportunity to submit a corrected version of the final report of study B1971016, which was included in the initial marketing authorisation application."

Action: For adoption

5.1.13. Viread - tenofovir disoproxil - EMEA/H/C/000419/II/0191

Gilead Sciences Ireland UC

Rapporteur: Joseph Emmerich, PRAC Rapporteur: Adrien Inoubli

Scope: "Extension of indication based on results from interim Week 48 clinical study report (CSR) for Study GS-US-174-0144: a 'Randomized, Double-Blind Evaluation of the Antiviral Efficacy, Safety and Tolerability of Tenofovir Disoproxil Fumarate Versus Placebo in Paediatric Patients with Chronic Hepatitis B Infection'. Following changes have been proposed:
1) Viread film coated tablets (123 mg; 163 mg; 204 mg): new chronic hepatitis B (CHB) indication to include treatment of CHB in paediatric patients aged 6 to < 12 years
2) Viread granules 33 mg/g: extension of the existing CHB indication for Viread granules to include treatment of CHB in paediatric patients aged 2 to < 12 years.
As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC have been updated for Viread 123 mg, 163 mg and 204 mg. Sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated for Viread 245 mg, whereas sections 4.1, 4.2, 4.4, 5.1 and 5.2. have been updated for Viread granules 33 mg/g.
The Package Leaflet has been updated accordingly for all the products concerned."

Action: For adoption

Request for Supplementary Information adopted on 13.12.2018.

5.1.14. Zinforo - ceftaroline fosamil - EMEA/H/C/002252/II/0041

Pfizer Ireland Pharmaceuticals

Rapporteur: Alar Irs, PRAC Rapporteur: Maia Uusküla

Scope: "Extension of indication to include paediatric patients from birth to less than 2 months old for Zinforo; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated based on results from study D3720C00009 (C2661002) an open-label, multicentre study to evaluate the safety, tolerability, pharmacokinetics, and efficacy of ceftaroline in neonates and young infants with late-onset sepsis. The Package Leaflet is updated in accordance. The RMP (v 17.0) has also been submitted."

Action: For adoption

5.1.15. WS1554
Riarify - beclometasone dipropionate / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004836/WS1554/0002
Trydonis - beclometasone dipropionate / formoterol fumarate dihydrate / glycopyrronium - EMEA/H/C/004702/WS1554/0002

Chiesi Farmaceutici S.p.A.

Lead Rapporteur: Janet Koenig, PRAC Rapporteur: Jan Neuhauser

Scope: “Extension of indication, based on results from two Phase III studies: Triple 7 (CCD-05993AA1-07) and Triple 8 (CCD-05993AA1-08), to include maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who are not adequately treated by combination of a long-acting beta2-agonist and a long-acting muscarinic antagonist. Sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated accordingly to reflect the studies’ results. The package leaflet and the risk management plan (version 6.0) are updated accordingly.”

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

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

Roche Registration GmbH

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

Scope: Letter from the applicant dated 20 February 2019 requesting an extension of clock-stop to respond to the request for supplementary information adopted on 31.01.2019

Request for Supplementary Information adopted on 31.01.2019.

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

No items

6. Ancillary medicinal substances in medical devices

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

No items

6.2. Update of Ancillary medicinal substances in medical devices

No items

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

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

No items

8. Pre-submission issues

8.1. Pre-submission issue

8.1.1. lefamulin - H0005048

Treatment of community-acquired pneumonia (CAP) in adults greater than or equal to 18 years of age

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

Action: For adoption

8.1.2. darolutamide - H0004790

Non-metastatic castration resistant prostate cancer

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

Action: For adoption

8.1.3. pexidartinib - Orphan - H0004832

Daiichi Sankyo Europe GmbH, Treatment of symptomatic tenosynovial giant cell tumor (TGCT), also known as pigmented villonodular synovitis (PVNS) and giant cell tumor of the tendon sheath (GCT-TS), where surgical resection is potentially associated with worsening functional limitation or severe morbidity

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

Action: For adoption

8.2. Priority Medicines (PRIME)

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

8.2.1. List of applications received

Action: For information

8.2.2. Recommendation for PRIME eligibility

Action: For adoption

9. Post-authorisation issues

9.1. Post-authorisation issues

9.1.1. Altargo - retapamulin - EMEA/H/C/000757

Glaxo Group Ltd

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Janet Koenig

Scope: Withdrawal of marketing authorisation

Action: For information

9.1.2. ATryn - antithrombin alfa - EMEA/H/C/000587/

Laboratoire Francais du Fractionnement et des Biotechnologies

Rapporteur: Alexandre Moreau, Co-Rapporteur: Nithyanandan Nagercoil

Scope: Withdrawal of marketing authorisation

Action: For information

9.1.3. Caprelsa - vandetanib - EMEA/H/C/002315/II/0028

Genzyme Europe BV

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: "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."

Action: For discussion

Request for Supplementary Information adopted on 18.10.2018, 26.04.2018, 14.12.2017.

9.1.4. Cetrotide - cetrorelix - EMEA/H/C/000233/II/0068

Merck Europe B.V.

Rapporteur: Martina Weise

Scope: "Update of section 4.2 of the SmPC based on literature review to add an alternative option for the treatment initiation to start once the leading follicle(s) reach a size that could lead to premature LH (Luteinizing Hormone) surge and ovulation.
The Package Leaflet (PL) is updated in accordance. Correction in section 3 of the PL regarding the timing of ovulation induction.
In addition, the Marketing authorisation holder (MAH) took the opportunity to delete the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.0."

Action: For discussion

Request for Supplementary Information adopted on 18.10.2018.

9.1.5. Imbruvica - ibrutinib - Orphan - EMEA/H/C/003791/II/0048

Janssen-Cilag International NV

Rapporteur: Filip Josephson, PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: "Update of section 4.4 of the SmPC Special warnings and precautions for use in order to add a warning under "bleeding-related events' based on the final clinical study reports results to evaluate the risks of major haemorrhage with the administration of IMBRUVICA® (ibrutinib)). The study is listed in section III.2 additional Pharmacovigilance Activities - A non-interventional PASS clinical study report (CSR) for serious haemorrhage - in the RMP.

In addition, the Marketing authorisation holder (MAH) took the opportunity to include a minor edit in the list of local representatives in the Package Leaflet."

CHMP request for PRAC advice

Action: For adoption

9.1.6. Increlex - mecasermin - EMEA/H/C/000704/S/0055

Ipsen Pharma

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

Scope: Update on annual re-assessment

Action: For discussion

9.1.7. Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0084

Pfizer Europe MA EEIG

Rapporteur: Greg Markey

Scope: "Update of section 4.2 of the SmPC in order to update the posology information in infants, following the final results from study MenACWY-TT-087 (Study 087); this is a phase IIIb, controlled, randomised, open study aimed to demonstrate the immunogenicity and safety of Nimenrix in healthy infants, given on a 3+1 primary and booster (2, 4, 6 and 15-18 months of age), a 1+1 primary and booster (6 and 15-18 months of age) or as a single dose at 15-18 months of age. The Package Leaflet is updated accordingly.
The MAH took the opportunity to include editorial changes in sections 4.4 and 4.8 of the SmPC."

Action: For discussion

Request for Supplementary Information adopted on 18.10.2018.

10. Referral procedures

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

No items

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

No items

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

No items

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

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

Syner-Medica Ltd

Rapporteur: Nithyanandan Nagercoil, Co-Rapporteur: Sol Ruiz

Scope: Opinion

Action: For adoption

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

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

No items

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

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

MAH various

Rapporteur: Jan Mueller-Berghaus, Co-rapporteur: Daniela Melchiorri

Scope: Oral Explanations, Report from SAG anti-infectives held on 12 February 2019

Oral explanations to be held on 26 February 2019 at time 16:00 and 17:00

The final list of experts to the SAG was adopted via written procedure on 11.02.2019

Action: For adoption

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

See 2.4

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

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

MAHs: various

Re-examination Rapporteur: John Joseph Borg, Re-examination Co-Rapporteur: Johann Lodewijk Hillege

Scope: Timetable, List of questions to SAG

Action: For adoption

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

10.8. 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

February 2019 Early Notification System on envisaged CHMP/CMDh outcome accompanied by communication to the general public.

Action: For information

12. Inspections

12.1. GMP inspections

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

12.2. GCP inspections

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

12.3. Pharmacovigilance inspections

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

12.4. GLP inspections

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

13. Innovation Task Force

13.1. Minutes of Innovation Task Force

Action: For information

13.2. Innovation Task Force briefing meetings

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

No items

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

13.3.1. EC request for EMA opinion on the definitions of pharmacological, immunological, metabolic and medical diagnosis

Final reports

Action: For adoption

13.4. Nanomedicines activities

No items

14. Organisational, regulatory and methodological matters

14.1. Mandate and organisation of the CHMP

14.1.1. Area of expertise of CHMP Co-opted Member

Discussion on area of expertise in light of Robert James Hemmings' resignation as of 06 February 2019.

Note: The area of expertise of Robert James Hemmings was Medical statistics (clinical-trial methodology / epidemiology).

Action: For discussion

14.2. Coordination with EMA Scientific Committees

14.2.1. Pharmacovigilance Risk Assessment Committee (PRAC)

Summary of recommendations and advice of PRAC meeting held on 11-14 February 2019

Action: For information

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

Action: For adoption

14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 20-22 February 2019
Action: For information

14.2.3. Paediatric Committee (PDCO)

PIPs reaching D30 at February 2019 PDCO

Action: For information

Report from the PDCO meeting held on 26-28 February 2019

Action: For information

14.2.4. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 19-21 February 2019
Action: For information

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

Report from the Coordination Group for Mutual Recognition and Decentralised Procedures –

Human (CMDh) on the meeting held on 26-28 February 2019

Action: For information

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

14.3.1. Scientific Advice Working Party (SAWP)

Report from the SAWP meeting held on 11-14 February 2019. Table of conclusions

Action: For information

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

Election of new SAWP chairperson

Action: for adoption

Nominations received

14.3.2. Name Review Group (NRG)

Table of Decisions of the NRG meeting held on 27 February 2019.

Action: For adoption

14.3.3. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP February 2019 meeting to CHMP for adoption:

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

Action: For adoption

14.3.4. Pharmacogenomics Working Party (PGWP)

Election of new PGWP chairperson

Action: For adoption

Nominations received

14.3.5. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink/Henrike Potthast

CMDh question to PKWP - Demonstration of bioequivalence for ezetimibe

14.3.6. **Action:** For adoptionQuality Working Party (QWP)

Election of new QWP chairperson

Action: For adoption

Nominations received

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

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)*

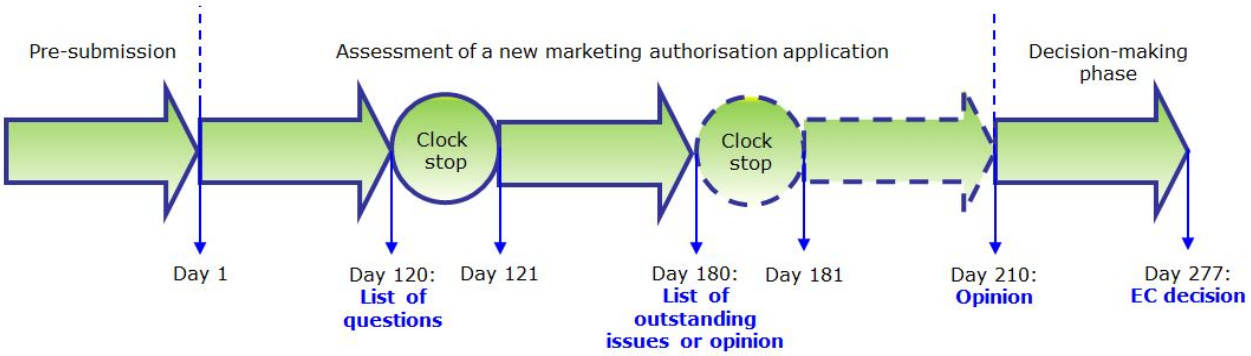
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

25 February 2019
EMA/CHMP/134787/2019

Annex to 25-28 February 2019 CHMP Agenda

Pre-submission and post-authorisations issues

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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 February 2019: **For adoption**

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

Final Outcome of Rapporteurship allocation for February 2019: **For adoption**

A.3. PRE-SUBMISSION ISSUES FOR INFORMATION

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

B. POST-AUTHORISATION PROCEDURES OUTCOMES

B.1. Annual re-assessment outcomes

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

Increlex - mecasermin -
EMEA/H/C/000704/S/0055
Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka

Naglazyme - galsulfase -
EMEA/H/C/000640/S/0073
BioMarin International Limited, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty
Request for Supplementary Information adopted on 15.11.2018.

Obizur - susoctocog alfa -
EMEA/H/C/002792/S/0023
Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski

Raxone - idebenone -
EMEA/H/C/003834/S/0012, Orphan
Santhera Pharmaceuticals (Deutschland) GmbH, Rapporteur: John Joseph Borg, PRAC Rapporteur: Amelia Cupelli
Request for Supplementary Information adopted on 31.01.2019.

Vedrop - tocofersolan -
EMEA/H/C/000920/S/0031
Orphan Europe SARL, Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Julia Pallos

B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

Zydelig - idelalisib -
EMEA/H/C/003843/R/0043
Gilead Sciences Ireland UC, Rapporteur: Filip Josephson, Co-Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Patrick Batty

B.2.2. Renewals of Marketing Authorisations for unlimited validity

Nuwiq - simoctocog alfa -
EMEA/H/C/002813/R/0027
Octapharma AB, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Andrea Laslop, PRAC Rapporteur: Ulla Wändel Liminga
Request for Supplementary Information adopted on 31.01.2019.

Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/R/0063
ViiV Healthcare B.V., Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber

B.2.3. Renewals of Conditional Marketing Authorisations

Natpar - parathyroid hormone -
EMEA/H/C/003861/R/0016, Orphan
Shire Pharmaceuticals Ireland Limited, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Rhea Fitzgerald
Request for Supplementary Information adopted on 31.01.2019.

Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (H5N1) (live attenuated, nasal) -
EMEA/H/C/003963/R/0019
AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Daniela Philadelphy
Request for Supplementary Information adopted on 31.01.2019.

B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

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

EMEA/H/C/PSUSA/00010006/201806
(5-aminolevulinic acid (keratosis))
CAPS:
Ameluz (EMEA/H/C/002204) (5-aminolevulinic acid), Biofrontera Bioscience GmbH, Rapporteur: Janet Koenig
NAPS:
ALACARE - PHOTONAMIC GMBH & CO. KG
EFFALA - PHOTONAMIC GMBH & CO. KG
PRAC Rapporteur: Martin Huber, "15-Jun-2015 to 14-Jun-2018."

EMEA/H/C/PSUSA/00010035/201807
(ingenol mebutate)
CAPS:
Picato (EMEA/H/C/002275) (ingenol mebutate), LEO Laboratories Ltd, Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, "01-February-2018 to 31-July-2018"

EMEA/H/C/PSUSA/00010111/201807
(lipegfilgrastim)
CAPS:
Lonquex (EMEA/H/C/002556) (lipegfilgrastim), Teva B.V., Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, "1 year"

EMEA/H/C/PSUSA/00010405/201807
(evolocumab)
CAPS:
Repatha (EMEA/H/C/003766) (evolocumab), Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Kimmo Jaakkola, "18 January 2018 - 17 July 2018"

EMEA/H/C/PSUSA/00010445/201807
(asparaginase (centrally authorised product))
CAPS:
Spectrila (EMEA/H/C/002661) (asparaginase), medac Gesellschaft fur klinische Spezialpraparate mbH, Rapporteur: Greg Markey, PRAC Rapporteur: Patrick Batty, "15.01.2018 - 14.07.2018"

EMEA/H/C/PSUSA/00010448/201807
(carfilzomib)
CAPS:
Kyprolis (EMEA/H/C/003790) (carfilzomib), Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Nikica Mirošević Skvrce, "20 January 2018 to 19 July 2018"

EMEA/H/C/PSUSA/00010457/201807

(pegaspargase (centrally authorised product))
CAPS:
Oncaspar (EMEA/H/C/003789) (pegaspargase), Les Laboratoires Servier, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Patrick Batty, "15-Jan-2018 to 14-Jul-2018"

EMEA/H/C/PSUSA/00010620/201807
(glecaprevir / pibrentasvir)
CAPS:
Maviret (EMEA/H/C/004430) (glecaprevir / pibrentasvir), AbbVie Deutschland GmbH & Co. KG, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Ana Sofia Diniz Martins, "26 January 2018 to 25 July 2018"

B.4. EPARs / WPARs

Efgratin - pegfilgrastim - EMEA/H/C/004789
Gedeon Richter Plc.; treatment of neutropenia, Similar biological application (Article 10(4) of Directive No 2001/83/EC)

Cavoley - pegfilgrastim - EMEA/H/C/005008
STADA Arzneimittel AG; treatment of neutropenia, Similar biological application (Article 10(4) of Directive No 2001/83/EC), Duplicate of Efgratin

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

Cerezyme - imiglucerase - EMEA/H/C/000157/II/0113/G Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege Opinion adopted on 07.02.2019.	Positive Opinion adopted by consensus on 07.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Dupixent - dupilumab - EMEA/H/C/004390/II/0013/G sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 14.02.2019.	Request for supplementary information adopted with a specific timetable.
Empliciti - elotuzumab - EMEA/H/C/003967/II/0013	

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Paula Boudewina van Hennik	
Firazyr - icatibant - EMEA/H/C/000899/II/0043/G, Orphan Shire Pharmaceuticals Ireland Limited, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 24.01.2019.	
Flixabi - infliximab - EMEA/H/C/004020/II/0034 Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 17.01.2019.	
Foclivia - influenza virus surface antigens (inactivated) of strain A/Vietnam/1194/2004 (H5N1) - EMEA/H/C/001208/II/0040/G Seqirus S.r.l, Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 07.02.2019.	Request for supplementary information adopted with a specific timetable.
Humira - adalimumab - EMEA/H/C/000481/II/0184/G AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder Request for Supplementary Information adopted on 06.12.2018.	
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0066/G Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 14.02.2019.	Request for supplementary information adopted with a specific timetable.
Keytruda - pembrolizumab - EMEA/H/C/003820/II/0067/G Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Matever - levetiracetam - EMEA/H/C/002024/II/0032 Pharmathen S.A., Generic, Generic of Keppra, Rapporteur: Ondřej Slanař Request for Supplementary Information adopted on 14.02.2019.	Request for supplementary information adopted with a specific timetable.
Nulojix - belatacept - EMEA/H/C/002098/II/0051	

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson Request for Supplementary Information adopted on 17.01.2019.	
Nulojix - belatacept - EMEA/H/C/002098/II/0052/G Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson Request for Supplementary Information adopted on 17.01.2019.	
Obizur - susoctocog alfa - EMEA/H/C/002792/II/0022/G Baxalta Innovations GmbH, Rapporteur: Nithyanandan Nagercoil Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 29.11.2018.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Ongentys - opicapone - EMEA/H/C/002790/II/0009 Bial - Portela & Cª, S.A., Rapporteur: Greg Markey Request for Supplementary Information adopted on 14.02.2019, 20.09.2018, 26.04.2018.	Request for supplementary information adopted with a specific timetable.
Ontruzant - trastuzumab - EMEA/H/C/004323/II/0015/G Samsung Bioepis NL B.V., Rapporteur: Koenraad Norga Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Orphacol - cholic acid - EMEA/H/C/001250/II/0025, Orphan Laboratoires CTRS, Rapporteur: Greg Markey Request for Supplementary Information adopted on 11.10.2018.	
Pandemic influenza vaccine H5N1 AstraZeneca - pandemic influenza vaccine (H5N1) (live attenuated, nasal) - EMEA/H/C/003963/II/0020/G AstraZeneca AB, Rapporteur: Jan Mueller-Berghaus Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pelgraz - pegfilgrastim - EMEA/H/C/003961/II/0002 Accord Healthcare Limited, Rapporteur: Sol Ruiz Opinion adopted on 07.02.2019.	Positive Opinion adopted by consensus on 07.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Pheburane - sodium phenylbutyrate - EMEA/H/C/002500/II/0019	

Eurocept International B.V., Rapporteur: Jayne Crowe Request for Supplementary Information adopted on 13.12.2018.	
Praxbind - idarucizumab - EMEA/H/C/003986/II/0014/G Boehringer Ingelheim International GmbH, Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 14.02.2019.	Request for supplementary information adopted with a specific timetable.
Synagis - palivizumab - EMEA/H/C/000257/II/0118 AbbVie Deutschland GmbH & Co. KG, Rapporteur: Mark Ainsworth Request for Supplementary Information adopted on 14.02.2019.	Request for supplementary information adopted with a specific timetable.
Taltz - ixekizumab - EMEA/H/C/003943/II/0025/G Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Tamiflu - oseltamivir - EMEA/H/C/000402/II/0135 Roche Registration GmbH, Rapporteur: Outi Mäki-Ikola Request for Supplementary Information adopted on 13.09.2018.	
Trulicity - dulaglutide - EMEA/H/C/002825/II/0033 Eli Lilly Nederland B.V., Rapporteur: Martina Weise Request for Supplementary Information adopted on 07.02.2019.	Request for supplementary information adopted with a specific timetable.
Vizarsin - sildenafil - EMEA/H/C/001076/II/0029 KRKA, d.d., Novo mesto, Generic, Generic of Viagra, Rapporteur: Alexandre Moreau Request for Supplementary Information adopted on 22.11.2018.	
Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0054/G Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez Request for Supplementary Information adopted on 14.02.2019.	Request for supplementary information adopted with a specific timetable.
WS1478	Positive Opinion adopted by consensus on

Saxenda-EMEA/H/C/003780/WS1478/0019 **Victoza-EMEA/H/C/001026/WS1478/0048** **Xultophy-EMEA/H/C/002647/WS1478/0027** Novo Nordisk A/S, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 06.12.2018.	14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1503/G **Prezista-EMEA/H/C/000707/WS1503/0100/G** **Rezolsta-EMEA/H/C/002819/WS1503/0029/G** **Symtuza-EMEA/H/C/004391/WS1503/0013/G** Janssen-Cilag International NV, Lead Rapporteur: Johann Lodewijk Hillege Request for Supplementary Information adopted on 13.12.2018.	
WS1519/G **HyQvia-EMEA/H/C/002491/WS1519/0047/G** **Kiovig-EMEA/H/C/000628/WS1519/0089/G** Baxter AG, Lead Rapporteur: Jan Mueller-Berghaus Request for Supplementary Information adopted on 14.02.2019.	Request for supplementary information adopted with a specific timetable.
WS1530/G **Aflunov-EMEA/H/C/002094/WS1530/0045/G** **Foclivia-EMEA/H/C/001208/WS1530/0039/G** Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri Request for Supplementary Information adopted on 07.02.2019.	Request for supplementary information adopted with a specific timetable.
WS1547 **PegIntron-EMEA/H/C/000280/WS1547/0136** **ViraferonPeg-EMEA/H/C/000329/WS1547/0129** Merck Sharp & Dohme B.V., Lead Rapporteur: Filip Josephson Opinion adopted on 07.02.2019.	Positive Opinion adopted by consensus on 07.02.2019. 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

Adempas - riociguat -
EMEA/H/C/002737/II/0028, Orphan
Bayer AG, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4 and 4.5 of the SmPC to include information for recommended starting dose for riociguat for patients who are on stable doses of strong multi pathway cytochrome P450 proteins (CYP) and P-gp/BCRP inhibitors based on date from Study 17957 which investigated the potential pharmacokinetic (PK) interaction of human immunodeficiency virus (HIV) antiretroviral agents as fixed-dose combination and riociguat in HIV patients, data from a statistical drug-drug interaction (DDI) which was evaluated in study 18634, in which PK data from study 17957 was compared to the historical PK data and data from a nonclinical study to elucidate the DDI potential of the different components included in the HIV combination products in vitro.
The package leaflet is updated accordingly."

Alprolix - eftrenonacog alfa -
EMEA/H/C/004142/II/0021, Orphan
Swedish Orphan Biovitrum AB (publ), Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.8 and 5.1 of the SmPC to include new clinical efficacy and safety data on long-term treatment with Alprolix. The submission includes integrated evaluation of data from the extension study (9HB01EXT (BYOND) which was submitted in a previous P46 procedure) and the pivotal parent studies. The PIL is updated accordingly. In addition, the MAH took the opportunity to update the product information to comply with the latest version of the "Excipients in the labelling and package leaflet of medicinal products for human use" guideline. The list of local representatives has been updated and other minor editorial changes have been included in the PIL."
Request for Supplementary Information adopted on 29.11.2018.

Atriance - nelarabine -
EMEA/H/C/000752/II/0046/G
Novartis Europharm Limited, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, "Update to the Annex II to remove the SOB based on final results from the Study

NLR506AUS02T (COG AALL0434) 'Intensified methotrexate, nelarabine and augmented BFM therapy for children and young adults with newly diagnosed T-ALL and T-LBL'. As a result sections 4.8 and 5.1 of the SmPC are updated. Additionally the MAH took the opportunity to update section 4.6 of the SmPC to revise information on the male and female contraception taking into consideration available non-clinical and clinical safety data as well as internal MAH's guidelines based on information from literature, health authority and working group guidelines. Moreover, the MAH took the opportunity to update details of the local representatives in the PL and introduce minor editorial changes in the PI. The revised RMP version 10 is included in this submission."	
AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0020 sanofi-aventis groupe, Rapporteur: Martina Weise, "Submission of the final report from study LTS 6050. This is a phase 3 long term interventional study to document the safety of two doses of teriflunomide (7 and 14 mg) in patients with multiple sclerosis with relapses." Request for Supplementary Information adopted on 17.01.2019, 22.11.2018.	
Axumin - fluciclovine (18F) - EMEA/H/C/004197/II/0010 Blue Earth Diagnostics Ireland Limited, Rapporteur: Janet Koenig, PRAC Rapporteur: Rugile Pilviniene, "Submission of an updated RMP version 2.0 in order to update to GVP Module V Rev.2 and introduce changes in line with the updated RMP template format; the update further includes new exposure information from both clinical trials and worldwide commercial exposure from US and EU countries and corrections to the effectiveness measurement of the image interpretation training from a review of self-assessment scores to normal pharmacovigilance activities." Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. 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/0073 GSK Vaccines S.r.l, Rapporteur: Kristina Dunder, "Update of sections 4.2 and 5.1 of the SmPC to	

add data on antibody persistence and response to a 3rd dose in children, adolescents and adults, based on clinical studies V72_28E1 and V72_75. Study V72_28E1 was a phase 3b, open label, multicentre extension study that evaluated the antibody persistence in children 4 through 12 years of age at 24 through 36 months after the last dose in follow-on subjects from the parent study V72_28. Study V72_75 was a phase 3b, open label, controlled, multicentre study that assessed the long-term antibody persistence of bactericidal activity at 4 to 7.5 years after 2-dose primary series of vaccination and the booster response to a third dose in adolescents and young adults 15 through 24 years of age who previously participated in studies V72P10 and V72_41. The Package Leaflet is updated accordingly."	
Brinavess - vernakalant - EMEA/H/C/001215/II/0034 Correvio, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.8 and 5.1 of the SmPC based on the final results from the non-interventional PASS SPECTRUM study, listed as a category 3 study in the RMP, in order to fulfil MEA 026.5; SPRECTRUM (6621-019) study is a prospective observational registry study to characterise normal conditions of use, dosing and safety following administration of vernakalant IV sterile concentrate." Request for Supplementary Information adopted on 14.02.2019.	Request for supplementary information adopted with a specific timetable.
Bydureon - exenatide - EMEA/H/C/002020/II/0057 AstraZeneca AB, Rapporteur: Kristina Dunder, "Update of sections 4.8 and 5.1 of the SmPC in order to implement minor changes in line with the revised study report for the DURATION 7 study (previously assessed as part of variation II/45). In addition, the MAH took the opportunity to implement editorial changes for increased clarity in the SmPC section 6.6 and the Package Leaflet of the pre-filled pen." Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0099 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of section 4.5 of the	Request for supplementary information adopted with a specific timetable.

SmPC in order to update the safety information for the concomitant administration of Cervarix with meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine (Nimenrix), based on results from study MENACWY-TT-054. This is a phase III, open, randomised, controlled, multicentre study aimed to assess the immunogenicity and reactogenicity of Nimenrix administered alone as compared to Nimenrix co-administered with HPV vaccine Cervarix or co-administered with Cervarix and tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine adsorbed (Boostrix) in female adolescents and adults at 9 to 25 years of age; as requested in the CHMP conclusion of procedure P46/093. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity update the package leaflet to correct inconsistencies related to the indication in males." Request for Supplementary Information adopted on 14.02.2019.	
Cetrotide - cetrorelix - EMEA/H/C/000233/II/0068 Merck Europe B.V., Rapporteur: Martina Weise, "Update of section 4.2 of the SmPC based on literature review to add an alternative option for the treatment initiation to start once the leading follicle(s) reach a size that could lead to premature LH (Luteinizing Hormone) surge and ovulation. The Package Leaflet (PL) is updated in accordance. Correction in section 3 of the PL to regarding the timing of ovulation induction. In addition, the Marketing authorisation holder (MAH) took the opportunity to delete the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.0." Request for Supplementary Information adopted on 18.10.2018.	See 9.1
Delstrigo - doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746/II/0001 Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information based on the results from the clinical study report P024: ' Phase III Multicenter,	

Open-Label, Randomized Study to Evaluate a Switch to MK-1439A in HIV-1-Infected Subjects Virologically Suppressed on a Regimen of a Ritonavir-boosted Protease Inhibitor and Two Nucleoside Reverse Transcriptase Inhibitors (NRTIs)'. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity implement editorial changes in the SmPC and patient leaflet."	
Eliquis - apixaban - EMEA/H/C/002148/II/0059 Bristol-Myers Squibb / Pfizer EEIG, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.3, 4.4 and 4.5 of the SmPC based on the current European Society of Cardiology (ESC) guideline for direct oral anti-coagulants (DOACs) and the literature including the AXAFA-AFNET 5 study, a major investigator's sponsored trial with apixaban, in order to include an exception to the contraindicated concomitant treatment with any other anticoagulant agent for heparin co-administration during catheter ablation for atrial fibrillation. In addition, the Marketing authorisation holder (MAH) took the opportunity to clarify the wording in section 4.2 of the SmPC to include a reference to transesophageal echocardiogram (TEE) guided cardioversion."	
EXJADE - deferasirox - EMEA/H/C/000670/II/0064 Novartis Europharm Limited, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "To update the Risk Management Plan (RMP) version 16.0 for Exjade® (deferasirox, EMEA/H/C/000670), covering all formulations (dispersible tablets, film-coated tablets and granules). With this update, the MAH introduces the alignment with requirements of the new RMP template (as per the revised Good Pharmacovigilance Practices (GVP) Module V Rev.2) and consequential removal of the food interaction and drug-drug interactions (DDI) from the list of important identified risks. In addition, "drug reaction with eosinophilia and systemic symptoms" (DRESS) has been reclassified from important potential risk to important identified risk. The reclassification of DRESS was agreed with the PRAC during a previous procedure	Request for supplementary information adopted with a specific timetable.

(EMEA/H/C/PSUSA/00000939/201710). Additional minor changes are have been also implemented in the RMP. With this variation, the Health Care Professional (HCP) guide is also updated." Request for Supplementary Information adopted on 14.02.2019.	
Fasenra - benralizumab - EMEA/H/C/004433/II/0012 AstraZeneca AB, Rapporteur: Fátima Ventura, "Update of sections 4.5 and 5.2 of the SmPC to reflect the outcome of the ALIZE study: a randomized, double-blind, parallel-group, placebo-controlled study designed to investigate the efficacy, safety, pharmacokinetics, and immunogenicity of a fixed dose of benralizumab (30 mg) administered subcutaneously on the humoral immune response following seasonal influenza virus vaccination in patients 12 to 21 years of age with severe asthma." Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Fasenra - benralizumab - EMEA/H/C/004433/II/0013 AstraZeneca AB, Rapporteur: Fátima Ventura, "Update of sections 4.8 and 5.1 of the SmPC in order to reflect the final results from study D3250C00021 (BORA) listed as a category 3 in the RMP; this is a randomised phase 3 study to evaluate the safety and tolerability of benralizumab in asthmatic adults and adolescents on inhaled corticosteroid plus long-acting β2 agnostic. In addition, section 4.2 of the SmPC is updated to reflect the extended PIP waiver age group" Request for Supplementary Information adopted on 14.02.2019.	Request for supplementary information adopted with a specific timetable.
Infanrix hexa - diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inact.) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/000296/II/0250 GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of section 5.1 of the SmPC in order to add information on the persistence of immunity against hepatitis B up to 14-15 years of age, based on results from study DTPa-HBV-IPV-115. This was a phase IV, open-label, multicentre study to assess the long-term persistence of antibodies against	Positive Opinion adopted by consensus on 07.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

hepatitis B and the immunogenicity and safety of a challenge dose of hepatitis B vaccine (Engerix-B Kinder SKF103860) in children aged 14-15 years, previously primed and boosted in the first two years of life with four doses of GSK Biologicals' DTPa-HBV-IPV/Hib (Infanrix hexa SB217744) vaccine. In addition, in line with the SmPC Guideline, the MAH took the opportunity to introduce in section 4.1 of the SmPC a statement regarding the use of Infanrix hexa in accordance with official recommendations." Opinion adopted on 07.02.2019.	
Jivi - damoctocog alfa pegol - EMEA/H/C/004054/II/0001, Orphan Bayer AG, Rapporteur: Sinan B. Sarac, "Submission of the final report from study (T103483-9, a 13- and 26-Week Intravenous Toxicity Study of BAY 94-9027 in the Nude Rat (Rowett nude rats, Crl:NIHFoxn1rnu) followed by a 26-Week Recovery Period) in fulfilment of recommendation adopted at the time of initial marketing authorisation opinion." Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kadcyla - trastuzumab emtansine - EMEA/H/C/002389/II/0042/G Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, "Submission of an updated RMP version 8 in order to remove MotHER study [MEA 011] from the European Union Risk Management Plan (EU RMP) and use the Global Enhanced Pharmacovigilance (PV) Pregnancy Program to fulfil the relevant commitment and to change the due date for the provision of the final study report for BO27938 (KATHERINE), a category 3 study in the RMP. In addition, the MAH took the opportunity to update the RMP in line with the version 2.0 of new GVP Module V. and include an update of Kadcyla Educational Material to reflect changes in the Prescribing information following the renewal of the marketing authorisation." Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 29.11.2018.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Kalydeco - ivacaftor - EMEA/H/C/002494/II/0076, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Concepcion Prieto Yerro, "Update of	

sections 4.4, and 5.1 of the SmPC to clarify the classification of the G970R CFTR mutation as a splicing mutation, based on data from the Study 770-112 G970R substudy (reviously submitted in procedure II/54) and an additional mRNA analysis (report N052)."

Keytruda - pembrolizumab - EMEA/H/C/003820/II/0062

Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Update of sections 4.2 and 5.1 of the SmPC to add an alternative dosing regimen of 400 mg every 6 weeks (Q6W) for all approved indications and indications currently under review in addition to the currently approved 200 mg every Q3W, based on modelling and simulation analysis. No new clinical or pre-clinical studies are being submitted as part of the current application. The Package Leaflet (section 3) is updated accordingly."
Request for Supplementary Information adopted on 13.12.2018.

Kolbam - cholic acid - EMEA/H/C/002081/II/0028, Orphan

Retrophin Europe Ltd, Rapporteur: Constantinos Markopoulos, "Submission of the final report from study CAC-002-01, listed as a category 3 study in the RMP. This is a Phase 3, open-label, single arm, non-randomized study investigating cholic acid in the treatment of subjects with inborn errors of bile acid metabolism.
The study was a continuation study that included eligible subjects who had previously received cholic acid in studies CAC-91-10-10 or CAC-001-01 as well as newly diagnosed subjects."

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

Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 to add a once-weekly dose regimen for carfilzomib (Kyprolis) at 20/70 mg/m2 in combination with dexamethasone (Kd) for the treatment of the currently indicated patient population. The MAH took the opportunity to implement editorial changes to the SmPC and Patient Information Leaflet (PIL) due to the revised excipients guideline (EMA/CHMP/302620/2017). The PIL is updated accordingly."

Request for Supplementary Information adopted on 15.11.2018.	
Luminity - perflutren - EMEA/H/C/000654/II/0026 Lantheus MI UK Ltd., Rapporteur: Peter Kiely, "Submission of the final report from study Luminity 422, a category 3 study in the RMP, in order to fulfil MEA 004.4. This is a phase IV, multi-centre, parallel-group, randomised, cross-over trial to compare the efficacy of Luminity and SonoVue in the evaluation of left ventricular border definition." Request for Supplementary Information adopted on 14.02.2019.	Request for supplementary information adopted with a specific timetable.
Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0038 GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus, "Submission of the final report from study Malaria-063; this is a phase III randomized, open, controlled study to evaluate the long term immune response to the hepatitis B antigen of the RTS,S/AS01E candidate vaccine, when administered as primary vaccination integrated into an Expanded Program on Immunization (EPI) regimen to infants living in sub-Saharan Africa." Request for Supplementary Information adopted on 13.12.2018.	
Nimenrix - meningococcal group A, C, W135 and Y conjugate vaccine - EMEA/H/C/002226/II/0084 Pfizer Europe MA EEIG, Rapporteur: Greg Markey, "Update of section 4.2 of the SmPC in order to update the posology information in infants, following the final results from study MenACWY-TT-087 (Study 087); this is a phase IIIb, controlled, randomised, open study aimed to demonstrate the immunogenicity and safety of Nimenrix in healthy infants, given on a 3+1 primary and booster (2, 4, 6 and 15-18 months of age), a 1+1 primary and booster (6 and 15-18 months of age) or as a single dose at 15-18 months of age. The Package Leaflet is updated accordingly. The MAH took the opportunity to include editorial changes in sections 4.4 and 4.8 of the SmPC." Request for Supplementary Information adopted	See 9.1

on 18.10.2018.

Pifeltro - doravirine -
EMEA/H/C/004747/II/0001
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information based on the results from the clinical study report P024: ' Phase III Multicenter, Open-Label, Randomized Study to Evaluate a Switch to MK-1439A in HIV-1-Infected Subjects Virologically Suppressed on a regimen of a ritonavir-boosted protease Inhibitor and two Nucleoside Reverse Transcriptase Inhibitors (NRTIs)'. The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder (MAH) took the opportunity implement editorial changes in the SmPC and patient leaflet."

Resolor - prucalopride -
EMEA/H/C/001012/II/0046
Shire Pharmaceuticals Ireland Limited, Rapporteur: Greg Markey, "Update of section 4.8 of the SmPC in order to add migraine and vertigo as uncommon adverse events, based on a reanalysis of the integrated safety information of 16 double-blind, placebo-controlled studies.
In addition, the Marketing authorisation holder (MAH) made editorial revision proposals for sections 4.4, 4.6 and 5.2 for alignment with Company Core Data Sheet version 12 and QRD templated wording.
The MAH also took the opportunity to propose minor editorial changes to Package Leaflet and sections 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC."
Request for Supplementary Information adopted on 13.12.2018.

Strensiq - asfotase alfa -
EMEA/H/C/003794/II/0035/G, Orphan
Alexion Europe SAS, Rapporteur: Daniela Melchiorri, "Update of sections 4.4, 4.6, 4.8 and 5.2 of the SmPC with the results of the integrated safety analysis of pooled asfotase alfa clinical studies, and section 5.1 of the SmPC with the final results of study ENB-002-08/ENB-003-08 (an open-label, non-randomised, non-controlled study) and study ENB-010-10 (a controlled, open label study to evaluate the efficacy, safety, and PK of asfotase alfa in infants and children ≤ 5 years of age with hypophosphatasia (HPP)). The

Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the SmPC and Package Leaflet."	
Symkevi - tezacaftor / ivacaftor - EMEA/H/C/004682/II/0002/G, Orphan Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Johann Lodewijk Hillege, "Update of section 4.5 of the SmPC with the results of the following 4 non-clinical drug-drug interaction (DDI) studies : Results from Study O092: Evaluation of VRT-1189001 as an Inducer of CYP1A2 and CYP2B6 using Primary Cryopreserved Human Hepatocytes Results from O093: Evaluation of VRT-0996107 as an Inducer of CYP2B6 using Primary Cryopreserved Human Hepatocytes Results from OPT-2018-041: Assessment of VRT-0893661, VRT-0996107, VRT-1189001 and VRT-1074233 as inhibitors of human OCT1, MATE1, MATE2-K, and BSEP mediated transport Results fOPT-2018-040: Assessment of VRT-0813077, VRT-0837018 and VRT-0842917 as substrates of human BCRP mediated transport. The MAH took the opportunity to introduce some additional minor updates in the Product information." Opinion adopted on 21.02.2019. Request for Supplementary Information adopted on 17.01.2019.	Positive Opinion adopted by consensus on 21.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
TECFIDERA - dimethyl fumarate - EMEA/H/C/002601/II/0054/G Biogen Netherlands B.V., Rapporteur: Martina Weise, "Type II grouped variation (3xC.I.13) for the submission of results of the below listed studies in order to fulfil LEG 004: 1. RSCH-2018-30: In vitro transcriptional profiling feasibility pilot study to determine the mechanism of action for lymphopenia in dimethyl fumarate-treated patients. 2. DMF-109MS301: Ex vivo transcriptional profiling study to assess the transcriptional changes induced by DMF in whole blood in 109MS301 and 109MS302 cohorts. 3. NLD-BGT-15-10945 (kinetic study): Characterisation of the immune-modulatory effects of Tecfidera in multiple sclerosis patients:	Positive Opinion adopted by consensus on 21.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

exploration of drug mechanism and methodological feasibility." Opinion adopted on 21.02.2019. Request for Supplementary Information adopted on 18.10.2018.	
Translarna - ataluren - EMEA/H/C/002720/II/0045, Orphan PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 4.5 of the SmPC in order to include information on Drug-Drug Interaction with sensitive probe substrate of organic anion transporting polypeptide 1B3 (OATP1B3) based on study PTC124-GD-042-HV (MEA016). The package leaflet is updated accordingly." Request for Supplementary Information adopted on 15.11.2018, 13.09.2018.	
Translarna - ataluren - EMEA/H/C/002720/II/0046, Orphan PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update information on patients with moderate to severe renal impairment based on results from study PTC124-GD-032-HV (MEA010). In addition the MAH took the opportunity to amend section 5.2 to propose correction of the biotransformation statement. The Package leaflet is updated accordingly." Request for Supplementary Information adopted on 20.09.2018.	
Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0009, Orphan Ipsen Pharma, Rapporteur: Janet Koenig, "Update of sections 4.2 and 5.2 of the SmPC in order to add PK information in subjects with mild, moderate and severe renal impairment based on study D-FR-01017-002 (A Phase I, open-label study to compare the pharmacokinetics of telotristat ethyl and its metabolite in subjects with impaired renal function to healthy subjects with normal renal function after a single dose of telotristat etiprate) (MEA005). The Package Leaflet is updated accordingly."	
Zostavax - shingles (herpes zoster) vaccine (live) - EMEA/H/C/000674/II/0120 MSD Vaccins, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.8 of the SmPC in order to	Negative Opinion adopted by consensus on 07.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

add the adverse reactions Guillain-Barré syndrome and facial paralysis with frequency "very rare" following a review post-marketing cases; the Package Leaflet is updated accordingly." Opinion adopted on 07.02.2019. Request for Supplementary Information adopted on 08.11.2018.	
Zykadia - ceritinib - EMEA/H/C/003819/II/0027 Novartis Europharm Limited, Rapporteur: Jorge Camarero Jiménez, "Submission of the final Biomarker annual update report from phase II studies (A2201 and A2203) in order to fulfil the following Post-Marketing Measure identified by the CHMP: To submit a yearly update of the biomarker program for ceritinib." Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 13.12.2018.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1401 **Genvoya-EMEA/H/C/004042/WS1401/0047** **Stribild-EMEA/H/C/002574/WS1401/0094** **Tybost-EMEA/H/C/002572/WS1401/0044** Gilead Sciences Ireland UC, Lead Rapporteur: Greg Markey, "Update of section 4.6 the SmPC for Tybost, Stribild and Genvoya based on pharmacokinetics data in pregnancy from IMPAACT study P1026s (ClinicalTrials.gov ID NCT00042289); this is an ongoing, nonrandomized, open-label, parallel-group, multi-centre phase 4 prospective study of antiretroviral (ARV) pharmacokinetics (PK) and safety in HIV-1 infected pregnant women that includes an arm for EVG/COBI. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to bring the PI in line with the latest QRD template version 10." Request for Supplementary Information adopted on 13.12.2018, 11.10.2018, 12.07.2018.	
WS1429 **Descovy-EMEA/H/C/004094/WS1429/0032** **Genvoya-EMEA/H/C/004042/WS1429/0048**	

Odefsey-EMEA/H/C/004156/WS1429/0033 Gilead Sciences Ireland UC, Lead Rapporteur: Greg Markey, "Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC with data in patients on chronic haemodialysis from the Study GS-US-292-1825; this is a Phase 3b Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of E/C/F/TAF Fixed Dose Combination (FDC) in HIV-1 Infected Subjects on Chronic Hemodialysis. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to introduce changes to the lactose wording for Genvoya and Odefsey and an administrative correction to the Genvoya Patient information leaflet (PIL) in order to add "lurasidone" to the second list of contra-indicated drugs appearing in the PIL. The WSA has also taken the opportunity to introduce some minor administrative amendments throughout the product information for all three products as well as to implement some minor linguistic amendments (MLAs) to the translations of the respective product information annexes: - Genvoya: DE, ES, FI, HR, HU, IS, IT, NO, SL and SV languages - Descovy: DA, DE, ES, FR, HR, NL, NO, PT and SL languages - Odefsey: CS, DE, LV, MT, NL, PL, SL and SV languages." Request for Supplementary Information adopted on 20.09.2018.	
WS1468 **Mekinist-EMEA/H/C/002643/WS1468/0030** **Tafinlar-EMEA/H/C/002604/WS1468/0034** Novartis Europharm Limited, Lead Rapporteur: Paula Boudewina van Hennik, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to reflect study results from study BRF117277, a Phase II, Open-Label, Multicentre Study of Dabrafenib plus Trametinib in Subjects with BRAF Mutation-Positive Melanoma that has Metastasized to the Brain (COMBI-MB)." Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 13.12.2018.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

WS1488 **Segluromet-EMEA/H/C/004314/WS1488/0004** **Steglatro-EMEA/H/C/004315/WS1488/0004** **Steglujan-EMEA/H/C/004313/WS1488/0006** Merck Sharp & Dohme B.V., Lead Rapporteur: Kristina Dunder, “Submission of the final CSR for Study P007/1017 - a Phase 3, randomized, double-blind, placebo-controlled, 26-week multicenter study with a 78-week extension to evaluate the efficacy and safety of ertugliflozin in subjects with type 2 Diabetes Mellitus and inadequate glycaemic control on metformin monotherapy - together with the final summarized data of all adjudicated confirmed fractures from the broad pool and pooled 2-year safety data from the 7 completed Phase 3 studies, including both 2-year studies P007/1017 and P002/1013.” Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 06.12.2018.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1495 **Lyrica-EMEA/H/C/000546/WS1495/0096** **Pregabalin** **Pfizer-EMEA/H/C/003880/WS1495/0026** Pfizer Europe MA EEIG, Lead Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.8 and 5.1 of the SmPC in order to reflect information from study A0081042 A Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study of the Efficacy and Safety of Pregabalin as Adjunctive Therapy in Children 1 Month through less than 4 Years of Age with Partial Onset Seizures. This submission relates to paediatric studies submitted according to Article 46 of the paediatric regulation (EC) No 1901/2006.” Request for Supplementary Information adopted on 13.12.2018.	
WS1523 **Epclusa-EMEA/H/C/004210/WS1523/0031** **Harvoni-EMEA/H/C/003850/WS1523/0072** **Sovaldi-EMEA/H/C/002798/WS1523/0054** **Vosevi-EMEA/H/C/004350/WS1523/0022** Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, “Update of sections 4.3, 4.4 and	Request for supplementary information adopted with a specific timetable.

4.5 of the SmPC in order implement additional guidance on the use of sofosbuvir-based therapy with concomitant drugs, based on final results from study GS-US-334-2130. This was a phase I study to evaluate the effects of cytochrome P450 and drug transporter inducers on sofosbuvir and probe drug pharmacokinetics in healthy subjects. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor editorial changes throughout the Product Information." Request for Supplementary Information adopted on 14.02.2019.	
WS1540 **Docetaxel** **Zentiva-EMEA/H/C/000808/WS1540/0057** **Taxotere-EMEA/H/C/000073/WS1540/0130** Aventis Pharma S.A., Lead Rapporteur: Alexandre Moreau, "Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information following review of a safety signal on secondary malignancies for docetaxel requested in follow-up to EMEA/H/C/PSUSA/00001152/201611; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to correct minor typos throughout the Product Information." Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

B.5.3. CHMP-PRAC assessed procedures

Aflunov - prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - **EMEA/H/C/002094/II/0044/G** Seqirus S.r.l, Rapporteur: Daniela Melchiorri, PRAC Rapporteur: Amelia Cupelli, "Update of sections 4.4, 4.6, 4.8 and 5.1 of the SmPC following clinical study reports of studies V87_25 and V87_26 listed as post approval commitments; these are Phase 3, stratified, randomized, controlled, observer-blind, multicenter studies; the Package Leaflet and Labelling are updated accordingly. The updated RMP version 3.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement some	

amendments to the PI and make some additional minor editorial corrections."
Request for Supplementary Information adopted on 20.09.2018.

Avonex - interferon beta-1a - EMEA/H/C/000102/II/0182/G
Biogen Netherlands B.V., Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Maria del Pilar Rayon, "2x type II (C.I.4):
1) Update of section 4.3, and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054).
2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles.
The Package leaflet has been updated accordingly.
This submission fulfils MEA 87.2 and 84."

Betaferon - interferon beta-1b - EMEA/H/C/000081/II/0124/G
Bayer AG, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "2x type II (C.I.4):
1) Update of section 4.3 and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054).
2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles.
The Package leaflet has been updated accordingly.
This submission fulfils MEA 024.2 and 21.
An updated RMP version 4.1 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes' and an update of the EU-RMP template (rev.2)."

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 18.10.2018, 26.04.2018, 14.12.2017.	
Daklinza - daclatasvir - EMEA/H/C/003768/II/0031 Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of section 5.1 of the SmPC in order to add information on long-term efficacy and drug resistance based on final results from study AI444046, listed as a category 3 study in the RMP. This is a phase 3 non-randomized, open-label, long-term follow-up and observational study of durability of efficacy, resistance and characterization of progression of liver disease in subjects with chronic hepatitis C previously treated with daclatasvir and/or asunaprevir. In addition, the Marketing authorisation holder (MAH) took the opportunity to postpone (from Q2 2021 to Q2 2023) the due date of the safety study AI444427 evaluating recurrence of hepatocellular carcinoma. Annex II is updated in accordance. The RMP version 6.0 has also been submitted." Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 17.01.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Extavia - interferon beta-1b - EMEA/H/C/000933/II/0096/G Novartis Europharm Limited, Informed Consent of Betaferon, Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, "2x type II (C.I.4): 1) Update of section 4.3 and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the	

European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054). 2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles. The Package leaflet has been updated accordingly. This submission fulfils MEA 022.2 and 019. An updated RMP version 4.1 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes' and an update of the EU-RMP template (rev. 2)."	
Fasenra - benralizumab - EMEA/H/C/004433/II/0014/G AstraZeneca AB, Rapporteur: Fátima Ventura, PRAC Rapporteur: David Olsen"B.IV.1.c – To add an autoinjector delivery device, Fasenra 30 mg solution for injection in pre-filled pen. C.I.4 – Update of sections 4.2, 6.4, 6.5, 6.6 of the SmPC in order to update the information for self-administration for Fasenra 30 mg solution for injection in pre-filled syringe. The labelling and the package leaflet are updated accordingly. In addition, the RMP (version 2.0) is updated to reflect the information about the new presentation, to include additional information about completed studies (ALIZE, GREGALE, AMES, GRECO), to add updated exposure data post MAA approval, and to reflect additional details on the post-authorisation safety studies (Pregnancy registry (D3250R00026) and Malignancy Post Authorization Safety Study (D3250R00042)). Furthermore, the RMP is revised in line with the RMP template (GVP Module V rev.2)."	
IBRANCE - palbociclib - EMEA/H/C/003853/II/0017/G Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Doris Stenver, "Update of section 5.3 of the SmPC in order to include information from two completed non-clinical studies: a 6-month carcinogenicity study in mice (20084764), and a 2-year carcinogenicity study in rats (20066483). Furthermore, the MAH submitted the final report from the non-clinical study 20084675, a Pre- and Postnatal Developmental Toxicity Study in rats.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

The MAH took the opportunity to introduce minor editorial changes in SmPC and PL." Opinion adopted on 14.02.2019.	
IMVANEX - smallpox vaccine (live modified vaccinia virus ankara) - EMEA/H/C/002596/II/0036 Bavarian Nordic A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, "Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update the safety information and to provide confirmation in terms of immunogenicity based on the results from study (POX-MVA-006) (a randomized, open-label phase III non-inferiority trial to compare indicators of efficacy for smallpox vaccine to the US licensed replicating smallpox vaccine in 18-42 year old healthy vaccinia-naïve subjects) listed as an obligation in the Annex II (ANX 004); the Package Leaflet is updated accordingly. The RMP version 7.2 has also been submitted." Request for Supplementary Information adopted on 14.02.2019, 04.10.2018.	Request for supplementary information adopted with a specific timetable.
Intuniv - guanfacine - EMEA/H/C/003759/II/0015 Shire Pharmaceuticals Ireland Limited, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Maria del Pilar Rayon, "Update of section 4.5 of the SmPC in order to remove the statement on potential drug interactions with drugs that inhibit OCT1 based on final results from study V8953M-SPD503; this is a non-clinical study (Transporter Interaction - OCT1 inhibition); The RMP version 3.0 has also been submitted." Request for Supplementary Information adopted on 14.02.2019.	Request for supplementary information adopted with a specific timetable.
Kineret - anakinra - EMEA/H/C/000363/II/0064/G Swedish Orphan Biovitrum AB (publ), Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, "Update of section 4.4 of the SmPC in order to add a warning on pulmonary events based on post-marketing data. The package leaflet is updated accordingly. Consequently, the important potential risks and the list of target medical events in the RMP (version 4.6) are updated to include pulmonary events and a specific follow-up questionnaire is created.	Request for supplementary information adopted with a specific timetable.

The RMP is also revised in line with the GVP Module V RMP template (revision 2). In addition, the due date for submission of the final study report for the post-authorisation study (Sobi ANAKIN-302) is proposed to be extended. Furthermore, the MAH took the opportunity to move the text about macrophage activation syndrome (MAS) and malignancies from section 4.8 to 4.4 of the SmPC." Request for Supplementary Information adopted on 14.02.2019.	
Mosquirix - plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - EMEA/H/W/002300/II/0036 GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jean-Michel Dogné, "Update of section 4.4 of the SmPC in order to modify the warning related to the waning of protection against Plasmodium falciparum malaria over time. This update is based on final results from study MALARIA-076 listed as a category 3 study in the RMP. This was an open extension to the phase III, multi-centre study MALARIA-055 PRI (110021) to evaluate long-term efficacy, safety and immunogenicity of the GSK Biologicals' candidate malaria vaccine in infants and children. The RMP version 4.1 has also been submitted." Request for Supplementary Information adopted on 14.02.2019, 31.10.2018.	Request for supplementary information adopted with a specific timetable.
Mysimba - naltrexone hydrochloride / bupropion hydrochloride - EMEA/H/C/003687/II/0029/G Orexigen Therapeutics Ireland Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber, "Group of variations consisting of the: 2) C.I.3.b: to update section 4.8 on the list of adverse drug reactions and their corresponding frequencies following the PRAC outcome on PSUR procedure (PSUSA/10366/201709). 2) C.I.4: to update sections 4.2,4.4 and 5.2 of the SmPC to add results from a phase I open label parallel study to evaluate the pharmacokinetics of a single oral dose of extended-release combination of naltrexone and bupropion in subjects with normal hepatic function or varying degrees of impaired hepatic function and remove the recommendation to not use	

naltrexone/bupropion in patients with mild hepatic impairment. The existing warning has also been updated accordingly. The warning related to contraindications has also been aligned to section 4.3 to add end-stage renal failure patients. Consequentially an updated RMP (version 11) has also been submitted. In addition, the MAH takes the opportunity to update the warning on lactose to be in accordance with EC guideline on Guideline on "Excipients in the labelling and package leaflet of medicinal products for human use"." Request for Supplementary Information adopted on 15.11.2018.	
Ontruzant - trastuzumab - EMEA/H/C/004323/II/0016 Samsung Bioepis NL B.V., Rapporteur: Koenraad Norga, PRAC Rapporteur: Brigitte Keller-Stanislawski "To add a new presentation with a new fill weight (420 mg) for Ontruzant (EU/1/17/1241/002); in addition the Marketing Authorisation Holder took the opportunity to introduce editorial changes in the PI in line with the originator product and to update the details of local representatives in the Package Leaflet. The RMP version 3.0 has been provided in accordance." Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Parsabiv - etelcalcetide - EMEA/H/C/003995/II/0010 Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, "Update of sections 4.8 to add convulsions secondary to hypocalceaemia as uncommon adverse reactions and further information on reports related to hypersensitivity reactions. Editorial correction is made to section 7. The Package Leaflet is update accordingly. Consequentially, RMP (version 2) has been submitted to reclassify some of the existing safety concerns." Request for Supplementary Information adopted on 29.11.2018.	
Plegridy - peginterferon beta-1a - EMEA/H/C/002827/II/0052/G Biogen Netherlands B.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ulla Wändel Liminga, "2x type II (C.I.4):	

1) Update of section 4.3, and 4.6 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054). 2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles. The Package leaflet has been updated accordingly. This submission fulfils MEA 8.2 and 002. An updated RMP version 4.1 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes' and an update of the EU-RMP template (rev. 2)."	
Rebif - interferon beta-1a - EMEA/H/C/000136/II/0137/G Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "2x type II (C.I.4): 1) Update of section 4.3, 4.6 and 5.3 of the SmPC in order to add information about pregnancy information and update the statement regarding breast-feeding following the completion of the European IFN Beta Pregnancy Registry (8th Annual and final report) and the Final CSR of the register-based study in the Nordic countries (EUPAS13054). 2) Update of section 4.6 of the SmPC in order to update the statement regarding breast-feeding following a review of studies, case reports and literature articles. The Package leaflet has been updated accordingly. This submission fulfils MEA 43.2 and 39. An updated RMP version 10.0 is included in the submission, including the deletion of the important potential risk 'Pregnancy outcomes' and an update of the EU-RMP template (rev.2)."	
SIRTURO - bedaquiline - EMEA/H/C/002614/II/0028, Orphan Janssen-Cilag International NV, Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, "Update of sections 4.2, 4.4 and 5.1 of the SmPC in order to improve clarity for prescribers and update the safety information	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

with inclusion of text on bedaquiline resistance, further to a request by the PRAC in the context of the assessment of PSUR procedure EMEA/H/C/PSUSA/00010074/201709 (LEG 011). The RMP version 3.3 has been approved. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet." Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 31.10.2018.	
Tremfya - guselkumab - EMEA/H/C/004271/II/0005 Janssen-Cilag International N.V., Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.4 and 4.8 of the SmPC in order to add hypersensitivity and rash as adverse drug reactions with the frequency uncommon, together with a statement describing the characteristics of the serious hypersensitivity events. The Package Leaflet is updated accordingly. The RMP has been updated to version 3.0." Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 29.11.2018.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
Uptravi - selexipag - EMEA/H/C/003774/II/0022 Janssen-Cilag International N.V., Rapporteur: Martina Weise, PRAC Rapporteur: Adrien Inoubli, "Update of Sections 4.2, 4.4 and 4.5 of the SmPC in order to update the safety information based on the final results from study AC-065-117 a listed category 3 study in the RMP which is a clinical pharmacology drug-drug interaction (DDI) study, evaluating the effect of clopidogrel a moderate inhibitor of CYP2C8, on the pharmacokinetics of selexipag and its active metabolite ACT-333679. The package leaflet is updated accordingly. The RMP version 6.1 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct minor discrepancies in the SmPC." Request for Supplementary Information adopted on 14.02.2019.	Request for supplementary information adopted with a specific timetable.
Venclyxto - venetoclax - EMEA/H/C/004106/II/0020, Orphan AbbVie Deutschland GmbH & Co. KG,	

Rapporteur: Filip Josephson, PRAC Rapporteur: Eva Jirsová, “Update of sections 4.2 and 5.2 of the SmPC in order to include that a 50% dose reduction of venetoclax is recommended in patients with severe hepatic impairment based on the final results from study M15-342 (listed as a category 3 study in the RMP): a study to evaluate the safety and pharmacokinetics of a single dose of ventoclax in female subjects with mild, moderate, or severe hepatic impairment. The package leaflet and the RMP (version 3.4) are updated accordingly. The RMP version 3.4 has also been submitted.”	
Vimpat - lacosamide - EMEA/H/C/000863/II/0073/G UCB Pharma S.A., Rapporteur: Filip Josephson, PRAC Rapporteur: Ulla Wändel Liminga, “Update of sections 4.4, 4.5 and 4.8 of the SmPC in order to include new safety information on cardiac arrhythmias based on safety signal assessment report (SSAR). Update of section 4.8 of the SmPC to update the frequency of some adverse events (AEs) based on data obtained from the updated safety pool analysis (Pool DBC-1). The Package Leaflet is updated accordingly. The RMP version 13 has also been submitted.” Request for Supplementary Information adopted on 14.02.2019, 04.10.2018.	Request for supplementary information adopted with a specific timetable.
WS1490 **IKERVIS-EMEA/H/C/002066/WS1490/0014** **Verkazia-EMEA/H/C/004411/WS1490/0001** Santen Oy, Lead Rapporteur: Peter Kiely, Lead PRAC Rapporteur: Jan Neuhauser, “Submission of an updated RMP version 7.0 in order to implement RMP revision 2 template, as a consequence safety concerns have been updated: all safety concerns were moved from important safety concerns to the new section of Risks not considered important for inclusion in the list of safety concerns in the RMP. The milestones for VERKAZIA PASS have also been updated. In addition, the MAH is proposing to align IKERVIS SmPC section 4.4 on concomitant therapy and effects on immune system with VERKAZIA SmPC in order to harmonize the routine risk minimization measures for both products. The MAH took this opportunity to	Request for supplementary information adopted with a specific timetable.

implement the latest QRD template and the safety features for IKERVIS." Request for Supplementary Information adopted on 14.02.2019.	

B.5.4. PRAC assessed procedures

PRAC Led **Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0148** Amgen Europe B.V., Rapporteur: Martina Weise, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Martina Weise, "Update of annex IID to implement information on education materials to address the incorrect self-administration of Aranesp via the SureClick pre-filled pen and associated dosing errors. The RMP (version 9.4) is updated accordingly and aligned to the latest GVP Module revision 2. In addition, a reference has been added to the PL with regards to the available training materials to help that caregivers are informed about the available training tools." Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 29.11.2018, 04.10.2018.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Colobreathe - colistimethate sodium - EMEA/H/C/001225/II/0039** Teva B.V., Rapporteur: Nithyanandan Nagercoil, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "Submission of the final report from study CLB-MD-08, a Category 3, non-interventional PASS. This is a Safety, Cross-sectional survey study to evaluate the effectiveness of the Colobreathe risk minimisation educational programme among healthcare professionals and patients. This submission also fulfils MEA 012.1." Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 31.10.2018.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Eurartesim - piperaquine tetraphosphate / artenimol - EMEA/H/C/001199/II/0032** Alfasigma S.p.A., Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "Submission of an updated RMP version 15.2 (in line with the revision 2 of	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

the RMP template) in order to close the Pregnancy Registry. In addition, the Marketing authorisation holder (MAH) took the opportunity to: - Distribution of a new version of the educational material. - Addition of two important potential risks: `Delayed haemolytic anaemia' and `Severe skin reactions´, such as Stevens- Johnson syndrome and Toxic Epidermal Necrolysis. - Limitation of the reproductive risk to the first trimester of pregnancy. - Update on several studies. - Inclusion of Eurartesim into the WHO Essential Medicines List. - Update the MAH details." Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 31.10.2018.	
PRAC Led **Farydak - panobinostat - EMEA/H/C/003725/II/0013, Orphan** Novartis Europharm Limited, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Patrick Batty, PRAC-CHMP liaison: Greg Markey, "Update of the RMP to version 5.0 in order to remove the commitment to conduct a non-interventional PASS study (LBH589D2408) of panobinostat use in relapsed or relapsed/refractory multiple myeloma patients who have received at least two prior regimens including bortezomib and an immunomodulatory agent in a real-world setting according to the current EU prescribing information and document adherence to dosing regimen (including the dosing card, blister pack) by describing clinical characteristics, frequency and severity of the medication error events; listed as a category 3 study in the RMP." Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 04.10.2018.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Forsteo - teriparatide - EMEA/H/C/000425/II/0050/G** Eli Lilly Nederland B.V., Rapporteur: Alexandre Moreau, PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final study reports of the European Union (EU) components of two	Request for supplementary information adopted with a specific timetable.

post-authorisation safety studies (PASS); Study B3DMC-GHBX(2.2) and Study B3D-MC-GHBX(2.3b) both US population-based comparative cohort studies undertaken to evaluate a potential association between teriparatide and adult Osteosarcoma. An updated RMP version 7.0 was submitted as part of the application." Request for Supplementary Information adopted on 14.02.2019.	
PRAC Led **Gardasil 9 - human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) - EMEA/H/C/003852/II/0029** MSD Vaccins, PRAC Rapporteur: Jean-Michel Dogné, PRAC-CHMP liaison: Bart Van der Schueren, "Submission of an updated RMP version 3.1 in order to bring it to the new revision 2 template. As a result, the safety concerns are being updated." Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Hemangiol - propranolol - EMEA/H/C/002621/II/0019** PIERRE FABRE DERMATOLOGIE, Rapporteur: Joseph Emmerich, Co-Rapporteur: Agnes Gyurasics, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Concepcion Prieto Yerro, "Update of Package Leaflet in order to strengthen the warning on Hypoglycemia and Bronchospasm following completion of Drug Utilisation Study (DUS) performed in Germany and France to evaluate off-label use and effectiveness of RMM in a real-life clinical setting (MEA 002). In additions editorial changes has been introduced in section 4.4 of the SmPC as well as changes in the PL in accordance with QRD template 10.0. RMP version 3.1 has been submitted in order to updates the additional RMMs as a consequence of the results of the DUS." Request for Supplementary Information adopted on 14.02.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **JETREA - ocriplasmin - EMEA/H/C/002381/II/0042/G** Oxurion NV, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, PRAC-CHMP liaison: Greg Markey, "C.I.13z: Submission of the final	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

report from 'ORBIT study (TG-MV-018): Ocriplasmin Research to Better Inform Treatment (ORBIT)'. This is a multicenter, prospective, observational study which assesses clinical outcomes and safety of JETREA® administered in a real-world setting for the treatment of symptomatic vitro macular adhesion (VMA). C.I.13z: Submission of the final report from 'Use of Intravitreal JETREA® in Clinical Practice: A European Prospective Drug Utilisation Study (TG-MV-017)' listed as a category 3 study in the RMP. This study is a European, multicentre, observational study. The study includes two parts, a drug utilisation study (DUS) and the Patient Educational Material Evaluation Survey (PEMES). The main objective of the DUS is to document JETREA utilisation patterns in real-life clinical practice. The objective of the PEMES is to assess the effectiveness of the risk minimisation measures (i.e. the patient educational material [PEM] provided to patients prior to the injection of JETREA). C.I.13z: Submission of the final report from 'INJECT: INvestigation of JETREA® in Patients with Confirmed Vitreomacular Traction'. This is a non-interventional, multi-centre, worldwide study in patients treated with JETREA® (ocriplasmin) for the approved indication in their country. The aim of the study is to evaluate safety, clinical effectiveness, and HRQoL outcomes in a real world setting among a large population of patients exposed to ocriplasmin across different countries according to country's approved indications. In addition, RMP V7.2 has been updated accordingly and the second revision of the RMP template has been implemented as well." Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 17.01.2019, 29.11.2018.	
PRAC Led **Kengrexal - cangrelor - EMEA/H/C/003773/II/0015** Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of an updated RMP version 2.0 in order to update the requirements for a study listed as category 3 in the RMP. In addition, the MAH took the opportunity to revise the RMP in	Request for supplementary information adopted with a specific timetable.

line with the RMP template version 2.0." Request for Supplementary Information adopted on 14.02.2019, 06.09.2018.	
PRAC Led **MabThera - rituximab - EMEA/H/C/000165/II/0152** Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Doris Stenver, PRAC-CHMP liaison: Sinan B. Sarac, "Submission of the final study report of the non-interventional drug utilisation study (DUS) BA28478 (MabThera drug utilisation study and patient alert card evaluation in non-oncology patients in Europe: an infusion centre-based approach); as a consequence, the RMP is also updated (version 19.1) to revise the text with the deletion of the safety concern 'off label use in autoimmune disease'." Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 29.11.2018, 06.09.2018.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Nulojix - belatacept - EMEA/H/C/002098/II/0050/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 (IM103074 and IM103077) listed as category 3 studies in the RMP. Study IM103074 is an observational study designed to assess the pattern of use of belatacept in US transplant recipients in routine clinical practice. Study IM103077 is an observational study designed to assess the patterns of use of belatacept in renal transplantation using the collaborative transplant study. An updated RMP (version 16.1) is submitted in order to reflect the results of the above studies. In addition, the MAH took the opportunity to update the RMP in line with the new RMP template (GVP Module V rev.2), to reflect minor editorial changes and to reflect the earlier completion dates for two remaining studies (IM103075 and IM103076) listed as category 3 studies in the RMP." Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 31.10.2018.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

PRAC Led **Onglyza - saxagliptin - EMEA/H/C/001039/II/0048** AstraZeneca AB, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 14 in order to introduce the new template (EMA/PRAC/613102/2015, GVP Module V, revision 2) and to reclassify or remove some of the safety concerns." Request for Supplementary Information adopted on 29.11.2018.	
PRAC Led **Ozempic - semaglutide - EMEA/H/C/004174/II/0006** Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 3.0 in order to reflect that the first milestones (Final protocol submission) for 2 of the additional pharmacovigilance activities have been fulfilled (for trials NN9535-4447 and NN9535-4352). Further the RMP is updated in line with the new template in accordance with Guideline on GVP Module V – Risk management systems (Rev 2)." Request for Supplementary Information adopted on 14.02.2019.	Request for supplementary information adopted with a specific timetable.
PRAC Led **Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0011** GlaxoSmithkline Biologicals SA, PRAC Rapporteur: Jan Neuhauser, PRAC-CHMP liaison: Andrea Laslop, "Submission of an updated RMP version 2 in order to extend the due dates of four category 3 studies (ZOSTER-002, ZOSTER-039, ZOSTER-041, ZOSTER-028) listed as required additional pharmacovigilance activities and to change the study design and due dates of a category 3 (EPI-ZOSTER-030 VS) listed as a required additional pharmacovigilance activity. In addition, the MAH took the opportunity to implement the new RMP template (Rev.2)." Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Tasmar - tolcapone - EMEA/H/C/000132/II/0061** Meda AB, Rapporteur: Jayne Crowe, PRAC	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Jayne Crowe, “Submission of an updated RMP version 7.0 in order to: - reflect currently available data from post-marketing experience and patient exposure data; - align the RMP with the new GVP RMP template rev.2; - remove the important identified risk ‘dopaminergic effects due to increased bioavailability of co-administered levodopa (e.g. dyskinesia)’ and the potential risks ‘drug interactions with significant clinical consequence including sudden sleep onset’, ‘melanoma’ and ‘intense urges’; - revise the targeted follow-up questionnaire for hepatic events and the Patient Diary.” Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 31.10.2018.	
PRAC Led **Thalidomide Celgene - thalidomide - EMEA/H/C/000823/II/0056, Orphan** Celgene Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, “Update of the RMP version 19.2 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 thalidomide and to provide more detail in relation to the pregnancy prevention. Consequently, Annex IID, SmPC sections 4.4 and 4.6 and the PL have been updated accordingly. Minor editorial changes have been introduced in the PI.” Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 29.11.2018, 04.10.2018.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Truvada - emtricitabine / tenofovir disoproxil - EMEA/H/C/000594/II/0159** Gilead Sciences Ireland UC, Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ana Sofia Diniz Martins, PRAC-CHMP liaison: Bruno Sepodes, “Submission of the final study report for the non-interventional study GS-EU-276-4027, a Cross-Sectional Post-authorisation Safety Study to Assess Healthcare Providers’ Level of	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

Awareness of Risk Minimisation Materials for Truvada for Pre-Exposure Prophylaxis (PrEP) in the European Union, listed as a Category 3 study in the EU Risk Management Plan. This submission fulfils the post-authorisation measure MEA 045.7." Opinion adopted on 14.02.2019.	
PRAC Led **Volibris - ambrisentan - EMEA/H/C/000839/II/0055** GlaxoSmithKline (Ireland) Limited, Rapporteur: Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, PRAC-CHMP liaison: Concepcion Prieto Yerro, "Submission of an updated Risk Management Plan (RMP) version 8.1 in order to remove the provision of the educational materials for healthcare professionals given the availability of the SmPC and the experience of using ambrisentan and to revise the educational materials for patients as requested by the PRAC in the PSUR procedure PSUSA/00000129/201706. The Annex II of the product information is updated accordingly. In addition, the MAH also took the opportunity to update the Annex II as requested by the Portuguese Agency following the approval of the last update to the educational materials (risks of decreases in haemoglobin or haematocrit, renal impairment, peripheral oedema and fluid retention, and hypersensitivity reaction) and to correct typographical errors." Opinion adopted on 14.02.2019. Request for Supplementary Information adopted on 29.11.2018, 12.07.2018.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **Xiapex - collagenase clostridium histolyticum - EMEA/H/C/002048/II/0106** Swedish Orphan Biovitrum AB (publ), Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber, PRAC-CHMP liaison: Janet Koenig, "Submission of the final report from a non-interventional post-authorisation safety study: Effectiveness of Xiapex educational material for healthcare professionals in the treatment of Peyronie's disease; listed as a category 3 study in the RMP." Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
PRAC Led **WS1510**	Request for supplementary information adopted with a specific timetable.

Mirapexin-EMEA/H/C/000134/WS1510/0089 **Sifrol-EMEA/H/C/000133/WS1510/0080** Boehringer Ingelheim International GmbH, Lead Rapporteur: Mark Ainsworth, Lead PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "RMP update to implement changes requested by PRAC in the context of the PSUSA procedure or in connection with a PRAC signal assessment procedure. The RMP update covers additionally the conversion into the new RMP template as per GVP Module V Revision 2 (EMA/838713/2011 Rev 2). Lastly the applicant takes the opportunity to adapt the medical search strategies and data retrieval approach without any impact on the overall safety conclusion." Request for Supplementary Information adopted on 14.02.2019.	
PRAC Led **WS1521** **Kivexa-EMEA/H/C/000581/WS1521/0079** **Trizivir-EMEA/H/C/000338/WS1521/0112** **Ziagen-EMEA/H/C/000252/WS1521/0105** ViiV Healthcare B.V., Lead PRAC Rapporteur: Adrien Inoubli, PRAC-CHMP liaison: Joseph Emmerich, "Submission of an RMP version 1.0 combining the RMPs for Ziagen, Kivexa and Trizivir into one Abacavir active-substance RMP" Request for Supplementary Information adopted on 14.02.2019.	Request for supplementary information adopted with a specific timetable.

B.5.5. CHMP-CAT assessed procedures

B.5.6. CHMP-PRAC-CAT assessed procedures

Imlygic - talimogene laherparepvec - EMEA/H/C/002771/II/0029, ATMP Amgen Europe B.V., Rapporteur: Olli Tenhunen, CHMP Coordinator: Tuomo Lapveteläinen, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 5.2 of the SmPC in order to update the pharmacokinetic properties information based on the final results from study 20120324, a phase 2, multicenter, single-arm trial to evaluate the biodistribution and shedding of talimogene laherparepvec in subjects with unresected, stage IIIB to IVM1c melanoma. This submission fulfils MEA 006.1. In addition, the Marketing	

authorisation holder (MAH) took the opportunity to update Annex II as per the already assessed EMEA/H/C/002771/ANX/001 procedure."	

B.5.7. PRAC assessed ATMP procedures

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

WS1497/G **Infanrix hexa-EMEA/H/C/000296/WS1497/0251/G** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren, Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1508/G **Herceptin-EMEA/H/C/000278/WS1508/0148/G** **MabThera-EMEA/H/C/000165/WS1508/0160/G** Roche Registration GmbH, Lead Rapporteur: Sinan B. Sarac Opinion adopted on 07.02.2019.	Positive Opinion adopted by consensus on 07.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1515 **Infanrix hexa-EMEA/H/C/000296/WS1515/0253** GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1522/G **Relvar Ellipta-EMEA/H/C/002673/WS1522/0041/G** **Revinty Ellipta-EMEA/H/C/002745/WS1522/0039/G** GlaxoSmithKline (Ireland) Limited, Lead Rapporteur: Concepcion Prieto Yerro Opinion adopted on 07.02.2019.	Positive Opinion adopted by consensus on 07.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1525 **Hexacima-EMEA/H/C/002702/WS1525/0086** **Hexaxim-EMEA/H/W/002495/WS1525/0091** **Hexyon-EMEA/H/C/002796/WS1525/0090** Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus	Request for supplementary information adopted with a specific timetable.

Request for Supplementary Information adopted on 14.02.2019.	
WS1533 **Fluenz Tetra-EMEA/H/C/002617/WS1533/0088** **Pandemic influenza vaccine H5N1 AstraZeneca-EMEA/H/C/003963/WS1533/0022** AstraZeneca AB, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1545 **Kivexa-EMEA/H/C/000581/WS1545/0080** **Trizivir-EMEA/H/C/000338/WS1545/0113** **Ziagen-EMEA/H/C/000252/WS1545/0106** ViiV Healthcare B.V., Lead Rapporteur: Joseph Emmerich	
WS1551 **Filgrastim** **Hexal-EMEA/H/C/000918/WS1551/0047** **Zarzio-EMEA/H/C/000917/WS1551/0048** Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.
WS1552 **Fluenz Tetra-EMEA/H/C/002617/WS1552/0087** **Pandemic influenza vaccine H5N1 AstraZeneca-EMEA/H/C/003963/WS1552/0021** AstraZeneca AB, Lead Rapporteur: Jan Mueller-Berghaus Opinion adopted on 14.02.2019.	Positive Opinion adopted by consensus on 14.02.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation.

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

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

WS1506/G **Nuwiq-EMEA/H/C/002813/WS1506/0026/G** **Vihuma-EMEA/H/C/004459/WS1506/0009/G** Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus "Update of sections 4.2, 4.8 and 5.1 of the SmPC based on clinical data from studies GENA-21 and GENA-13. The Package Leaflet is updated accordingly." Request for Supplementary Information adopted on 13.12.2018.	Request by the applicant dated 08 January 2019 for an extension of clock-stop to respond to the request for supplementary information adopted in 13.12.2018

B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

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

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

autologous CD34+ cell enriched population that contains hematopoietic stem cells transduced with lentiglobin BB305 lentiviral vector encoding the beta-A-T87Q-globin gene - EMEA/H/C/003691, Orphan, ATMP
bluebird bio GmbH, treatment of transfusion-dependent β-thalassaemia (TDT)
List of Questions adopted on 25.01.2019.

enasidenib - EMEA/H/C/004324, Orphan
Celgene Europe Limited, treatment of acute myeloid leukaemia (AML)
List of Questions adopted on 18.10.2018.

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

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/0008, Orphan
Merck Europe B.V., Rapporteur: Filip Josephson,
PRAC Rapporteur: Anette Kirstine Stark

Translarna - ataluren -
EMEA/H/C/002720/R/0051, Orphan
PTC Therapeutics International Limited,
Rapporteur: Johann Lodewijk Hillege,
Co-Rapporteur: Concepcion Prieto Yerro, PRAC
Rapporteur: Liana Gross-Martirosyan

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

B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

Accofil - filgrastim -
EMEA/H/C/003956/II/0028/G
Accord Healthcare S.L.U., Rapporteur: Outi
Mäki-Ikola

Bemfola - follitropin alfa - EMEA/H/C/002615/II/0021/G
Gedeon Richter Plc., Rapporteur: Paula Boudewina van Hennik

Benlysta - belimumab - EMEA/H/C/002015/II/0064/G
GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder

Docetaxel Kabi - docetaxel - EMEA/H/C/002325/II/0022
Fresenius Kabi Deutschland GmbH, Generic, Generic of Taxotere, Rapporteur: Alexandre Moreau

Entyvio - vedolizumab - EMEA/H/C/002782/II/0039
Takeda Pharma A/S, Rapporteur: Daniela Melchiorri

Flucelvax Tetra - influenza vaccine surface antigen inactivated prepared in cell cultures - EMEA/H/C/004814/II/0003
Seqirus Netherlands B.V., Rapporteur: Sol Ruiz

Humira - adalimumab - EMEA/H/C/000481/II/0189
AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder

Lymphoseek - tilmanocept - EMEA/H/C/002085/II/0017
Norgine B.V., Rapporteur: Jayne Crowe

Orencia - abatacept - EMEA/H/C/000701/II/0125
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola

Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0145
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus

ProQuad - measles, mumps, rubella and varicella vaccine (live) - EMEA/H/C/000622/II/0132
MSD Vaccins, Rapporteur: Jan Mueller-Berghaus

TachoSil - human thrombin / human fibrinogen - EMEA/H/C/000505/II/0092
Takeda Austria GmbH, Rapporteur: Jan Mueller-Berghaus

Tysabri - natalizumab -

EMEA/H/C/000603/II/0113/G
Biogen Netherlands B.V., Rapporteur: Jan Mueller-Berghaus

Visudyne - verteporfin - EMEA/H/C/000305/II/0098/G
Novartis Europharm Limited, Rapporteur: Alexandre Moreau

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

Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0151
Amgen Europe B.V., Rapporteur: Martina Weise, "Submission of the final analysis of clinical study report (CSR, 10 May 2018) for Study 20110226 to fulfill the post-marketing authorization measure (category 3 pharmacovigilance activity in the Aranesp EU Risk Management Plan (RMP). Study 20110226 is a phase 3, multicenter, randomized, double-blind, parallel group study - START-CKD: Strategies Using Darbepoetin alfa to Avoid Transfusions in Chronic Kidney."

AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0022
sanofi-aventis groupe, Rapporteur: Martina Weise, "Submission of the final report of the nonclinical 7-Week oral administration juvenile toxicity study in the rat (JUV0024 Aubagio), which is part of the agreed PIP for Aubagio (EMEA-001094-PIP01-10)."

Cyramza - ramucirumab - EMEA/H/C/002829/II/0030
Eli Lilly Nederland B.V., Rapporteur: Paula Boudewina van Hennik, "Update of section 4.8 of the SmPC in order to add haemangioma and thrombotic microangiopathy (TMA) as new adverse drug reactions (ADRs) based on review of clinical trials, post-marketing cases and the published scientific literature. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Estonia, Latvia and Lithuania in the Package Leaflet."

Delstrigo - doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746/II/0003
Merck Sharp & Dohme B.V., Rapporteur: Filip

Josephson, “Submission of the final week 96 report from study P021, a phase 3 multicenter, double-blind, randomized active comparator-controlled clinical trial to evaluate the safety and efficacy of MK-1439A once-daily versus ATRIPLA once-daily in treatment-naïve HIV-1 infected patients.”

Gilenya - fingolimod -
EMEA/H/C/002202/II/0053

Novartis Europharm Limited, Rapporteur: Alexandre Moreau, “Type II (C.I.4):
- to update section 4.4 of the SmPC (subsection 'Return of disease activity (rebound)' and subsection 'Stopping therapy') to add information to prescriber's on the timing of reported events and further recommendations on monitoring of patients.
- to update section 4.6 of the SmPC to add a warning for women stopping treatment for the purpose of becoming pregnant and for pregnant women, and addition of a cross-reference to section 4.4 subsection 'Return of disease activity (rebound)'.
- to update section 4.8 of the SmPC to add a new adverse reaction ‘Severe exacerbation of disease after Gilenya discontinuation' with frequency 'Not known'.
The package leaflet is updated accordingly.”

Orgalutran - ganirelix -
EMEA/H/C/000274/II/0043

Merck Sharp & Dohme B.V., Rapporteur: Outi Mäki-Ikola, “Update of sections 4.4 and 4.8 of the SmPC to include anaphylaxis (including anaphylactic shock), angioedema, and urticaria under hypersensitivity reactions.
In addition, the MAH took the opportunity to include minor editorial corrections in the SmPC and to update the list of local representatives (PT and NL) in the Package Leaflet.”

Pifeltro - doravirine -
EMEA/H/C/004747/II/0003

Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, “Submission of the final week 96 report from study P021, a phase 3 multicenter, double-blind, randomized active comparator-controlled clinical trial to evaluate the safety and efficacy of MK-1439A once-daily versus ATRIPLA once-daily in treatment-naïve HIV-1 infected patients.”

Rubraca - rucaparib -
EMEA/H/C/004272/II/0009, Orphan
Clovis Oncology Ireland Limited, Rapporteur: Jorge Camarero Jiménez, “Submission of a final report CHVI-283298 describing development and qualification of a test method capable of confirming the absence of monomethyl sulfate (MMS) in fulfilment of Recommendation 2.”

Thyrogen - thyrotropin alfa -
EMEA/H/C/000220/II/0102
Genzyme Europe BV, Rapporteur: Peter Kiely, “Update of sections 4.4 and 5.1 of the SmPC in order to update the safety information with with HiLo and ESTIMABL1 long term follow-up data study results as well as fulfill FUM35. Additionally, the sodium content provision wording in the Package Leaflet is aligned to the Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal products for human use" (SANTE-2017-11668). Few editorial changes are also made and the name of an excipient in the German translation is also corrected.”

Tyverb - lapatinib -
EMEA/H/C/000795/II/0059
Novartis Europharm Limited, Rapporteur: Filip Josephson, “Update of section 5.1 of the SmPC in order to update Table 8 based on updated/corrected results from study EGF114299/LAP016A2307, an interventional study with progression free survival rate as primary objective, original report submitted during procedure EMEA/H/C/00795/II/0051.”

Victoza - liraglutide -
EMEA/H/C/001026/II/0050
Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.2 and 5.1 of the SmPC, based on the phase 3b study NN2211-4315 (LIRA-ADD2SGLT2i), to include data on liraglutide vs placebo as add-on to SGLT2 inhibitors (+/- metformin) in subjects with type 2 diabetes mellitus. The Package Leaflet has been updated accordingly.”

Xeloda - capecitabine -
EMEA/H/C/000316/II/0083
Roche Registration GmbH, Rapporteur: Janet Koenig, “Update of section 4.6 of the SmPC in order to add advice on post treatment contraception period and wash out period before

initiation of breastfeeding. The Package leaflet is updated accordingly."	
XGEVA - denosumab - EMEA/H/C/002173/II/0068 Amgen Europe B.V., Rapporteur: Kristina Dunder, "Update of section 4.8 of the SmPC to include the new ADR 'lichenoid drug eruptions' and information in the description of selected adverse reactions based on post-marketing experiences. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in the Package Leaflet."	
WS1527/G **Cymbalta-EMEA/H/C/000572/WS1527/0078/G** **Duloxetine** **Lilly-EMEA/H/C/004000/WS1527/0014/G** **Xeristar-EMEA/H/C/000573/WS1527/0081/G** **Yentreve-EMEA/H/C/000545/WS1527/0063/G** Eli Lilly Nederland B.V., Duplicate, Duplicate of Ariclaim, Yentreve, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Maria del Pilar Rayon, "C.I.4 (Type II) - Update of sections 4.4 and 4.6 of the SmPC in order to add a warning on the risk of postpartum haemorrhage based on final results from study Study F1J-MC-B057 listed as a category 3 in the RMP; this is an observational study to assess maternal and foetal outcomes following exposure to duloxetine. The Package Leaflet is updated accordingly. C.I.11.z (Type IB) - to stop enrolment of Study F1J-MC-B034 (study B034), another study included in the current EU-RMP Version 12.4 as an additional pharmacovigilance activities to address missing information regarding duloxetine exposure due to pregnancy. The RMP version 13 has also been submitted. In addition, the Worksharing applicant (WSA) took the opportunity to correct the term "sucrase-isomaltase" in section 4.4 of the SmPC in line with the Annex to the EC guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (EMA/CHMP/302620/2017 corr. 1*) and to bring the PI in line with the latest QRD template version 10.	

The Xeristar 30 mg SmPC & Xeristar 60 mg SmPC and the Yentreve 20 mg SmPC & Yentreve 40 mg SmPC have been combined in a single SmPC, respectively, following the Policy on combined SmPCs (EMA/333423/2015)."	

B.6.10. CHMP-PRAC assessed procedures

Flebogamma DIF - human normal immunoglobulin - EMEA/H/C/000781/II/0059/G Instituto Grifols, S.A., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of section 4.8 of the SmPC for Flebogamma DIF 100 mg/ml in order to update the safety information based on the final results from study IG0601: A multi-center, prospective, open-label, clinical trial to assess the safety and the efficacy of a new intravenous immune globulin (IGIV3I Grifols 10%) in patients with idiopathic (immune) thrombocytopenic purpura. The Package Leaflet is updated accordingly. Update of section 4.8 of the SmPC to revise the adverse drug reactions for both strengths based on all completed studies previously submitted. The Package Leaflet is updated accordingly. Update of SmPC according to the Guideline on core SmPC for human normal immunoglobulin for intravenous administration (IVIg) which came into effect on 01 January 2019. With this submission, the MAH proposes the following changes in alignment with the guideline: - Inclusion of Chronic inflammatory demyelinating polyneuropathy (CIDP) and Multifocal motor neuropathy (MMN) as new therapeutic indications - Modification of Secondary immunodeficiencies (SID) therapeutic indication definition. The Package Leaflet is updated accordingly. The RMP version 7.0 has also been submitted."	
Movymia - teriparatide - EMEA/H/C/004368/II/0010 STADA Arzneimittel AG, Duplicate, Duplicate of Terrosa, Rapporteur: Milena Stain, PRAC Rapporteur: Ronan Grimes, "Submission of the final clinical study report from Study RGB1023O31; a Phase III, multi-centre, randomised, active-controlled, parallel-group,	

comparative efficacy/safety study. An updated RMP version 1.3 was provided as part of the application."

Tecentriq - atezolizumab - EMEA/H/C/004143/II/0022

Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of sections 4.2 and 5.2 of the SmPC in order to add 2 dosing regimens, 840 mg every 2 weeks and 1680 mg every 4 weeks administered as an IV infusion for the approved indications, based on results of population pharmacokinetics modelling and simulation analyses (report No. 1085557) and supported by exposure-response analyses (report No. 1087176). The package leaflet is updated accordingly.
An updated RMP is also provided in order to reflect the proposed new dosing regimens, and to align the indication statement for metastatic urothelial carcinoma with the SmPC.
Moreover, the due date for submission of RMP commitments and an Annex II condition are proposed to be updated."

Terrosa - teriparatide - EMEA/H/C/003916/II/0009

Gedeon Richter Plc., Rapporteur: Milena Stain, PRAC Rapporteur: Ronan Grimes, "Submission of the final clinical study report from Study RGB1023O31; a Phase III, multi-centre, randomised, active-controlled, parallel-group, comparative efficacy/safety study. An updated RMP version 1.3 was provided as part of the application."

WS1518
Epclusa-EMEA/H/C/004210/WS1518/0034
Harvoni-EMEA/H/C/003850/WS1518/0077
Sovaldi-EMEA/H/C/002798/WS1518/0055
Vosevi-EMEA/H/C/004350/WS1518/0025

Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, Lead PRAC Rapporteur: Ana Sofia Diniz Martins, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC (Epclusa, Harvoni), sections 4.2, 4.4, 5.1 and 5.2 (Sovaldi) and 4.2, 4.8 and 5.2 (Vosevi) in order to add new information regarding the use of the sofosbuvir-containing products in patients with

renal impairment, based on final results from studies GS-US-342-4062, GS-US-337-4063 and GS-US-334-0154, listed as a category 3 study in the RMP and study GS-US-338-1125.
Study GS-US-342-4062 was a phase 2, multi-centre, open-label study to evaluate the efficacy and safety of sofosbuvir/velpatasvir for 12 Weeks in subjects with chronic HCV infection who are on dialysis for end stage renal disease.
Study GS-US-337-4063 was a phase 2, multi-centre, open-label study to evaluate the efficacy and safety of ledipasvir/sofosbuvir in subjects with genotype 1, 4, 5 and 6 chronic HCV infection who are on dialysis for end stage renal disease.
Study GS-US-334-0154 was a phase 2b, open label study of 200 mg or 400 mg Sofosbuvir+ribavirin for 24 Weeks in Genotype 1 or 3 HCV infected subjects with renal insufficiency.
Study GS-US-338-1125 was a phase 1, open-label, parallel-group, single-dose study to evaluate the pharmacokinetics of voxilaprevir in subjects with normal renal function and severe renal impairment.
The Package Leaflet is updated accordingly. The RMPs have also been submitted for each of the products in this work-sharing procedure."

B.6.11. PRAC assessed procedures

PRAC Led
Adasuve - loxapine -
EMEA/H/C/002400/II/0030
Ferrer Internacional s.a., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Liana Gross-Martirosyan, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of the category 3 final report from Drug Utilization study AMDC-204-403 EU (A Multinational Retrospective Medical Record Review to Evaluate Utilization Patterns of Adasuve-Staccato loxapine for inhalation in agitated persons in routine clinical care). An updated RMP version 9.1 is proposed accordingly."

PRAC Led
Fasenra - benralizumab -
EMEA/H/C/004433/II/0017
AstraZeneca AB, Rapporteur: Fátima Ventura,

PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Bjorg Bolstad, “Update of section 4.4 of the SmPC in order to add a warning on the risk of anaphylactic reaction and update the safety information following a safety review. The package Leaflet is updated accordingly. The RMP version 2 November 2018 has also been submitted.”

PRAC Led

Flixabi - infliximab -

EMEA/H/C/004020/II/0039

Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, “Update of the RMP to replace the current registries with one company-sponsored initiated registry (PERFUSE) and three IBD registries (CEDUR, CREDIT, and DREAM)”

PRAC Led

Kyprolis - carfilzomib -

EMEA/H/C/003790/II/0034, Orphan

Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Nikica Mirošević Skvrce, PRAC-CHMP liaison: Katarina Vučić, “Update of the RMP (v. 10) for Kyprolis to align with the revised guideline GVP Module V (Revision 2), resulting in the reclassification and removal of a number of identified and potential risks and missing information.”

PRAC Led

OPDIVO - nivolumab -

EMEA/H/C/003985/II/0062

Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, “Submission of an updated RMP version 13.5 in order to introduce a Patient Information Brochure (PIB) as an additional risk minimization measure (ARMM) for nivolumab. The annex IID is updated accordingly.”

PRAC Led

Prolia - denosumab -

EMEA/H/C/001120/II/0081

Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, “Submission of an updated RMP version 26 in order to amend the category 3 study 20090522

to include the study population men and women who receive denosumab with glucocorticoid exposure, and related study objectives. The pharmacovigilance plan and all corresponding sections of the EU RMP have been updated to include revised details for study 20090522. The amended protocol for study 20090522 has also been added to the appropriate annex of the RMP."

PRAC Led
WS1568
Relvar Ellipta-EMEA/H/C/002673/
WS1568/0043
Revinty Ellipta-EMEA/H/C/002745/
WS1568/0041
GlaxoSmithKline (Ireland) Limited, Lead Rapporteur: Concepcion Prieto Yerro, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Concepcion Prieto Yerro, "Submission of the final report from study HZC102972 listed as a category 3 study in the RMP. This is a post-authorisation safety study to further characterise the important potential risk of decreased bone mineral density (BMD) and associated fractures with FF/VI in the treatment of chronic obstructive pulmonary disease (COPD) byevaluating the effect of the inhaled corticosteroid fluticasone furoate (FF) on bone mineral density by comparing fluticasone furoate (FF)/vilanterol (VI) treatment with VI treatment in subjects with moderate COPD."

B.6.12. CHMP-CAT assessed procedures

No items

B.6.13. CHMP-PRAC-CAT assessed procedures

No items

B.6.14. PRAC assessed ATMP procedures

No items

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

WS1498/G
Infanrix hexa-EMEA/H/C/000296/
WS1498/0252/G
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

WS1564
Fiasp-EMEA/H/C/004046/WS1564/0011
NovoMix-EMEA/H/C/000308/WS1564/0097
NovoRapid-EMEA/H/C/000258/WS1564/0125
Ryzodeg-EMEA/H/C/002499/WS1564/0031
Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder

WS1571
Keppra-EMEA/H/C/000277/WS1571/0174
UCB Pharma S.A., Lead Rapporteur: Koenraad Norga

WS1578
M-M-RVAXPRO-EMEA/H/C/000604/WS1578/0093
ProQuad-EMEA/H/C/000622/WS1578/0131
MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus

WS1579
Axura-EMEA/H/C/000378/WS1579/0081
Memantine
Merz-EMEA/H/C/002711/WS1579/0017
Merz Pharmaceuticals GmbH, Lead Rapporteur: Concepcion Prieto Yerro

WS1580
Juluca-EMEA/H/C/004427/WS1580/0012
Tivicay-EMEA/H/C/002753/WS1580/0046
ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson

WS1584
Nuwiq-EMEA/H/C/002813/WS1584/0029
Vihuma-EMEA/H/C/004459/WS1584/0011
Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus

Mosquirix-EMEA/H/W/002300/WS1556/0040/G
Shingrix-EMEA/H/C/004336/WS1556/0014/G
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

Hexacima-EMEA/H/C/002702/WS1574/0087
Hexaxim-EMEA/H/W/002495/WS1574/

0092
Hexyon-EMEA/H/C/002796/WS1574/
0091
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

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

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

B.7.2. Monthly Line listing for Type I variations

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

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

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

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

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

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

E. Annex E - EMEA CERTIFICATION OF PLASMA MASTER FILES

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

E.1. PMF Certification Dossiers:

E.1.1. Annual Update

E.1.2. Variations:

E.1.3. Initial PMF Certification:

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

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

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

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

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

G. ANNEX G

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

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

G.2. PRIME

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

G.2.1. List of procedures concluding at 25-28 February 2019 CHMP plenary:

G.2.2. List of procedures starting in February 2019 for March 2019 CHMP adoption of outcomes

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