21 June 2019
EMA/CHMP/341563/2019
Inspections, Human Medicines Pharmacovigilance and Committees Division

# Committee for medicinal products for human use (CHMP)

## Final Minutes for the meeting on 23-26 April 2019

Chair: Harald Enzmann – Vice-Chair: Bruno Sepodes

**Disclaimers**

Some of the information contained in the minutes 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, the minutes are a working document primarily designed for CHMP members and the work the Committee undertakes.

**Note on access to documents**

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

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# 1. Introduction

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

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced the restricted involvement of some meeting participants in upcoming discussions as included in the pre-meeting list of participants and restrictions. See (current) April 2019 CHMP minutes for the list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the CHMP plenary session held 23-26 April 2019 (to be published post May 2019 CHMP meeting).

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 22 or more members were present in the room). All decisions, recommendations and advice were agreed by consensus, unless otherwise specified.

## 1.2. Adoption of agenda

CHMP agenda for 23-26 April 2019

The CHMP adopted the agenda.

## 1.3. Adoption of the minutes

CHMP minutes for 25-28 March 2019

ORGAM minutes for 15 April 2019

The CHMP minutes for 25-28 March 2019 were adopted.

The Minutes of the April 2019 CHMP ORGAM meeting held on 15 April 2019, together with all decisions taken at that meeting, were adopted.

# 2. Oral Explanations

## 2.1. Pre-authorisation procedure oral explanations

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

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

Scope: Possible oral explanation/List of outstanding issues

**Action**: Possible oral explanation to be held on Wednesday, 24 April 2019 at 11:00

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

The CHMP agreed that no oral explanation is needed this time.

See 3.2.

### 2.1.2. cannabidiol - Orphan - EMEA/H/C/004675

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

Scope: Oral explanation/List of outstanding issues

**Action**: Oral explanation to be held on Wednesday, 24 April 2019 at time 14:00

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

An oral explanation was held on Wednesday, 24 April 2019. The presentation mainly focused on efficacy data including subgroup analysis.

See 3.2

### 2.1.3. edaravone - Orphan - EMEA/H/C/004938

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

Scope: Oral explanation, List of experts for the SAG Neurology meeting scheduled on 15 April 2019 adopted via written procedure on 12 April 2019

**Action**: Oral explanation to be held on Wednesday, 24 April 2019 at time 09:00

List of Outstanding Issues adopted on 28.02.2019. List of Questions adopted on 20.09.2018.

Participation of a patient representative.

The members noted the report from the SAG Neurology.

An oral explanation was held on Wednesday, 24 April 2019. The presentation by the applicant mainly focused on efficacy data as well as post-authorisation commitments.

### 2.1.4. glutamine - Orphan - EMEA/H/C/004734

Emmaus Medical Europe Ltd; treatment of sickle cell disease

Scope: Oral explanation

**Action**: Oral explanation to be held on Thursday, 25 April 2019 at time 09:00

List of Outstanding Issues adopted on 31.01.2019. List of Questions adopted on 28.06.2018.

An oral explanation was held on Thursday, 25 April 2019. The presentation by the applicant mainly focused on efficacy data, including subgroup analysis.

## 2.2. Re-examination procedure oral explanations

No items

## 2.3. Post-authorisation procedure oral explanations

No items

## 2.4. Referral procedure oral explanations

No items

# 3. Initial applications

## 3.1. Initial applications; Opinions

### 3.1.1. Ambrisentan Mylan - ambrisentan - EMEA/H/C/004985

MYLAN S.A.S; treatment of pulmonary arterial hypertension (PAH)

Scope: Opinion

**Action**: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of Volibris

List of Outstanding Issues adopted on 28.02.2019. List of Questions adopted on 20.09.2018.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

The CHMP adopted the similarity CHMP assessment report.

### 3.1.2. Cabazitaxel Teva - cabazitaxel - EMEA/H/C/004951

Teva B.V.; treatment of prostate cancer

Scope: Opinion

**Action**: For adoption

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

List of Outstanding Issues adopted on 28.02.2019. List of Questions adopted on 20.09.2018.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The CHMP adopted a negative opinion by consensus, recommending the refusal of the marketing authorisation application. The CHMP adopted the assessment report.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The refusal question and answers document was circulated for information.

### 3.1.3. Doptelet - avatrombopag - EMEA/H/C/004722

Dova Pharmaceuticals Ireland Limited; treatment of thrombocytopenia

Scope: Opinion

**Action**: For adoption

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

List of Outstanding Issues adopted on 28.02.2019. List of Questions adopted on 20.09.2018.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that avatrombopag is a new active substance, as claimed by the applicant.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The CHMP noted the letter of recommendation dated 18 April 2019.

The legal status was agreed as medicinal product subject to medical prescription.

The summary of opinion was circulated for information.

### 3.1.4. Dovato - dolutegravir / lamivudine - EMEA/H/C/004909

ViiV Healthcare B.V.; treatment of Human Immunodeficiency Virus type 1 (HIV-1)

Scope: Opinion

**Action**: For adoption

Fixed combination application (Article 10b of Directive No 2001/83/EC)

List of Questions adopted on 31.01.2019.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

### 3.1.5. Esperoct - turoctocog alfa pegol - Orphan - EMEA/H/C/004883

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

Scope: Opinion

**Action**: For adoption

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

List of Outstanding Issues adopted on 28.03.2019, 15.11.2018. List of Questions adopted on 26.07.2018.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that turoctocog alfa pegol is a new active substance, as claimed by the applicant.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The CHMP noted the letter of recommendation dated 15 April 2019.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

### 3.1.6. Grasustek - pegfilgrastim - EMEA/H/C/004556

Juta Pharma GmbH; reduction in the duration of neutropenia and the incidence of febrile neutropenia

Scope: Opinion

**Action**: For adoption

Similar biological application (Article 10(4) of Directive No 2001/83/EC)

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

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The CHMP noted the letter of recommendation dated 23 April 2019.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

### 3.1.7. Libtayo - cemiplimab - EMEA/H/C/004844

Regeneron Ireland U.C.; as monotherapy, indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma

Scope: Opinion

**Action**: For adoption

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

List of Outstanding Issues adopted on 28.03.2019, 31.01.2019. List of Questions adopted on 26.07.2018.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a conditional marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that cemiplimab is a new active substance, as claimed by the applicant.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The CHMP noted the letters of recommendation dated 23 April 2019.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

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

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

Scope: Opinion

**Action**: For adoption

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

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

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by majority (20 positive out of 30 votes) together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that botulinum toxin type A is not a new active substance, as claimed by the applicant.

The Norwegian Member was not in agreement with the CHMP recommendation.

The divergent position (Andrea Laslop, Romaldas Mačiulaitis, Greg Markey, Constantinos Markopoulos, Jan Mueller-Berghaus, Koenraad Norga, Sinan B. Sarac, Bart Van der Schueren, Martina Weise, Alexandre Moreau, Bjorg Bolstad) was appended to the opinion.

The CHMP noted the letter of recommendation dated 24 April 2019.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

### 3.1.9. Sixmo - buprenorphine - EMEA/H/C/004743

L. Molteni & C. dei Fratelli Alitti Societa di Esercizio S.p.A.; Substitution treatment for opioid drug dependence

Scope: Opinion

**Action**: For adoption

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

List of Outstanding Issues adopted on 28.02.2019, 15.11.2018. List of Questions adopted on 22.03.2018.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to special and restricted medical prescription.

The summary of opinion was circulated for information.

### 3.1.10. Striascan - ioflupane (123i) - EMEA/H/C/004745

CIS BIO International; indicated for detecting loss of functional dopaminergic neuron terminals in the striatum

Scope: Opinion

**Action**: For adoption

Generic application (Article 10(1) of Directive No 2001/83/EC), Generic of DaTSCAN

List of Outstanding Issues adopted on 28.02.2019. List of Questions adopted on 20.09.2018.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

### 3.1.11. TALZENNA - talazoparib - EMEA/H/C/004674

Pfizer Europe MA EEIG; 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: Opinion

**Action**: For adoption

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

List of Outstanding Issues adopted on 28.02.2019. List of Questions adopted on 20.09.2018.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considered that talazoparib is a new active substance, as claimed by the applicant.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

### 3.1.12. Temybric Ellipta - fluticasone furoate / umeclidinium / vilanterol - EMEA/H/C/005254

GlaxoSmithKline Trading Services; treatment of adult patients with chronic obstructive pulmonary disease (COPD)

Scope: Opinion

**Action**: For adoption

Informed consent application (Article 10c of Directive No 2001/83/EC), Informed Consent of Trelegy Ellipta

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to medical prescription.

The summary of opinion was circulated for information.

### 3.1.13. Ultomiris - ravulizumab - Orphan - EMEA/H/C/004954

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

Scope: Opinion

**Action**: For adoption

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

List of Outstanding Issues adopted on 28.02.2019. List of Questions adopted on 15.11.2018.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

Furthermore, the CHMP considers that ravulizumab is a new active substance, as claimed by the applicant.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The CHMP noted the letter of recommendation dated 18 April 2019.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

### 3.1.14. Xromi - hydroxycarbamide - EMEA/H/C/004837

Nova Laboratories Ireland Limited; prevention of complications of Sickle Cell disease

Scope: Opinion

**Action**: For adoption

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

Oral explanation held on 28.03.2019. List of Outstanding Issues adopted on 28.03.2019, 28.02.2019, 15.11.2018. List of Questions adopted on 28.06.2018.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion recommending the granting of a marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The legal status was agreed as medicinal product subject to restricted medical prescription.

The summary of opinion was circulated for information.

### 3.1.15. Zynteglo - Autologous CD34$^{+}$ cells encoding $\beta^{A\text{-}T87Q}$-globin gene- Orphan - ATMP - EMEA/H/C/003691

bluebird bio (Netherlands) B.V.; treatment of transfusion-dependent β-thalassaemia (TDT)

Scope: Re-adoption of opinion

**Action**: For adoption

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

Opinion adopted on 28.03.2019. List of Questions adopted on 25.01.2019.

The CHMP noted the discussion and the re-adopted draft opinion taken by the CAT at their April meeting.

The CHMP re-adopted a positive opinion recommending the granting of a conditional marketing authorisation by consensus together with the CHMP assessment report and translation timetable.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

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

### 3.2.1. sodium oxybate - EMEA/H/C/004962

medium to long-term maintenance of alcohol abstinence and treatment of mild to moderate alcohol withdrawal syndrome

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 15.11.2018.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

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

treatment of severe hypoglycaemia

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 13.12.2018.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

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

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

Scope: List of outstanding issues

**Action**: For adoption

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

The Committee was reminded of the status of this application and its remaining outstanding issues.

The CHMP agreed that no oral explanation is needed this time. See 2.1.

The Committee adopted a 2nd list of outstanding issues with a specific timetable.

### 3.2.4. cannabidiol - Orphan - EMEA/H/C/004675

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

Scope: Oral explanation/List of outstanding issues

**Action**: Oral explanation to be held on Wednesday, 24 April 2019 at time 14:00

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

The Committee was reminded of the status of this application and its remaining outstanding issues.

An oral explanation was held on Wednesday, 24 April 2019. The presentation mainly focused on efficacy data including subgroup analysis.

See 2.1

The Committee adopted a 3rd list of outstanding issues with a specific timetable.

The CHMP agreed to consult the SAG Neurology and adopted a list of questions to this group.

### 3.2.5. enasidenib - Orphan - EMEA/H/C/004324

Celgene Europe BV; treatment of acute myeloid leukaemia (AML)

Scope: List of outstanding issues

**Action**: For adoption

List of Questions adopted on 18.10.2018.

The Committee was reminded of the status of this application and its remaining outstanding issues.

The Committee adopted a list of outstanding issues with a specific timetable.

The CHMP agreed to consult the SAG-Oncology and adopted a list of questions to this group.

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

### 3.3.1. arsenic trioxide - EMEA/H/C/005175

treatment of relapsed acute promyelocytic leukaemia (APL)

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

### 3.3.2. budesonide / glycopyrronium / formoterol fumarate dihydrate - EMEA/H/C/004983

as a maintenance treatment in adult patients with moderate to very severe chronic obstructive pulmonary disease (COPD)

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

### 3.3.3. dexmedetomidine - EMEA/H/C/005152

light to moderate sedation

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

### 3.3.4. tagraxofusp - Orphan - EMEA/H/C/005031

**Accelerated assessment**

TMC Pharma (EU) Limited; treatment of adult patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN)

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

### 3.3.5. polatuzumab vedotin - Orphan - EMEA/H/C/004870

**Accelerated assessment**

Roche Registration GmbH; Treatment of mature B cell lymphomas

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

### 3.3.6. selinexor - Orphan - EMEA/H/C/005127

Karyopharm Europe GmbH; treatment of patients with relapsed refractory multiple myeloma (RRMM)

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

### 3.3.7. lifitegrast - EMEA/H/C/004653

treatment of moderate to severe dry eye disease in adults for whom prior artificial tears has not been sufficient

Scope: List of questions

**Action**: For adoption

The Committee discussed the issues identified in this application.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

### 3.4.1. clofarabine - EMEA/H/C/005039

treatment of acute lymphoblastic leukaemia

Scope: Request by the applicant dated 12.04.2019 for an extension to the clock stop to respond to the List of Questions adopted on 31.01.2019.

List of Questions adopted on 31.01.2019.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the List of Questions adopted on 31.01.2019.

### 3.4.2. rituximab - EMEA/H/C/004696

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

Scope: Amended timetable

**Action**: For adoption

Amended list of questions adopted on 28.03.2019. List of questions adopted on 13.12.2018.

The CHMP adopted the amended timetable.

### 3.4.3. ibalizumab - EMEA/H/C/004961

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

Scope: List of experts for the SAG HIV/viral diseases meeting scheduled on 11.04.2019 adopted via written procedure on 05.04.2019

**Action**: For information

Request for supplementary information adopted on 28.02.2019. List of Questions adopted on 11.12.2018.

The CHMP noted the list of experts to the SAG HIV/viral diseases adopted via written procedure on 05.04.2019.

### 3.4.4. Doxolipad - doxorubicin hydrochloride - EMEA/H/C/004110

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

Scope: Draft list of experts for the ad-hoc expert group and call for nomination of experts

**Action**: For information

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.

The CHMP noted the draft list of experts and the call for nomination.

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

No items

## 3.6. Initial applications in the decision-making phase

No items

## 3.7. Withdrawals of initial marketing authorisation application

No items

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

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

No items

## 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

### 4.3.1. Humalog - insulin lispro - EMEA/H/C/000088/X/0169

Eli Lilly Nederland B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: quality

**Action**: For adoption

The Committee discussed the issues identified in this application, mainly relating to the quality part.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

Vertex Pharmaceuticals (Ireland) Limited

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

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

**Action**: For adoption

The Committee discussed the issues identified in this application, mainly relating to the pharmacokinetics and the dosing recommendations for children.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

### 4.3.3. Liprolog - insulin lispro - EMEA/H/C/000393/X/0130

Eli Lilly Nederland B.V.

Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: quality

**Action**: For adoption

The Committee discussed the issues identified in this application, mainly relating to the quality part.

The Committee adopted the CHMP recommendation and scientific discussion together with the list of questions.

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

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

Celltrion Healthcare Hungary Kft.

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

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

An updated list of questions was adopted via written procedure on 17.04.2019.

**Action**: For information

List of Questions adopted on 28.03.2019.

The CHMP noted the updated list of questions adopted via written procedure on 17.04.2019

### 4.4.2. Pemetrexed Fresenius Kabi - pemetrexed - EMEA/H/C/003895/X/0009

Fresenius Kabi Deutschland GmbH

Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Ghania Chamouni

Scope: "Extension application to introduce a new pharmaceutical form (concentrate for solution for infusion) associated with new strength 25 mg/ml."

Request by the applicant for an extension to the clock stop to respond to the list of questions adopted on 31.01.2019

**Action**: For adoption

List of Questions adopted on 31.01.2019.

The CHMP agreed to the request by the applicant for an extension to the clock stop to respond to the list of questions adopted on 31.01.2019

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

Bristol-Myers Squibb Pharma EEIG

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

Scope: "Extension of indication to include treatment in combination with pomalidomide and dexamethasone of adult patients with multiple myeloma. As a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 4.9, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.
The RMP (version 2.0) is updated to reflect the new indication."

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

**Action**: For adoption

Request for Supplementary Information adopted on 13.12.2018.

The Committee discussed the issues identified in this application, mainly concerning the claim of significant benefit in relation to the request for 1 year market protection.

The Committee adopted a 2nd request for supplementary information with a specific timetable.

### 5.1.2. Fiasp - insulin aspart - EMEA/H/C/004046/II/0010

Novo Nordisk A/S

Rapporteur: Kristina Dunder, Co-Rapporteur: Ingrid Wang, PRAC Rapporteur: Amelia Cupelli

Scope: "Extension of indication to include treatment of children and adolescents aged 1 year and above based on data from the phase 3b clinical trial NN1218-4101 (assessed as part of PAM P46-002, fulfilled), supported by data from the Clinical Pharmacology trials NN1218-4371 (PAM P46-003, submitted on the 02-Jan-2019) and NN1218-3888 which was included in the initial MAA.
As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC and the corresponding sections of the Package Leaflet are updated accordingly.
In addition, the Marketing Authorisation Holder (MAH) took the opportunity to make other non-related minor or editorial changes throughout the EU PI to increase readability/consistency."

**Action**: For adoption

The Committee discussed the issues identified in this application, relating to some clinical aspects and the RMP.

The Committee adopted a request for supplementary information with a specific timetable.

### 5.1.3. Keytruda - pembrolizumab - EMEA/H/C/003820/II/0069

Merck Sharp & Dohme B.V.

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

Scope: "Extension of indication to include first line treatment of advanced or metastatic renal cell carcinoma (RCC) as combination therapy of pembrolizumab together with axitinib based on the results of the first Interim Analysis (IA1) from the pivotal study, KN426, an ongoing, Phase 3, randomized, open-label, multicenter, global study, to evaluate the efficacy and safety of pembrolizumab in combination with axitinib versus sunitinib in previously untreated subjects with advanced/metastatic RCC. It also includes supportive data from KEYNOTE-427 Cohort A (pembrolizumab monotherapy) and a Sponsored Study A4061051 (axitinib monotherapy). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated in order to update the safety information. The Package Leaflet is updated in accordance.
In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.
The risk management plan (RMP) Version 24.1 is submitted."

**Action**: For adoption

The Committee discussed the issues identified in this application, mainly relating to efficacy data in the relevant subgroups.

The Committee adopted a request for supplementary information with a specific timetable.

### 5.1.4. 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 (tablet formulation) as monotherapy for the maintenance treatment of adult patients with advanced (FIGO stages III and IV) BRCA1/2-mutated (germline and/or somatic) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy. As a consequence of this new indication, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC of the tablet formulation have been updated. Sections 4.2, 4.4, 4.8 and 5.1 of the SmPC of the capsule formulation have also been modified to reflect information that is also relevant to the capsule formulation. The Package Leaflet has been updated accordingly. The RMP version 17.4 has also been accepted"

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

**Action**: For adoption

Request for Supplementary Information adopted on 28.02.2019, 13.12.2018.

The Committee confirmed that all issues previously identified in this application had been addressed.

The Committee adopted a positive opinion by consensus together with the CHMP Assessment Report and translation timetable.

The Icelandic and Norwegian CHMP members were in agreement with the CHMP recommendations.

The summary of opinion was circulated for information.

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

Alexion Europe SAS

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

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

**Action**: For adoption

The Committee discussed the issues identified in this application, mainly relating to long term efficacy data and the wording of the indication.

The Committee adopted a request for supplementary information with a specific timetable.

### 5.1.6. Stelara - ustekinumab - EMEA/H/C/000958/II/0071

Janssen-Cilag International NV

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

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

**Action**: For adoption

The Committee discussed the issues identified in this application, mainly relating to the wording of the indication and the target population.

The Committee adopted a request for supplementary information with a specific timetable.

### 5.1.7. WS1539
### Ebymect - dapagliflozin / metformin - EMEA/H/C/004162/WS1539/0035
### Edistride - dapagliflozin - EMEA/H/C/004161/WS1539/0029
### Forxiga - dapagliflozin - EMEA/H/C/002322/WS1539/0048
### Xigduo - dapagliflozin / metformin - EMEA/H/C/002672/WS1539/0046

AstraZeneca AB

Lead Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin

Scope: "Update of sections 4.1, 4.2, 4.4, 4.8, and 5.1 of Forxiga, Edistride, Xigduo and Ebymect of the SmPC to modify the current indication for improvement of glycaemic control based on final results from study D1693C00001 (DECLARE), which is listed as a category 3 study in the RMP (Forxiga: MEA 005):
- For the prevention of new or worsening HF or CV death
- For the prevention of new or worsening nephropathy
The Package Leaflets (PL) are updated accordingly. The updated dapagliflozin Risk Management Plan (RMP) version 17 and dapagliflozin/metformin fixed dose combination (FDC) RMP version 11 have also been submitted.
In addition, the Worksharing Applicant took the opportunity to correct a typo error in Edistride marketing authorisation number in section 8 of SmPC and add the latest renewal date for Xigduo in section 9 of SmPC. Besides, the lactose wording in SmPC section 4.4 has been updated in line with the updated excipient guideline. The revised PI also includes proposal for minor administrative changes for consistency throughout the PI."

**Action**: For adoption

The Committee discussed the issues identified in this application, mainly relating to the wording of the indication and how to best reflect the final results from study D1693C00001in the SmPC.

The Committee adopted a request for supplementary information with a specific timetable.

### 5.1.8. WS1542
### Bretaris Genuair - aclidinium - EMEA/H/C/002706/WS1542/0040
### Eklira Genuair - aclidinium - EMEA/H/C/002211/WS1542/0040

AstraZeneca AB

Lead Rapporteur: Ewa Balkowiec Iskra, Lead Co-Rapporteur: Peter Kiely

Scope: "Extension of indication to include reduction of COPD exarcerbations for Eklira Genuair

and Bretaris Genuair; as a consequence, sections 4.1, 4.4, 4.8 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance.
In addition, the Worksharing Applicant (WSA) took the opportunity to update the list of local representatives in the Package Leaflet for Bretaris Genuair and to implement minor editorial changes in sections 4.4, 4.6, 5.3 of the SmPC and section 2 of the PL for both Eklira Genuair and Bretaris Genuair."

**Action**: For adoption

The Committee discussed the issues identified in this application, mainly relating to efficacy data and the wording of the indication.

The Committee adopted a request for supplementary information with a specific timetable.

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

### 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. lisocabtagene maraleucel - PRIME – Orphan – ATMP - H0004731/0004

Celgene Europe Ltd; intended for the treatment of adult patients with relapsed or refractory large B-cell lymphoma including diffuse large B-cell lymphoma (DLBCL), primary mediastinal

B-cell lymphoma (PMBCL), and follicular lymphoma grade 3B (FL3B) after at least 2 lines of therapy

Scope: Request for combination pack

**Action:** For adoption

The CHMP agreed to the request for a combination pack.

### 8.1.2. isatuximab - Orphan - H0004977

sanofi-aventis groupe; Isatuximab in combination with pomalidomide and dexamethasone is indicated for the treatment of patients with refractory or relapsed multiple myeloma who have received at least 2 lines of prior therapy including lenalidomide and a proteasome inhibitor.

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

**Action**: For adoption

The CHMP did not agree to the request for accelerated assessment and adopted the briefing note and Rapporteurs' recommendation on the Request for Accelerated Assessment.

## 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

The CHMP noted the list of applications received.

### 8.2.2. Recommendation for PRIME eligibility

**Action:** For adoption

The CHMP adopted the recommendation for PRIME eligibility. The CHMP reviewed 1 recommendation for eligibility to PRIME, which was denied.

The individual outcomes are listed in PRIME Monthly Report on EMA website.

# 9. Post-authorisation issues

## 9.1. Post-authorisation issues

### 9.1.1. Tyverb - lapatinib - EMEA/H/C/000795/II/0059

Novartis Europharm Limited

Rapporteur: Filip Josephson

Scope: "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."

**Action**: For discussion

The Committee discussed the issues identified in this application. The members were informed that the MAH submitted corrections to errors that were found in the results of EGF114299 study. The results from that study led in variation II/0051 to an alteration of the indication wording, which was now questioned.

While the corrected data are under assessment in variation EMEA/H/C/00795/II/0059 the CHMP agreed to update the SmPC of Tyverb immediately reverting back to the previous indication wording and removing the erroneous results from study EGF114299 (EMEA/H/C/00795/IB/0061).

The Committee adopted a request for supplementary information with a specific timetable.

### 9.1.2. Revlimid - lenalidomide - Orphan - EMEA/H/C/000717/II/0102/G

Celgene Europe BV

Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

Scope: Letter from third party regarding the opinion adopted on 28.03.2019

**Action:** For information

The CHMP noted the letter from the third party.

### 9.1.3. Tecentriq - atezolizumab - EMEA/H/C/004143/II/0022

Roche Registration GmbH

Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: "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."

**Action**: For discussion

The Committee discussed the issues identified in this application, mainly relating to the exposure-response relationship and the dosing regimen.

The Committee adopted a request for supplementary information with a specific timetable.

# 10. Referral procedures

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

### 10.1.1. Lartruvo – olaratumab – EMEA/H/A-20/1479/C/4216/015

Eli Lilly Nederland B.V.

Rapporteur: Jorge Camarero Jiménez, Co-Rapporteur: Daniela Melchiorri

Scope: Opinion

**Action:** For adoption

Review of benefit-risk balance following preliminary results of the ANNOUNCE study (I5B-MC-JGDJ) which did not meet the primary endpoint of prolongation of overall survival in the study population.

The CHMP adopted an opinion by consensus, recommending that Lartruvo lacks therapeutic efficacy and that the risk-benefit balance of Lartruvo is not favourable. Therefore, the CHMP was of the opinion that the marketing authorisation(s) for Lartruvo should be revoked.

The CHMP adopted the assessment report.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

The CHMP agreed to the public health communication.

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

### 10.2.1. Norethisterone Ethinylestradiol-meta-analysis - EMEA/H/A-5(3)/1477

MAH various

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

Scope: Opinion

**Action**: For adoption

Request from the UK for a CHMP opinion on a recently published meta-analysis study on the developmental effect of norethisterone acetate and ethinylestradiol and any potential clinical implications on the human foetus.

The CHMP adopted an opinion by consensus, concluding that the conclusions of the meta-analysis cannot be considered reliable. Due to the multiple limitations of the meta-analysis study, the results described in this manuscript cannot be used to further expand clinical knowledge. As a consequence, the conclusion, that current clinical data available do not support a signal of teratogenicity of a combination of norethisterone/ethinylestradiol remains valid. The CHMP therefore, did not recommend any regulatory action based on the above data.

The CHMP adopted the assessment report.

The Icelandic and Norwegian Members were in agreement with the CHMP recommendation.

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

No items

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

No items

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

### 10.5.1. Septanest and associated names - articaine (hydrochloride)/adrenaline (tartare) - EMEA/H/A-30/1461

MAH Septodont group of companies and associated companies

Rapporteur: Romaldas Maciulaitis, Co-rapporteur: Fatima Ventura

Scope: Final opinion documents

**Action:** For information

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

Opinion adopted on 28.03.2019

The CHMP noted the final documents.

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

No items

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

No items

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

No items

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

No items

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

No items

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

### 10.11.1. Basiron AC – benzoyl peroxide, hydrous – EMEA/H/A-13/1475

MAH: Galderma Nordic AB

Re-examination Rapporteur: Romaldas Maciulaitis, Re-examination Co-Rapporteur: Alexandre Moreau

Initial Referral Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege

Scope: Re-examination, Appointment of Re-examination Rapporteurs

**Action:** For adoption

This procedure concerns a Type II Quality WS variation (SE/H/xxxx/WS/190). The notification received by the reference authority (SE) on 26/10/2018, notifying of the start of a referral under Article 13 of Commission regulation (EC) No 1234/2008.

The CHMP appointed Romaldas Maciulaitis as re-examination Rapporteur and Alexandre Moreau as re-examination Co-Rapporteur.

# 11. Pharmacovigilance issue

## 11.1. Early Notification System

April 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

No items

## 13.2. Innovation Task Force briefing meetings

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

No items

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

No items

## 13.4. Nanomedicines activities

No items

# 14. Organisational, regulatory and methodological matters

## 14.1. Mandate and organisation of the CHMP

### 14.1.1. CHMP co-opted member

Call for nomination of a CHMP co-opted member with the area of expertise:

Expertise in biostatistics, principally on clinical trial methodology, and at least basic knowledge of the EU regulatory framework

**Action:** For information

The CHMP agreed to extend the deadline for nominations.

Nominations should be sent.

## 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 8-11 April 2019

**Action:** For information

The CHMP noted the information.

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

**Action:** For adoption

The CHMP adopted the EURD list.

### 14.2.2. Committee for Advanced Therapies (CAT)

CAT draft minutes of meeting held on 15-17 April 2019

**Action:** For information

The CHMP noted the draft minutes.

### 14.2.3. Paediatric Committee (PDCO)

PIPs reaching D30 at April 2019 PDCO

**Action:** For information

The CHMP noted the information.

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

**Action:** For information

The CHMP noted the report.

### 14.2.4. Committee for Orphan Medicinal Products (COMP)

Report from the COMP meeting held on 15-17 April 2019

**Action:** For information

The CHMP noted the report.

### 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 23-25 April 2019

**Action:** For information

The CHMP noted the report.

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

### 14.3.1. Scientific Advice Working Party (SAWP)

Chair: Anja Schiel

Report from the SAWP meeting held on 5 April 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.

The CHMP noted the report.

### 14.3.2. Biologics Working Party (BWP)

Chair: Sol Ruiz/Nanna Aaby Kruse

Reports from BWP April 2019 meeting to CHMP for adoption:

- 6 reports on products in scientific advice and protocol assistance
- 5 reports on products in pre-authorisation procedures

**Action:** For adoption

The CHMP adopted the reports.

## 14.4. Cooperation within the EU regulatory network

### 14.4.1. Antimicrobial Advice ad hoc Expert Group (AMEG)

Scope: Overview of comments received by stakeholders during the public consultation on the AMEG scientific advice on the impact on public health and animal health of the use of antibiotics in animals - preliminary risk profiling for new antimicrobials

**Action:** For information

The CHMP noted the overview of comments.

### 14.4.2. Pharmacokinetics Working Party (PKWP)

Chair: Jan Welink/Henrike Potthast

CMDh question to PKWP - Biowaiver for oral solutions with the “same concentration”

**Action:** For adoption

The CHMP agreed to the CMDh questions to PKWP.

### 14.4.3. Ad-hoc Influenza Working Group

Scope:

Amended EU Strain selection for the Influenza Vaccines for the Season 2019/2020: Report from the Ad Hoc Influenza working group to the BWP

Amended EU Recommendation for the Seasonal Influenza Vaccine Composition for the Season 2019/2020

**Action:** Adopted via written procedure on 10.04.2019

The CHMP noted the amended documents adopted via written procedure on 10 April 2019.

## 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 discussion

The CHMP noted the update.

## 16. List of participants

List of participants including any restrictions with respect to involvement of members/alternates/experts following evaluation of declared interests for the April 2019 CHMP meeting

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Harald Enzmann | Chair | Germany | No interests declared | |
| Andrea Laslop | Member | Austria | No interests declared | |
| Milena Stain | Alternate | Austria | No interests declared | |
| Bart Van der Schueren | Member | Belgium | No interests declared | |
| Mila Vlaskovska | Member | Bulgaria | No interests declared | |
| Selma Arapovic Dzakula | Alternate | Croatia | No interests declared | |
| Emilia Mavrokordatou | Member | Cyprus | No interests declared | |
| Ondřej Slanař | Member | Czech Republic | No interests declared | |
| Sinan B. Sarac | Member | Denmark | No interests declared | |
| Mark Ainsworth | Alternate | Denmark | No interests declared | |
| Alar Irs | Member | Estonia | No restrictions applicable to this meeting | |
| Outi Mäki-Ikola | Member | Finland | No restrictions applicable to this meeting | |
| Tuomo Lapveteläinen | Alternate | Finland | No interests declared | |
| Alexandre Moreau | Member | France | No interests declared | |
| Martina Weise | Member | Germany | No restrictions applicable to this meeting | |
| Janet Koenig | Alternate | Germany | No interests declared | |
| Constantinos Markopoulos | Member | Greece | No interests declared | |
| Eleftheria Nikolaidi | Alternate | Greece | No interests declared | |
| Agnes Gyurasics | Member | Hungary | No interests declared | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Hrefna Gudmundsdottir | Alternate | Iceland | No interests declared | |
| Jayne Crowe | Member | Ireland | No interests declared | |
| Peter Kiely | Alternate | Ireland | No interests declared | |
| Daniela Melchiorri | Member | Italy | No restrictions applicable to this meeting | |
| Natalja Karpova | Member | Latvia | No interests declared | |
| Romaldas Mačiulaitis | Member | Lithuania | No participation in final deliberations and voting on: | polatuzumab vedotin (EMEA/H/C/004870) |
| Johann Lodewijk Hillege | Member | Netherlands | No interests declared | |
| Paula Boudewina van Hennik | Alternate | Netherlands | No interests declared | |
| Bjorg Bolstad | Member | Norway | No restrictions applicable to this meeting | |
| Ingrid Wang | Alternate | Norway | No interests declared | |
| Ewa Balkowiec Iskra | Member | Poland | No interests declared | |
| Bruno Sepodes | Member(Vice-Chair) | Portugal | No interests declared | |
| Fatima Ventura | Alternate | Portugal | No restrictions applicable to this meeting | |
| Simona Badoi | Member | Romania | No interests declared | |
| Francisek Drafi | Member | Slovakia | No interests declared | |
| Rajko Kenda | Member | Slovenia | No restrictions applicable to this meeting | |
| Maria Concepcion Prieto Yerro | Member | Spain | No interests declared | |
| Jorge Camarero Jiménez | Alternate | Spain | No participation in final deliberations and voting on: | polatuzumab vedotin (EMEA/H/C/004870) |
| Kristina Dunder | Member | Sweden | No interests declared | |
| Filip Josephson | Alternate | Sweden | No interests declared | |
| Greg Markey | Member | United Kingdom | No interests declared | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Koenraad Norga | Co-opted member | Belgium | No restrictions applicable to this meeting | |
| Jan Mueller-Berghaus | Co-opted member | Germany | No interests declared | |
| Blanka Hirschlerova | Co-opted member | Czech Republic | No interests declared | |
| Sol Ruiz | Co-opted member | Spain | No interests declared | |
| Anja Schiel | Expert - in person* | Norway | No interests declared | |
| Kristina Bech Jensen | Expert - in person* | Denmark | No interests declared | |
| Eskild Colding-Jørgensen | Expert - via telephone* | Denmark | No restrictions applicable to this meeting | |
| Aldana Rosso | Expert - via telephone* | Denmark | No interests declared | |
| Zane Neikena | Expert - via telephone* | Latvia | No interests declared | |
| Donal O'Connor | Expert - via telephone* | Ireland | No interests declared | |
| Laurens de Leur | Expert - via telephone* | Netherlands | No interests declared | |
| Ingrid Schellens | Expert - via telephone* | Netherlands | No interests declared | |
| Liesbeth Van Vlijmen | Expert - via telephone* | Netherlands | No interests declared | |
| Jutta Dedorath | Expert - via telephone* | Germany | No interests declared | |
| Susanna Hausmann | Expert - via telephone* | Germany | No interests declared | |
| Marion Haberkamp | Expert - via telephone* | Germany | No interests declared | |
| Justyna Pilecka | Expert - via telephone* | Poland | No interests declared | |
| Peter Morgan Warren | Expert - via telephone* | United Kingdom | No interests declared | |
| Yolanda Barbachano | Expert - via telephone* | United Kingdom | No interests declared | |
| Serge Bakchine | Expert - via telephone* | France | No interests declared | |
| Ines Reis | Expert - via telephone* | United Kingdom | No restrictions applicable to this meeting | |
| Larissa Higgins | Expert - via telephone* | Ireland | No interests declared | |
| Lisbeth Bregnhoj | Expert - via telephone* | Denmark | No interests declared | |
| Sebastian Liebau | Expert - via telephone* | Germany | No restrictions applicable to this meeting | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Andreas Kirisits | Expert - via Adobe* | Austria | No interests declared | |
| Regine Magdalene Lehnert | Expert - via Adobe* | Germany | No interests declared | |
| Sylvia Kuehn | Expert - via Adobe* | Germany | No restrictions applicable to this meeting | |
| Kendra Schafti | Expert - via Adobe* | Germany | No interests declared | |
| Olga Kholmanskikh | Expert - via Adobe* | Belgium | No interests declared | |
| George Aislaitner | Expert - via Adobe* | Germany | No interests declared | |
| Meeting run with the help of EMA staff | | | | |

*Experts were only evaluated against the product(s) they have been invited to talk about.

## 17. 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)*

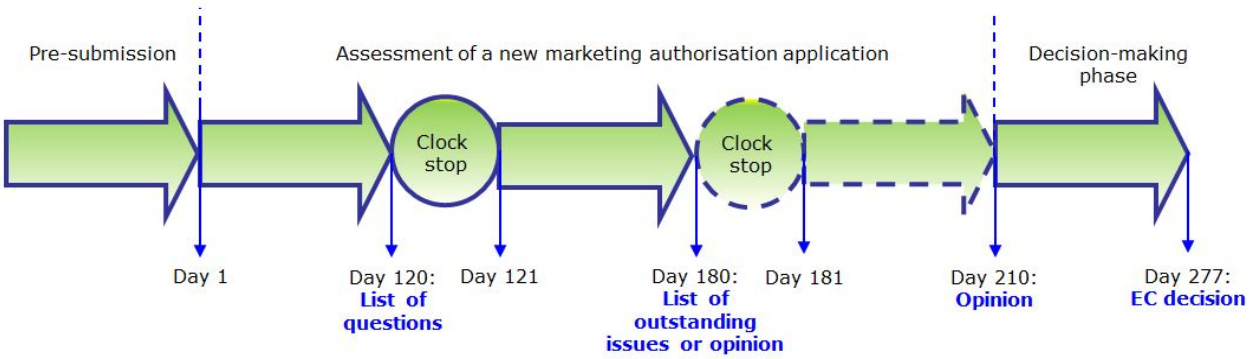
The items listed in this section are those for which marketing authorisation holders (MAHs) or applicants have been invited to the CHMP plenary meeting to address questions raised by the Committee. Oral explanations normally relate to on-going applications (section 3, 4 and 5) or referral procedures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

21 June 2019
EMA/CHMP/341564/2019

# Final Annex to 23-26 April 2019 CHMP Minutes

Pre-submission and post-authorisations issues

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## A. PRE SUBMISSION ISSUES

### A.1. ELIGIBILITY REQUESTS

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| Report on Eligibility to Centralised Procedure for April 2019: **For adoption** | Adopted. |

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

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| Final Outcome of Rapporteurship allocation for April 2019: **For adoption** | Adopted. |

### 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

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| **Increlex - mecasermin - EMEA/H/C/000704/S/0055**<br>Ipsen Pharma, Rapporteur: Outi Mäki-Ikola, PRAC Rapporteur: Kirsti Villikka<br>Request for Supplementary Information adopted on 28.02.2019. | Positive Opinion adopted by consensus together with the CHMP assessment report.<br>The Marketing Authorisation remains under exceptional circumstances.<br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion. |
| **Kolbam - cholic acid - EMEA/H/C/002081/S/0029, Orphan**<br>Retrophin Europe Ltd, Rapporteur: Constantinos Markopoulos, PRAC Rapporteur: Agni Kapou<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Obizur - susoctocog alfa - EMEA/H/C/002792/S/0023**<br>Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, PRAC Rapporteur: Brigitte Keller-Stanislawski<br>Request for Supplementary Information adopted on 28.02.2019. | Positive Opinion adopted by consensus together with the CHMP assessment report.<br>The Marketing Authorisation remains under exceptional circumstances.<br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion. |
| **Orphacol - cholic acid - EMEA/H/C/001250/S/0026, Orphan**<br>Laboratoires CTRS, Rapporteur: Constantinos Markopoulos, PRAC Rapporteur: Sofia Trantza<br>Request for Supplementary Information adopted on 28.02.2019. | Positive Opinion adopted by consensus together with the CHMP assessment report.<br>The Marketing Authorisation remains under exceptional circumstances.<br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion. |

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| **SCENESSE - afamelanotide - EMEA/H/C/002548/S/0023, Orphan**<br>Clinuvel Europe Limited, Rapporteur: Janet Koenig, PRAC Rapporteur: Martin Huber | Positive Opinion adopted by consensus together with the CHMP assessment report.<br><br>The Marketing Authorisation remains under exceptional circumstances.<br><br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion. |
| **Vyndaqel - tafamidis - EMEA/H/C/002294/S/0047, Orphan**<br>Pfizer Europe MA EEIG, Rapporteur: Joseph Emmerich, PRAC Rapporteur: Ghania Chamouni<br>Request for Supplementary Information adopted on 28.03.2019. | Positive Opinion adopted by consensus together with the CHMP assessment report.<br><br>The Marketing Authorisation remains under exceptional circumstances.<br><br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP opinion. |

## B.2. RENEWALS OF MARKETING AUTHORISATIONS OUTCOMES

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

### B.2.2. Renewals of Marketing Authorisations for unlimited validity

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| **Accofil - filgrastim - EMEA/H/C/003956/R/0026**<br>Accord Healthcare S.L.U., Rapporteur: Outi Mäki-Ikola, Co-Rapporteur: Sol Ruiz, PRAC Rapporteur: Kirsti Villikka | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br><br>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.<br><br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion. |
| **Adjupanrix - pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - EMEA/H/C/001206/R/0062**<br>GlaxoSmithkline Biologicals SA, Informed Consent of Pandemrix (EXP), Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Menno van der Elst<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Busulfan Fresenius Kabi - busulfan - EMEA/H/C/002806/R/0010**<br>Fresenius Kabi Deutschland GmbH, Generic, Generic of Busilvex, Rapporteur: John Joseph Borg, PRAC Rapporteur: Eva A. Segovia | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br><br>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity. |

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| | The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion. |
| **Imbruvica - ibrutinib - EMEA/H/C/003791/R/0049, Orphan**<br>Janssen-Cilag International NV, Rapporteur: Filip Josephson, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Nikica Mirošević Skvrce | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br><br>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.<br><br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion. |
| **Instanyl - fentanyl - EMEA/H/C/000959/R/0049**<br>Takeda Pharma A/S, Rapporteur: Alexandre Moreau, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Ghania Chamouni<br>Request for Supplementary Information adopted on 31.01.2019. | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br><br>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.<br><br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion. |
| **Triumeq - dolutegravir / abacavir / lamivudine - EMEA/H/C/002754/R/0063**<br>ViiV Healthcare B.V., Rapporteur: Filip Josephson, Co-Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Martin Huber<br>Request for Supplementary Information adopted on 28.02.2019. | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br><br>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.<br><br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion. |
| **Trulicity - dulaglutide - EMEA/H/C/002825/R/0036**<br>Eli Lilly Nederland B.V., Rapporteur: Martina Weise, Co-Rapporteur: Ondřej Slanař, PRAC Rapporteur: Amelia Cupelli<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Vargatef - nintedanib - EMEA/H/C/002569/R/0025**<br>Boehringer Ingelheim International GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Agni Kapou<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Xultophy - insulin degludec / liraglutide -** | Positive Opinion adopted by consensus together |

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| **EMEA/H/C/002647/R/0028**<br>Novo Nordisk A/S, Rapporteur: Kristina Dunder, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Menno van der Elst<br>Request for Supplementary Information adopted on 28.03.2019. | with the CHMP assessment report and translation timetable.<br><br>Based on the review of the available information, the CHMP was of the opinion that the renewal of the marketing authorisation can be granted with unlimited validity.<br><br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion. |

### B.2.3. Renewals of Conditional Marketing Authorisations

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| **Bavencio - avelumab - EMEA/H/C/004338/R/0008, Orphan**<br>Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark | Positive Opinion adopted by consensus together with the CHMP assessment report and translation timetable.<br><br>The CHMP was of the opinion that the renewal for this conditional Marketing Authorisation can be granted.<br><br>The Marketing Authorisation remains conditional.<br><br>The Icelandic and Norwegian CHMP Members were in agreement with the CHMP Opinion. |
| **Translarna - ataluren - EMEA/H/C/002720/R/0051, Orphan**<br>PTC Therapeutics International Limited, Rapporteur: Johann Lodewijk Hillege, Co-Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Liana Gross-Martirosyan<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |

### B.3. POST-AUTHORISATION PHARMACOVIGILANCE OUTCOMES

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| **Signal detection**<br><br>PRAC recommendations on signals adopted at the PRAC meeting held on 8-11 April 2019 PRAC: | Adopted. |
| **Signal of recurrent thrombosis in patients with antiphospholipid syndrome**<br><br>Direct oral anticoagulants (DOACs) (rivaroxaban; apixaban; dabigatran; edoxaban) – Xarelto, Pradaxa, Eliquis, Lixiana, Roteas – PRAC recommendation on a variation<br><br>**Action**: For adoption | |

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| PSUR procedures for which PRAC adopted a recommendation for variation of the terms of the MA at its April 2019 meeting: | Noted. |
| **EMEA/H/C/PSUSA/00000954/201809** (denosumab (indicated for osteoporosis and for bone loss associated with hormone ablation in prostate cancer)) CAPS: **Prolia** (EMEA/H/C/001120) (denosumab), Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "From: 26/09/2017 To: 26/09/2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br><br>Update of section 4.4 of the SmPC to reflect the fact that fatal cases of hypocalcaemia have been observed, and section 4.8 of the SmPC to add 'Lichenoid drug eruptions' as a new uncommon ADR and 'Alopecia' as a new common ADR. The Package leaflet is updated accordingly.<br><br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00001749/201809** (insulin aspart) CAPS: **Fiasp** (EMEA/H/C/004046) (insulin aspart), Novo Nordisk A/S, Rapporteur: Kristina Dunder **NovoMix** (EMEA/H/C/000308) (insulin aspart), Novo Nordisk A/S, Rapporteur: Kristina Dunder **NovoRapid** (EMEA/H/C/000258) (insulin aspart), Novo Nordisk A/S, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "From: 01/10/2017 To: 30/09/2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br><br>Update of section 4.8 of the SmPC for Fiasp to add "anaphylactic reactions" with a frequency "not known".<br><br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00002653/201809** (rivaroxaban) CAPS: **Xarelto** (EMEA/H/C/000944) (rivaroxaban), Bayer AG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, "From: 15/09/2017 To: 15/09/2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br><br>Update of section 4.8 of the SmPC to delete the footnote 'A: observed in prevention of VTE in adult patients undergoing elective hip or knee replacement surgery' is deleted for the adverse |

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| | drug reaction ‘renal impairment (incl. blood creatinine increased, blood urea increased)’. Update of section 3 of the Package Leaflet in order to move the statement ‘You must take Xarelto together with a meal’ before the statement ‘Swallow the tablet(s) preferably with water’ and the text is amended to stress the importance of this instruction.<br><br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010052/201809** (vortioxetine)<br>CAPS:<br>**Brintellix** (EMEA/H/C/002717) (vortioxetine), H. Lundbeck A/S, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Laurence de Fays, “From: 29/09/2017 To: 29/09/2018” | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br><br>Update of section 4.4 of the SmPC to change the class warning on haemorrhage accordingly, to add that haemorrhage has been reported with vortioxetine as well.<br><br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010055/201809** (alemtuzumab)<br>CAPS:<br>**Lemtrada** (EMEA/H/C/003718) (alemtuzumab), Sanofi Belgium, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, “13-Sep-2017 – 12-Sep-2018” | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br><br>Update of section 4.4 of the SmPC to add a warning on serious reactions temporally associated with LEMTRADA infusion including pulmonary alveolar haemorrhage, myocardial infarction, stroke (including ischaemic and haemorrhagic stroke), cervicocephalic (e.g. vertebral, carotid) arterial dissection, to add a warning on haemophagocytic lymphohistiocytosis and on autoimmune hepatitis and hepatic injury, and to revise a warning on use of alemtuzumab in patients with thyroid disorders.<br><br>Update of section 4.8 of the SmPC to add the adverse reactions pulmonary alveolar |

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| | haemorrhage, myocardial infarction, stroke (including ischaemic and haemorrhagic stroke), cervicocephalic (e.g. vertebral, carotid) arterial dissection with a frequency unknown, haemophagocytic lymphohistiocytosis with a frequency rare and neutropaenia with a frequency very common. The Package leaflet is updated accordingly.<br><br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010317/201809**<br>(naloxegol)<br>CAPS:<br>**Moventig** (EMEA/H/C/002810) (naloxegol), Kyowa Kirin Holdings B.V., Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ronan Grimes, "16-Mar-2018 – 15-Sept-2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br><br>Update of sections 4.4 and 4.8 of the SmPC to strengthen the warning on gastrointestinal perforation and add gastrointestinal perforation with a frequency 'not known'. The Package leaflet is updated accordingly.<br><br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010366/201809**<br>(naltrexone / bupropion)<br>CAPS:<br>**Mysimba** (EMEA/H/C/003687) (naltrexone hydrochloride / bupropion hydrochloride), Orexigen Therapeutics Ireland Limited, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber, "From: 10/09/2017 To: 09/09/2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br><br>Update of sections 4.4 and 4.7 to include a warning that naltrexone/bupropion may affect the ability to drive and section 4.8 of the SmPC to add somnolence and loss of consciousness as common and rare adverse reactions, respectively. The Package leaflet should be updated accordingly.<br><br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010480/201809**<br>(dexamethasone (centrally authorised product indicated in symptomatic multiple myeloma)) | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation |

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| CAPS:<br>**Neofordex** (EMEA/H/C/004071) (dexamethasone), Laboratoires CTRS, Rapporteur: Greg Markey, PRAC Rapporteur: Ghania Chamouni, “17-Sep-2017 – 16-Sep-2018” | and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br><br>Update of section 4.4 of the SmPC to add a warning on the risk of tumour lysis syndrome. The Package leaflet is updated accordingly.<br><br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010635/201809** (avelumab)<br>CAPS:<br>**Bavencio** (EMEA/H/C/004338) (avelumab), Merck Europe B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark, “From: 22/03/2018 To: 22/09/2018” | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br><br>Update of section 4.8 of the SmPC to add pancreatitis as an adverse drug reaction (ADR) with the frequency rare. Sections 4.2 and 4.4 are amended consequentially to add pancreatitis to the list of immune-related ADR. The package leaflet (PL) is updated accordingly. The MAH also took the opportunity to harmonise SmPC and PL to correct the wrong reference to sepsis in section 4 of the PL.<br><br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010637/201809** (trientine)<br>CAPS:<br>**Cuprior** (EMEA/H/C/004005) (trientine), GMP-Orphan SA, Rapporteur: Jayne Crowe, PRAC Rapporteur: Ana Sofia Diniz Martins, “06-Mar-2018 – 05-Sep-2018” | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 and Article 107g(3) of Directive 2001/83/EC the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus the variation to the terms of the marketing authorisation(s) for the medicinal products containing the above referred active substance(s), concerning the following change(s):<br><br>Update of section 4.9 of the SmPC to add the description of the symptoms and signs observed after an overdose case.<br><br>The Icelandic and the Norwegian CHMP members |

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| | agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010655/201809** (niraparib) CAPS: **Zejula** (EMEA/H/C/004249) (niraparib), Tesaro Bio Netherlands B.V., Rapporteur: Bjorg Bolstad, PRAC Rapporteur: Jan Neuhauser, "From: 25/03/2018 To: 25/09/2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended , recommends by consensus the variation to the terms of the marketing authorisation for the above mentioned medicinal product, concerning the following changes:<br><br>Update of section 4.8 of the SmPC to add the adverse drug reaction febrile neutropenia with the frequency uncommon.<br><br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |
| **EMEA/H/C/PSUSA/00010662/201809** (ocrelizumab) CAPS: **Ocrevus** (EMEA/H/C/004043) (ocrelizumab), Roche Registration GmbH, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Brigitte Keller-Stanislawski, "From: 27/03/2018 To: 27/09/2018" | The CHMP, having considered in accordance with Article 28 of Regulation (EC) No 726/2004 the PSUR on the basis of the PRAC recommendation and the PRAC assessment report as appended, recommends by consensus, the variation to the terms of the marketing authorisation(s) for the above mentioned medicinal product(s), concerning the following change(s):<br><br>To update the SmPC section 4.8 with regards to association between low Ig level and risk of serious infections.<br><br>The Icelandic and the Norwegian CHMP members agree with the above-mentioned recommendation of the CHMP. |

**B.4. EPARs / WPARs**

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| **Zynteglo - 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 (Netherlands) B.V, treatment of transfusion-dependent β-thalassaemia (TDT), New active substance (Article 8(3) of Directive No 2001/83/EC) | For information only. Comments can be sent to the EPL in case necessary. |

## B.5. TYPE II VARIATION, WORKSHARING PROCEDURE OUTCOMES

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

### B.5.1. CHMP assessed procedures scope: Pharmaceutical aspects

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| **Apealea - paclitaxel - EMEA/H/C/004154/II/0003/G**<br>Oasmia Pharmaceutical AB, Rapporteur: Bart Van der Schueren<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Benlysta - belimumab - EMEA/H/C/002015/II/0064/G**<br>GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder<br>Opinion adopted on 26.04.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Benlysta - belimumab - EMEA/H/C/002015/II/0068**<br>GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Benlysta - belimumab - EMEA/H/C/002015/II/0069/G**<br>GlaxoSmithKline (Ireland) Limited, Rapporteur: Kristina Dunder<br>Opinion adopted on 26.04.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Docetaxel Kabi - docetaxel - EMEA/H/C/002325/II/0022**<br>Fresenius Kabi Deutschland GmbH, Generic, Generic of Taxotere, Rapporteur: Alexandre Moreau<br>Request for Supplementary Information adopted on 11.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Entyvio - vedolizumab - EMEA/H/C/002782/II/0039**<br>Takeda Pharma A/S, Rapporteur: Daniela Melchiorri<br>Opinion adopted on 26.04.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Flixabi - infliximab - EMEA/H/C/004020/II/0031**<br>Samsung Bioepis NL B.V., Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 26.04.2019.<br>Request for Supplementary Information adopted on 27.09.2018. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| **Ilumetri - tildrakizumab - EMEA/H/C/004514/II/0005/G**<br>Almirall S.A, Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Lymphoseek - tilmanocept - EMEA/H/C/002085/II/0017**<br>Norgine B.V., Rapporteur: Jayne Crowe<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Nucala - mepolizumab - EMEA/H/C/003860/II/0023**<br>GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely<br>Opinion adopted on 26.04.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Orencia - abatacept - EMEA/H/C/000701/II/0125**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Outi Mäki-Ikola<br>Opinion adopted on 26.04.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Praxbind - idarucizumab - EMEA/H/C/003986/II/0014/G**<br>Boehringer Ingelheim International GmbH, Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 04.04.2019.<br>Request for Supplementary Information adopted on 14.02.2019. | Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Privigen - human normal immunoglobulin - EMEA/H/C/000831/II/0145**<br>CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **ProQuad - measles, mumps, rubella and varicella vaccine (live) - EMEA/H/C/000622/II/0132**<br>MSD Vaccins, Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 04.04.2019. | Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Repaglinide Accord - repaglinide - EMEA/H/C/002318/II/0009/G**<br>Accord Healthcare S.L.U., Generic, Generic of NovoNorm, Rapporteur: Agnes Gyurasics<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Repatha - evolocumab - EMEA/H/C/003766/II/0026/G** | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP |

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| Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 17.01.2019, 19.07.2018. | Members were in agreement with the CHMP recommendation. |
| **Simponi - golimumab - EMEA/H/C/000992/II/0087/G**<br>Janssen Biologics B.V., Rapporteur: Kristina Dunder<br>Opinion adopted on 26.04.2019.<br>Request for Supplementary Information adopted on 21.03.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Synagis - palivizumab - EMEA/H/C/000257/II/0118**<br>AbbVie Deutschland GmbH & Co. KG, Rapporteur: Mark Ainsworth<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 14.02.2019. | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **TachoSil - human thrombin / human fibrinogen - EMEA/H/C/000505/II/0092**<br>Takeda Austria GmbH, Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 26.04.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Trulicity - dulaglutide - EMEA/H/C/002825/II/0033**<br>Eli Lilly Nederland B.V., Rapporteur: Martina Weise<br>Opinion adopted on 04.04.2019.<br>Request for Supplementary Information adopted on 07.02.2019. | Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Tysabri - natalizumab - EMEA/H/C/000603/II/0113/G**<br>Biogen Netherlands B.V., Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 04.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Visudyne - verteporfin - EMEA/H/C/000305/II/0098/G**<br>Novartis Europharm Limited, Rapporteur: Alexandre Moreau<br>Request for Supplementary Information adopted on 04.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Zytiga - abiraterone acetate - EMEA/H/C/002321/II/0054/G**<br>Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez | Request for Supplementary Information adopted with a specific timetable. |

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| Request for Supplementary Information adopted on 26.04.2019, 14.02.2019. | |

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

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| **Aclasta - zoledronic acid - EMEA/H/C/000595/II/0072**<br>Novartis Europharm Limited, Rapporteur: Kristina Dunder, "Update of sections 4.2 and 5.1 upon request of the CHMP following assessment of P46/036 based on final results from study ZOL446H2337; this is a randomised, double-blind, placebo-controlled efficacy and safety study of intravenous zoledronic acid administered twice yearly compared to placebo in children with glucocorticoid-induced osteoporosis (GIO) which was part of the main clinical measure of the Aclasta Paediatric Investigational plan (PIP).<br>In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet."<br><br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Aranesp - darbepoetin alfa - EMEA/H/C/000332/II/0151**<br>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."<br>Request for Supplementary Information adopted on 04.04.2019.<br>Letter from the applicant dated 18.04.2019 requesting a clock stop extension. **For information.** | Request for Supplementary Information adopted with a specific timetable. |
| **AUBAGIO - teriflunomide - EMEA/H/C/002514/II/0022**<br>sanofi-aventis groupe, Rapporteur: Martina Weise, "Submission of the final report of the non-clinical 7 weeks repeated-dose oral juvenile toxicity study with 8 weeks recovery period in the rat (study no. JUV0024), which was earlier agreed in the PIP (EMEA-001094-PIP01-10)." | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| Opinion adopted on 26.04.2019. | |
| **Biktarvy - bictegravir / emtricitabine / tenofovir alafenamide - EMEA/H/C/004449/II/0011**<br>Gilead Sciences Ireland UC, Rapporteur: Joseph Emmerich, "Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information based on the pooling of 96-week data from two randomized, double-blind, active controlled studies GS-US-380-1489 and GS-US-380-1490 in HIV-1 infected, antiretroviral treatment-naïve adults receiving Biktarvy compared with each of the comparator treatment groups (i.e. pooled Biktarvy (BVY) vs abacavir /dolutegravir /lamivudine and pooled BVY vs dolutegravir + emtricitabine/tenofovir alafenamide).<br>In addition the Marketing authorisation holder (MAH) took the opportunity to introduce some minor linguistic amendments in the SmPC and the Package Leaflet"<br>Opinion adopted on 26.04.2019.<br>Request for Supplementary Information adopted on 28.03.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **CellCept - mycophenolate mofetil - EMEA/H/C/000082/II/0146**<br>Roche Registration GmbH, Rapporteur: Sinan B. Sarac, "Update of sections 4.7 and 4.8 of the SmPC to update the safety information based on the reassessment of all available evidence from clinical trials and post-marketing experience, in order to present adverse drug reactions (ADRs) rather than adverse events (AEs). Additionally, section 5.2 of the SmPC is updated based on current literature on the pharmacokinetics in geriatric patients. The Package Leaflet and Labelling are updated accordingly.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes throughout the PI and to bring the PI in line with the latest QRD template version 10."<br><br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Cerdelga - eliglustat - EMEA/H/C/003724/II/0021, Orphan**<br>Genzyme Europe BV, Rapporteur: Johann Lodewijk Hillege, "Submission of the final report from study PKM14281 , A Randomized, | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| Three-Period Crossover Study of Single and Repeated Doses for Three Different Strengths of Eliglustat in Healthy Adult, CYP2D6 Extensive and Poor Metabolizers, to characterize dose proportionality of 21, 42 and 84 mg eliglustat dosage strengths, in line with CHMP recommendation. Consequently section 5.2 of the Summary Product Characteristics (SmPC) was updated accordingly."<br>Opinion adopted on 26.04.2019.<br>Request for Supplementary Information adopted on 21.03.2019. | |
| **Cervarix - human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - EMEA/H/C/000721/II/0099**<br>GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, "Update of section 4.5 of the 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.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity update the package leaflet to correct inconsistencies related to the indication in males."<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 14.02.2019. | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Cyramza - ramucirumab - EMEA/H/C/002829/II/0030**<br>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 as common and rare, respectively based on review of clinical trials, post-marketing cases and the published scientific | Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| 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."<br>Opinion adopted on 04.04.2019. | |
| **Delstrigo - doravirine / lamivudine / tenofovir disoproxil - EMEA/H/C/004746/II/0003**<br>Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, "Update of section 5.1 of the SmPC in order to reflect the week-96 results from studies P021, a phase 3 multicenter, double-blind, randomized active comparator-controlled clinical trial to evaluate the safety and efficacy of doravirine/ /lamivudine/ tenofovir disoproxil fumarate once daily compared with efavirenz/emtricitabine/tenofovir disoproxil fumarate once daily in treatment-naïve HIV-1 infected patients, as well as the study P018, a phase 3 multicenter, double-blind, randomized, active-comparator-controlled trial to evaluate the safety, efficacy, and pharmacokinetics of doravirine compared with ritonavir-boosted darunavir, each given in combination with emtricitabine/ tenofovir disoproxil fumarate or abacavir/lamivudine, in treatment-naïve HIV-1 infected patients.<br>In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC."<br>Opinion adopted on 26.04.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Dynastat - parecoxib - EMEA/H/C/000381/II/0075**<br>Pfizer Europe MA EEIG, Duplicate, Duplicate of Xapit (SRD), Rapporteur: Jayne Crowe, "Update section 4.4 of the SmPC in regard of the co-administration of NSAIDs and antiplatelet drugs as a class, and the association with an increased risk of gastrointestinal bleeding. The opportunity has been taken for minor editorial amendments to be made in the SmPC, Labelling and Package Leaflet."<br>Opinion adopted on 04.04.2019.<br>Request for Supplementary Information adopted on 17.01.2019. | Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **ELOCTA - efmoroctocog alfa - EMEA/H/C/003964/II/0030**<br>Swedish Orphan Biovitrum AB (publ), | Request for Supplementary Information adopted with a specific timetable. |

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| Rapporteur: Jan Mueller-Berghaus, “Update of sections 4.2 and 4.8 of the SmPC in order to remove the class wording that no data are available in previously untreated patients and update the Frequency category for Blood and lymphatic system disorders in previously untreated patients following interim results from study 997HA306, this is an ongoing open-label, single-arm, multicentre study evaluating the safety and efficacy of rFVIIIFc in paediatric previously untreated patients with severe haemophilia A when used according to local standard of care; the Package Leaflet is updated accordingly.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to delete the non-mandatory list of local representatives.”<br>Request for Supplementary Information adopted on 04.04.2019, 31.01.2019. | |
| **Fasenra - benralizumab - EMEA/H/C/004433/II/0013**<br>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”<br>Request for Supplementary Information adopted on 11.04.2019, 14.02.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Kalydeco - ivacaftor - EMEA/H/C/002494/II/0076, Orphan**<br>Vertex Pharmaceuticals (Ireland) Limited, Rapporteur: Maria 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 (previously submitted in procedure II/54) and an additional mRNA analysis (report N052).”<br>Opinion adopted on 26.04.2019.<br>Request for Supplementary Information adopted on 28.02.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Lartruvo - olaratumab - EMEA/H/C/004216/II/0012, Orphan** | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP |

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| Eli Lilly Nederland B.V., Rapporteur: Jorge Camarero Jiménez, "Submission of the final report from Study 15B-EW-JGDI (JGDI) - An Open-Label Study to Evaluate the Pharmacokinetics of Doxorubicin Following the Concomitant Intravenous Administration of Olaratumab (IMC-3G3) to Patients with Advanced Soft Tissue Sarcoma."<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 13.12.2018. | Members were in agreement with the CHMP recommendation. |
| **Luminity - perflutren - EMEA/H/C/000654/II/0026**<br>Lantheus EU Limited, 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."<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 14.02.2019. | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Ongentys - opicapone - EMEA/H/C/002790/II/0015**<br>Bial - Portela & Cª, S.A., Rapporteur: Greg Markey, "Submission of the analytical data results on M10 in patients treated once daily for more than 6 months using a validated analytical method. This variation fulfills the commitment made in REC 002."<br>Opinion adopted on 04.04.2019.<br>Request for Supplementary Information adopted on 13.12.2018. | Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Orgalutran - ganirelix - EMEA/H/C/000274/II/0043**<br>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.<br>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."<br>Opinion adopted on 26.04.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Pifeltro - doravirine - EMEA/H/C/004747/II/0003** | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP |

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| Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, “Update of section 5.1 of the SmPC in order to reflect the week-96 results from studies P021, a phase 3 multicenter, double-blind, randomized active comparator-controlled clinical trial to evaluate the safety and efficacy of doravirine/ /lamivudine/ tenofovir disoproxil fumarate once daily compared with efavirenz/emtricitabine/tenofovir disoproxil fumarate once daily in treatment-naïve HIV-1 infected patients, as well as the study P018, a phase 3 multicenter, double-blind, randomized, active-comparator-controlled trial to evaluate the safety, efficacy, and pharmacokinetics of doravirine compared with ritonavir-boosted darunavir, each given in combination with emtricitabine/ tenofovir disoproxil fumarate or abacavir/lamivudine, in treatment-naïve HIV-1 infected patients.<br>In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC.”<br>Opinion adopted on 26.04.2019. | Members were in agreement with the CHMP recommendation. |
| **Rubraca - rucaparib - EMEA/H/C/004272/II/0009, Orphan**<br>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 a regulatory recommendation.”<br>Opinion adopted on 11.04.2019. | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Shingrix - herpes zoster vaccine (recombinant, adjuvanted) - EMEA/H/C/004336/II/0012**<br>GlaxoSmithkline Biologicals SA, Rapporteur: Bart Van der Schueren, “Update of section 4.8 of the SmPC in order to add "hypersensitivity reactions including rash, urticaria and angioedema" as an adverse drug reaction with frequency "rare". This update is based on data from clinical trials, literature and post-marketing surveillance reports.<br>The Package Leaflet is updated accordingly.”<br>Opinion adopted on 26.04.2019.<br>Request for Supplementary Information adopted on 14.03.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Strensiq - asfotase alfa - EMEA/H/C/003794/II/0035/G, Orphan** | Request for Supplementary Information adopted with a specific timetable. |

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| 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.”<br>Request for Supplementary Information adopted on 26.04.2019, 28.02.2019. | |
| **Telzir - fosamprenavir - EMEA/H/C/000534/II/0094/G**<br>ViiV Healthcare B.V., Rapporteur: Joseph Emmerich, “Update of sections 4.3 and 4.5 of the SmPC in order to implement information on a drug-drug interaction between fosamprenavir (with or without ritonavir) and the antipsychotic lurasidone and update of sections 4.4 and 4.5 of the SmPC in order to implement information on a drug-drug interaction between fosamprenavir (with or without ritonavir) and various antineoplastic agents (including dasatinib, nilotinib, ibrutinib, vinblastine, everolimus), based on an assessment of recent safety data. The drug-drug-interactions table in section 4.5 was also updated to remove active substances withdrawn from the market and to differentiate between tenofovir disoproxil and tenofovir alafenamide.<br>The Package Leaflet is updated accordingly.”<br>Opinion adopted on 26.04.2019.<br>Request for Supplementary Information adopted on 31.01.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Thyrogen - thyrotropin alfa - EMEA/H/C/000220/II/0102**<br>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 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 | Request for Supplementary Information adopted with a specific timetable. |

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| 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."<br>Request for Supplementary Information adopted on 26.04.2019. | |
| **Translarna - ataluren - EMEA/H/C/002720/II/0046, Orphan**<br>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."<br>Opinion adopted on 26.04.2019.<br>Request for Supplementary Information adopted on 28.02.2019, 20.09.2018. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Tyverb - lapatinib - EMEA/H/C/000795/II/0059**<br>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."<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Victoza - liraglutide - EMEA/H/C/001026/II/0050**<br>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."<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Xeloda - capecitabine - EMEA/H/C/000316/II/0081**<br>Roche Registration GmbH, Rapporteur: Janet | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP |

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| Koenig, “Update of sections 4.2, 4.4, 4.8 and 6.6 of the SmPC in relation to cutting or crushing of Xeloda tablets. The Package Leaflet is updated accordingly. In addition, the MAH is taking the opportunity to make some editorial changes to the Product Information.”<br>Opinion adopted on 26.04.2019.<br>Request for Supplementary Information adopted on 28.03.2019. | recommendation. |
| **Xeloda - capecitabine - EMEA/H/C/000316/II/0083**<br>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.”<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Xermelo - telotristat ethyl - EMEA/H/C/003937/II/0009, Orphan**<br>Ipsen Pharma, Rapporteur: Martina Weise, “Update of sections 4.2 and 5.2 of the SmPC in order to amend posology recommendations and add PK information in relation to 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.”<br>Opinion adopted on 26.04.2019.<br>Request for Supplementary Information adopted on 28.02.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **XGEVA - denosumab - EMEA/H/C/002173/II/0068**<br>Amgen Europe B.V., Rapporteur: Kristina Dunder, “Update of section 4.8 of the SmPC based on post-marketing experience to include the new ADR ‘lichenoid drug eruptions’ with a frequency category of ‘uncommon’. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in Ireland and Portugal in the Package Leaflet.”<br>Opinion adopted on 11.04.2019. | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Zinforo - ceftaroline fosamil -** | Positive Opinion adopted by consensus on |

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| **EMEA/H/C/002252/II/0042**<br>Pfizer Ireland Pharmaceuticals, Rapporteur: Alar Irs, "Update of section 4.8 of the SmPC to include revised frequency of the adverse drug reaction (ADR) eosinophilia from not known to rare. The Package leaflet is updated accordingly."<br>Opinion adopted on 26.04.2019.<br>Request for Supplementary Information adopted on 31.01.2019. | 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1429**<br>**Descovy-EMEA/H/C/004094/WS1429/0032**<br>**Genvoya-EMEA/H/C/004042/WS1429/0048**<br>**Odefsey-EMEA/H/C/004156/WS1429/0033**<br>Gilead Sciences Ireland UC, Lead Rapporteur: Greg Markey, "Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC of Descovy, Genvoya and Odefsey 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 Haemodialysis. The Package Leaflet is updated accordingly.<br>In addition, the Worksharing applicant (WSA) took the opportunity to remove boceprevir drug-drug interaction information in section 4.5 of the SmPC since this medicinal product has been withdrawn from the EU market, as well as to introduce some minor amendments throughout the product information of Descovy, Genvoya and Odefsey. The Package Leaflet is updated accordingly.<br>Moreover, the Package Leaflet of Genvoya and Odefsey have been updated regarding the lactose wording, as per the revised Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'; as well as an administrative correction to the Genvoya Package Leaflet in order to add "lurasidone" to the second list of contra-indicated drugs."<br>Opinion adopted on 26.04.2019.<br>Request for Supplementary Information adopted on 28.02.2019, 20.09.2018. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1506/G**<br>**Nuwiq-EMEA/H/C/002813/WS1506/0026** | Request for Supplementary Information adopted with a specific timetable. |

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| **/G**<br>**Vihuma-EMEA/H/C/004459/WS1506/0009/G**<br>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.”<br>Request for Supplementary Information adopted on 26.04.2019, 13.12.2018. | |
| **WS1523**<br>**Epclusa-EMEA/H/C/004210/WS1523/0031**<br>**Harvoni-EMEA/H/C/003850/WS1523/0072**<br>**Sovaldi-EMEA/H/C/002798/WS1523/0054**<br>**Vosevi-EMEA/H/C/004350/WS1523/0022**<br>Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, “Update of sections 4.3, 4.4 and 4.5 of the SmPC in order to 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.”<br>Request for Supplementary Information adopted on 26.04.2019, 14.02.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **WS1527/G**<br>**Cymbalta-EMEA/H/C/000572/WS1527/0078/G**<br>**Duloxetine Lilly-EMEA/H/C/004000/WS1527/0014/G**<br>**Xeristar-EMEA/H/C/000573/WS1527/0081/G**<br>**Yentreve-EMEA/H/C/000545/WS1527/0063/G**<br>Eli Lilly Nederland B.V., Duplicate, Duplicate of Ariclaim, Yentreve, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Maria del Pilar Rayon, “C.I.4 (Type II) - Update of sections 4.4 and 4.6 of the SmPC in order to add a warning on the risk of postpartum haemorrhage based on final results from study F1J-MC-B057 listed as a category 3 in the RMP; this is an observational study to assess maternal and foetal | Request for Supplementary Information adopted with a specific timetable. |

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| outcomes following exposure to duloxetine. The Package Leaflet is updated accordingly.<br>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 activity to address missing information regarding duloxetine exposure due to pregnancy.<br>The RMP version 13 has also been submitted.<br>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.<br>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).”<br>Request for Supplementary Information adopted on 11.04.2019. | |

### B.5.3. CHMP-PRAC assessed procedures

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| **Avastin - bevacizumab - EMEA/H/C/000582/II/0106/G**<br>Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Anette Kirstine Stark, “1) Type II Variation (C.I.4): Update of section 5.1 of the SmPC to reflect final overall survival data from the long-term follow-up study JO25567 in order to fulfil ANX 085 for study JO29424. Annex II.D and the RMP (ver 29.1) have been updated accordingly.<br>2) Type IB Variation (C.I.11.z): Change in the deadline for the fulfilment of ANX 086 from Q4 2018 to Q2 2019.<br>The RMP is submitted according to template Rev 2 and consolidates the approved versions (27.1 & 28.1).”<br>Opinion adopted on 26.04.2019.<br>Request for Supplementary Information adopted on 31.01.2019, 18.10.2018. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Flebogamma DIF - human normal immunoglobulin - EMEA/H/C/000781/II/0059/G** | Request for Supplementary Information adopted with a specific timetable. |

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| 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.<br>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.<br>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:<br>- Inclusion of Chronic inflammatory demyelinating polyneuropathy (CIDP) and Multifocal motor neuropathy (MMN) as new therapeutic indications<br>- Modification of Secondary immunodeficiencies (SID) therapeutic indication definition.<br>The Package Leaflet is updated accordingly. The RMP version 7.0 has also been submitted.”<br>Request for Supplementary Information adopted on 26.04.2019. | |
| **Hulio - adalimumab - EMEA/H/C/004429/II/0004**<br>Mylan S.A.S, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ulla Wändel Liminga, “Submission of the final report from study (FKB327-003) listed as a category 3 study in the RMP. This is an open-label extension study to compare the long term efficacy, safety, immunogenicity and pharmacokinetics of Hulio and Humira in patients with rheumatoid arthritis on concomitant methotrexate (ARABESC-OLE). The RMP version 2.0 is updated accordingly.”<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 17.01.2019. | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **IMVANEX - smallpox vaccine (live modified vaccinia virus ankara) - EMEA/H/C/002596/II/0036** | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP |

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| Bavarian Nordic A/S, Rapporteur: Greg Markey, PRAC Rapporteur: Julie Williams, “Update of sections 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 Annex II is updated accordingly. Minor consequential changes to section 4.4 of the SmPC are introduced and the Package Leaflet is updated accordingly. The RMP version 7.2 has also been submitted.”<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 14.02.2019, 04.10.2018. | recommendation. |
| **Intuniv - guanfacine - EMEA/H/C/003759/II/0015**<br>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);<br>The RMP version 3.0 has also been submitted.”<br>Request for Supplementary Information adopted on 11.04.2019, 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/0036**<br>GlaxoSmithkline Biologicals SA, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Jean-Michel Dogné, “Update of section 4.4 of the SmPC in order to indicate that protection against Plasmodium falciparum malaria wanes over time and vaccination may delay the acquisition of natural immunity. In addition, section 5.1 of the SmPC has been updated with long-term efficacy data. 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 | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| and immunogenicity of the GSK Biologicals' candidate malaria vaccine in infants and children. The RMP version 4.3 has also been submitted."<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 14.02.2019, 31.10.2018. | |
| **Movymia - teriparatide - EMEA/H/C/004368/II/0010**<br>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."<br>Request for Supplementary Information adopted on 11.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **OPDIVO - nivolumab - EMEA/H/C/003985/II/0060/G**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to include information from studies CA209171 (A Phase 2, single-arm, open-label, multicentre clinical trial with nivolumab monotherapy in subjects with advanced or metastatic squamous (Sq) cell non-small cell lung cancer (NSCLC) who have received at least one prior systemic regimen for the treatment of Stage IIIb/IV Sq NSCLC) and CA209172 (A Phase 2, single-arm, open-label, multicentre clinical trial with nivolumab monotherapy in subjects with histologically confirmed Stage III (unresectable) or Stage IV melanoma progressing after prior treatment containing an anti-CTLA-4 monoclonal antibody). In addition, the MAH takes the occasion to update Annex II to reflect already fulfilled requirement regarding biomarkers (ANX 005.3, ANX 006, ANX 023, ANX 024, ANX 026 and ANX 027). The RMP has been updated accordingly (final version 13.6)."<br>Opinion adopted on 26.04.2019.<br>Request for Supplementary Information adopted on 28.03.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Tecentriq - atezolizumab - EMEA/H/C/004143/II/0022** | Request for Supplementary Information adopted with a specific timetable. |

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| 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.<br>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.<br>Moreover, the due date for submission of RMP commitments and an Annex II condition are proposed to be updated.”<br>Request for Supplementary Information adopted on 26.04.2019. | |
| **Terrosa - teriparatide - EMEA/H/C/003916/II/0009**<br>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.”<br>Request for Supplementary Information adopted on 11.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **Uptravi - selexipag - EMEA/H/C/003774/II/0022**<br>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.<br>The RMP version 6.1 has also been submitted.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to correct minor | Request for Supplementary Information adopted with a specific timetable. |

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| discrepancies in the SmPC."<br>Request for Supplementary Information adopted on 11.04.2019, 14.02.2019. | |
| **Vimpat - lacosamide - EMEA/H/C/000863/II/0073/G**<br>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."<br>Request for Supplementary Information adopted on 11.04.2019, 14.02.2019, 04.10.2018. | Request for Supplementary Information adopted with a specific timetable. |
| **WS1490**<br>**IKERVIS-EMEA/H/C/002066/WS1490/0014**<br>**Verkazia-EMEA/H/C/004411/WS1490/0001**<br>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 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.<br>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 implement the latest QRD template and the safety features for IKERVIS."<br>Request for Supplementary Information adopted on 11.04.2019, 14.02.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **WS1518**<br>**Epclusa-EMEA/H/C/004210/WS1518/0034**<br>**Harvoni-EMEA/H/C/003850/WS1518/0077** | Request for Supplementary Information adopted with a specific timetable. |

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| **Sovaldi-EMEA/H/C/002798/WS1518/0055**<br>**Vosevi-EMEA/H/C/004350/WS1518/0025**<br>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.<br>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.<br>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.<br>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.<br>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.<br>The Package Leaflet is updated accordingly. The RMPs have also been submitted for each of the products in this work-sharing procedure."<br>Request for Supplementary Information adopted on 11.04.2019. | |

### B.5.4. PRAC assessed procedures

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| PRAC Led<br>**Adasuve - loxapine -**<br>**EMEA/H/C/002400/II/0030**<br>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 | Request for Supplementary Information adopted with a specific timetable. |

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| 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."<br>Request for Supplementary Information adopted on 11.04.2019. | |
| PRAC Led<br>**Bydureon - exenatide - EMEA/H/C/002020/II/0054**<br>AstraZeneca AB, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final study report, upon request by PRAC following the assessment of MEA 11.5, from study H8O-MC-B015 extension/ D5550R00003; 'Incidence of Pancreatic Malignancy and Thyroid Neoplasm in Type 2 Diabetes Mellitus Patients who Initiate Exenatide Compared to Other Antihyperglycemic Drugs', as well as the feasibility study 'Incidence of pancreatic cancer and thyroid neoplasm among type 2 diabetes patients who initiated Bydureon (exenatide) as compared with those who initiated other glucose lowering drugs'. An updated RMP (version 32) was agreed during the procedure."<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 17.01.2019. | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**Flixabi - infliximab - EMEA/H/C/004020/II/0039**<br>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)"<br>Request for Supplementary Information adopted on 11.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| PRAC Led<br>**Humira - adalimumab - EMEA/H/C/000481/II/0185**<br>AbbVie Deutschland GmbH & Co. KG, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of the final report | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| from The Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT) registry, an ongoing long-term observational cohort study initiated in Germany in 2001 by The German Society of Rheumatology to investigate the long-term safety, effectiveness, and costs of biologic therapies for rheumatoid arthritis, listed as a category 3 study in the RMP."<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 17.01.2019. | |
| PRAC Led<br>**Kengrexal - cangrelor - EMEA/H/C/003773/II/0015**<br>Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Amelia Cupelli, PRAC-CHMP liaison: Daniela Melchiorri, "Submission of an updated RMP (version 3.1) in order to revise the objectives, the safety concerns to address and the milestones for a study listed as category 3 in the RMP: a multicentre retrospective observational study of patients undergoing percutaneous coronary intervention (PCI) who receive cangrelor and transition to either clopidogrel, prasugrel or ticagrelo (ARCANGELO – Italian prospective study on cangrelor). The protocol synopsis of the PASS is included in the Annex to the RMP. In addition, the RMP and the list of safety concerns are revised in accordance with the GVP Module V guideline (rev. 2)."<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 14.03.2019, 14.02.2019, 06.09.2018. | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**Kyprolis - carfilzomib - EMEA/H/C/003790/II/0034, Orphan**<br>Amgen Europe B.V., Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Nikica Mirošević Skvrce, PRAC-CHMP liaison: Selma Arapovic Dzakula, "Update of the RMP (v.10.1) 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."<br>Opinion adopted on 11.04.2019. | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**Ozempic - semaglutide - EMEA/H/C/004174/II/0006** | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP |

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| Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Annika Folin, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 3.1 in order to reflect that final protocols for Studies NN9535-4447 and NN9535-4352 have been provided (included as milestones under 'additional pharmacovigilance activities' in the RMP). Further the RMP is updated in line with the new template in accordance with Guideline on GVP Module V – Risk management systems (Rev 2)."<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 14.02.2019. | recommendation. |
| PRAC Led<br>**Prolia - denosumab - EMEA/H/C/001120/II/0078/G**<br>Amgen Europe B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 27 in order to add a retrospective cohort database study as a new category 3 study, upon request by PRAC following the assessment of EMEA/H/C/PSUSA/000954/201709, in order to further characterize the potential increased risk of cerebrovascular events (e.g. stroke) and other serious cardiovascular events in subjects with osteoporosis. Further, the important identified and potential risks and missing information in the RMP have been updated in accordance with the Guideline on GVP Module V – Risk management systems (Rev 2)."<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 17.01.2019. | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**Prolia - denosumab - EMEA/H/C/001120/II/0081**<br>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 study objectives for the category 3 study 20090522 to include the study population 'men and women who receive denosumab with glucocorticoid exposure'. The amended protocol for study 20090522 has also been added to the appropriate annex of the RMP." | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| Opinion adopted on 11.04.2019. | |
| PRAC Led<br>**Remicade - infliximab - EMEA/H/C/000240/II/0218**<br>Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder,<br>"Submission of the final study report on Remicade for the RABBIT Cohort 2 portion of the registry.<br>Rheumatoide Arthritis - Beobachtung der Biologika-Therapie (RABBIT) is a German RA registry established as a prospective observational cohort study on the long-term safety and effectiveness of biologic disease-modifying anti-rheumatic drugs in patients with RA.<br>RMP (v19) was updated with the conclusion of the study. The MAH also revised the list of safety concerns in the RMP as requested in the assessment of LEG 156."<br>Request for Supplementary Information adopted on 11.04.2019, 17.01.2019. | Request for Supplementary Information adopted with a specific timetable. |
| PRAC Led<br>**Simponi - golimumab - EMEA/H/C/000992/II/0085**<br>Janssen Biologics B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder,<br>"Submission of the final report from study (CNTO148ART4002) listed as a category 3 study in the RMP. This is an observational phase 4 study using the Optum Research Database (ORD) to estimate the long-term safety profile in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) who are initiating Simponi treatment and/or other types of biologic and non-biologic treatments. In addition, the RMP (version 19.0) is updated to reflect the final study report from study CNTO148ART4002 and to revise the list of safety concerns in accordance with the GVP Module V guideline (rev. 2)."<br>Request for Supplementary Information adopted on 11.04.2019, 17.01.2019. | Request for Supplementary Information adopted with a specific timetable. |
| PRAC Led<br>**WS1510 Mirapexin-EMEA/H/C/000134/WS1510/0089** | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

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| **Sifrol-EMEA/H/C/000133/WS1510/0080**<br>Boehringer Ingelheim International GmbH, Lead Rapporteur: Mark Ainsworth, Lead PRAC Rapporteur: Anette Kirstine Stark, PRAC-CHMP liaison: Sinan B. Sarac, "To introduce RMP version 10.0, the RMP has been converted into the new RMP template as per GVP Module V Revision 2 (EMA/838713/2011 Rev 2). In addition, the applicant takes the opportunity to adapt the medical search strategies and data retrieval approach without any impact on the overall safety conclusion."<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 14.02.2019. | |
| PRAC Led<br>**WS1521**<br>**Kivexa-EMEA/H/C/000581/WS1521/0079**<br>**Trizivir-EMEA/H/C/000338/WS1521/0112**<br>**Ziagen-EMEA/H/C/000252/WS1521/0105**<br>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 and revision of the important identified /potential risk for abacavir containing products in accordance with the revised GVP on RMP version 2, based on the post-marketing data."<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 14.02.2019. | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| PRAC Led<br>**WS1568**<br>**Relvar Ellipta-EMEA/H/C/002673/WS1568/0043**<br>**Revinty Ellipta-EMEA/H/C/002745/WS1568/0041**<br>GlaxoSmithKline (Ireland) Limited, Lead Rapporteur: Maria Concepcion Prieto Yerro, Lead PRAC Rapporteur: Maria del Pilar Rayon, PRAC-CHMP liaison: Maria 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) by evaluating the effect of the inhaled | Request for Supplementary Information adopted with a specific timetable. |

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| corticosteroid fluticasone furoate (FF) on bone mineral density by comparing fluticasone furoate (FF)/vilanterol (VI) treatment with VI treatment in subjects with moderate COPD."<br>Request for Supplementary Information adopted on 11.04.2019. | |

### B.5.5. CHMP-CAT assessed procedures

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| **YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0003, Orphan, ATMP**<br>Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus, "Update of sections 4.8 and 5.1 of the SmPC based on the 24-month data analysis of a Phase 1/2 Multicenter Study Evaluating the Safety and Efficacy of KTE-C19 in Subjects with Refractory Aggressive Non-Hodgkin Lymphoma (ZUMA-1). The Package Leaflet has been updated accordingly. Additionally, section 5.2 of the SmPC has been updated with further information on the kinetics and persistence of CAR-T cells. Furthermore, editorial changes have been introduced throughout the PI."<br>Opinion adopted on 26.04.2019, 17.04.2019.<br>Request for Supplementary Information adopted on 22.03.2019, 25.01.2019. | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0006, Orphan, ATMP**<br>Kite Pharma EU B.V., Rapporteur: Jan Mueller-Berghaus, CHMP Coordinator: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 17.04.2019. | Request for Supplementary Information adopted with a specific timetable. |

### B.5.6. CHMP-PRAC-CAT assessed procedures

### B.5.7. PRAC assessed ATMP procedures

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

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| **WS1493/G**<br>**Rivastigmine 1A Pharma-EMEA/H/C/001181/WS1493/0025/G** | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP |

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| **Rivastigmine Hexal-EMEA/H/C/001182/WS1493/0026/G**<br>**Rivastigmine Sandoz-EMEA/H/C/001183/WS1493/0027/G**<br>Hexal AG, Informed Consent of Exelon, Lead Rapporteur: Alexandre Moreau<br>Opinion adopted on 26.04.2019.<br>Request for Supplementary Information adopted on 24.01.2019. | recommendation. |
| **WS1498/G**<br>**Infanrix hexa-EMEA/H/C/000296/WS1498/0252/G**<br>GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren<br>Opinion adopted on 04.04.2019. | Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1525**<br>**Hexacima-EMEA/H/C/002702/WS1525/0086**<br>**Hexaxim-EMEA/H/W/002495/WS1525/0091**<br>**Hexyon-EMEA/H/C/002796/WS1525/0090**<br>Sanofi Pasteur Europe, Duplicate, Duplicate of Hexacima, Lead Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 11.04.2019.<br>Request for Supplementary Information adopted on 14.02.2019. | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1564**<br>**Fiasp-EMEA/H/C/004046/WS1564/0011**<br>**NovoMix-EMEA/H/C/000308/WS1564/0097**<br>**NovoRapid-EMEA/H/C/000258/WS1564/0125**<br>**Ryzodeg-EMEA/H/C/002499/WS1564/0031**<br>Novo Nordisk A/S, Lead Rapporteur: Kristina Dunder<br>Opinion adopted on 04.04.2019. | Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1571**<br>**Keppra-EMEA/H/C/000277/WS1571/0174**<br>UCB Pharma S.A., Lead Rapporteur: Koenraad Norga<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **WS1578**<br>**M-M-RVAXPRO-EMEA/H/C/000604/WS1578/0093** | Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP |

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| **ProQuad-EMEA/H/C/000622/WS1578/0131**<br>MSD Vaccins, Lead Rapporteur: Jan Mueller-Berghaus<br>Opinion adopted on 04.04.2019. | recommendation. |
| **WS1579**<br>**Axura-EMEA/H/C/000378/WS1579/0081**<br>**Memantine Merz-EMEA/H/C/002711/WS1579/0017**<br>Merz Pharmaceuticals GmbH, Lead Rapporteur: Maria Concepcion Prieto Yerro<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **WS1580**<br>**Juluca-EMEA/H/C/004427/WS1580/0012**<br>**Tivicay-EMEA/H/C/002753/WS1580/0046**<br>ViiV Healthcare B.V., Lead Rapporteur: Filip Josephson<br>Opinion adopted on 11.04.2019. | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **WS1584**<br>**Nuwiq-EMEA/H/C/002813/WS1584/0029**<br>**Vihuma-EMEA/H/C/004459/WS1584/0011**<br>Octapharma AB, Lead Rapporteur: Jan Mueller-Berghaus<br>Request for Supplementary Information adopted on 26.04.2019. | Request for Supplementary Information adopted with a specific timetable. |
| **WS1604**<br>**Filgrastim Hexal-EMEA/H/C/000918/WS1604/0048**<br>**Zarzio-EMEA/H/C/000917/WS1604/0049**<br>Hexal AG, Duplicate, Duplicate of Zarzio, Lead Rapporteur: Johann Lodewijk Hillege<br>Opinion adopted on 04.04.2019. | Positive Opinion adopted by consensus on 04.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Mosquirix-EMEA/H/W/002300/WS1556/0040/G**<br>**Shingrix-EMEA/H/C/004336/WS1556/0014/G**<br>GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren<br>Opinion adopted on 11.04.2019. | Positive Opinion adopted by consensus on 11.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |
| **Hexacima-EMEA/H/C/002702/WS1574/0087**<br>**Hexaxim-EMEA/H/W/002495/WS1574/0092**<br>**Hexyon-EMEA/H/C/002796/WS1574/0091** | Positive Opinion adopted by consensus on 26.04.2019. The Icelandic and Norwegian CHMP Members were in agreement with the CHMP recommendation. |

Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus
Opinion adopted on 26.04.2019.

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

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| PRAC Led<br>**OPDIVO - nivolumab -**<br>**EMEA/H/C/003985/II/0062**<br>Bristol-Myers Squibb Pharma EEIG, Rapporteur: Jorge Camarero Jiménez, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus<br>Withdrawal request submitted on 03.04.2019. | The MAH withdrew the procedure on 03.04.2019. |

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

## B.6. START OF THE PROCEDURES TIMETABLES FOR INFORMATION

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

### 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

**dapagliflozin / saxagliptin / metformin hydrochloride - EMEA/H/C/004910**
to improve glycaemic control when metformin with or without sulphonylurea (SU) does not provide adequate glycaemic control and where simultaneous addition of dapagliflozin and saxagliptin is considered necessary - to improve glycaemic control when metformin with or without sulphonylurea (SU) and either dapagliflozin or saxagliptin does not provide adequate glycaemic control - when already being treated with dapagliflozin and saxagliptin and metformin.
List of Questions adopted on 15.11.2018.

**deferasirox - EMEA/H/C/005014**
treatment of chronic iron overload,
List of Questions adopted on 15.11.2018.

**erlotinib - EMEA/H/C/005071**
treatment of lung and pancreatic cancers
List of Questions adopted on 13.12.2018.

**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
List of Questions adopted on 20.09.2018.

**levodopa - EMEA/H/C/004786**
treatment of symptoms of OFF periods in Parkinson's disease
List of Questions adopted on 20.09.2018.

**siponimod - EMEA/H/C/004712**
treatment of secondary progressive multiple sclerosis (SPMS)
List of Questions adopted on 31.01.2019.

**Nucala - mepolizumab - EMEA/H/C/003860/X/0018**
GlaxoSmithKline Trading Services Limited, Rapporteur: Peter Kiely, PRAC Rapporteur: Brigitte Keller-Stanislawski, "Extension application to introduce a new pharmaceutical form, solution for injection (in pre-filled syringe or in pre-filled pen)."
List of Questions adopted on 31.01.2019.

**delafloxacin - EMEA/H/C/004860**
treatment of Acute Bacterial Skin and Skin Structure Infection (ABSSSI) in adults
List of Questions adopted on 20.09.2018.

**Tecentriq - atezolizumab - EMEA/H/C/004143/X/0017**
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, Co-Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Extension application to add a new strength of 840 mg (60 mg/ml) for Tecentriq concentrate for solution for infusion in a vial and a new indication (metastatic triple-negative breast cancer (TNBC)). The new indication applies only to the 840mg strength."
List of Questions adopted on 31.01.2019.
Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004)

**tigecycline - EMEA/H/C/005114**
Treatment of soft tissue and intra-abdominal infections
- complicated skin and soft tissue infections, excluding diabetic foot infections
- complicated intra-abdominal infections

should be used only in situations where it is known or suspected that other alternatives are not suitable
List of Questions adopted on 13.12.2018.

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

**Evoltra - clofarabine - EMEA/H/C/000613/S/0063**
Genzyme Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni

**Firdapse - amifampridine - EMEA/H/C/001032/S/0064, Orphan**
BioMarin International Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Ulla Wändel Liminga

**Lamzede - velmanase alfa - EMEA/H/C/003922/S/0004, Orphan**
Chiesi Farmaceutici S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Jan Neuhauser

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

**Cosentyx - secukinumab - EMEA/H/C/003729/R/0050**
Novartis Europharm Limited, Rapporteur: Tuomo Lapveteläinen, Co-Rapporteur: Kristina Dunder, PRAC Rapporteur: Eva A. Segovia

**Duavive - estrogens conjugated / bazedoxifene - EMEA/H/C/002314/R/0021**
Pfizer Europe MA EEIG, Rapporteur: Martina Weise, Co-Rapporteur: Mark Ainsworth, PRAC Rapporteur: Martin Huber

**Firdapse - amifampridine - EMEA/H/C/001032/R/0062, Orphan**
BioMarin International Limited, Rapporteur: Kristina Dunder, Co-Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Ulla Wändel Liminga

**Lynparza - olaparib - EMEA/H/C/003726/R/0029**
AstraZeneca AB, Rapporteur: Alexandre Moreau, Co-Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Amelia Cupelli

**Otezla - apremilast -**

**EMEA/H/C/003746/R/0027**
Celgene Europe BV, Rapporteur: Peter Kiely, Co-Rapporteur: Janet Koenig, PRAC Rapporteur: Eva A. Segovia

**Rasagiline ratiopharm - rasagiline - EMEA/H/C/003957/R/0014**
Teva B.V., Rapporteur: Bruno Sepodes, Co-Rapporteur: Jayne Crowe, PRAC Rapporteur: Ana Sofia Diniz Martins

**Rixubis - nonacog gamma - EMEA/H/C/003771/R/0029**
Baxalta Innovations GmbH, Rapporteur: Andrea Laslop, Co-Rapporteur: Alexandre Moreau, PRAC Rapporteur: Brigitte Keller-Stanislawski

**Trevicta - paliperidone - EMEA/H/C/004066/R/0022**
Janssen-Cilag International NV, Informed Consent of Xeplion, Rapporteur: Kristina Dunder, Co-Rapporteur: Martina Weise, PRAC Rapporteur: Ulla Wändel Liminga

**Zalmoxis - nalotimagene carmaleucel - EMEA/H/C/002801/R/0015, Orphan, ATMP**
MolMed S.p.A, Rapporteur: Johannes Hendrikus Ovelgonne, Co-Rapporteur: Sol Ruiz, CHMP Coordinators: Paula Boudewina van Hennik and Maria Concepcion Prieto Yerro, PRAC Rapporteur: Brigitte Keller-Stanislawski

### 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

**Dupixent - dupilumab - EMEA/H/C/004390/II/0017**
sanofi-aventis groupe, Rapporteur: Jan Mueller-Berghaus, Co-Rapporteur: Peter Kiely, PRAC Rapporteur: Kimmo Jaakkola, “Extension of indication to include a new indication in adults patients with chronic rhinosinusitis with nasal polyposis. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. An updated RMP is submitted (V 4.0)”

**OFEV - nintedanib - EMEA/H/C/003821/II/0026, Orphan**
Boehringer Ingelheim International GmbH,

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| Rapporteur: Jayne Crowe, Co-Rapporteur: Ewa Balkowiec Iskra, PRAC Rapporteur: Nikica Mirošević Skvrce, “Extension of indication to include new indication for OFEV for the treatment of Systemic Sclerosis associated Interstitial Lung Disease (SSc-ILD).<br>As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The MAH takes this opportunity to also introduce minor<br>linguistic corrections to the Annexes for France and Sweden. The RMP version 7.0 has also been submitted.”<br>Request for 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004) | |
| **Suliqua - insulin glargine / lixisenatide - EMEA/H/C/004243/II/0011**<br>sanofi-aventis groupe, Rapporteur: Kristina Dunder, PRAC Rapporteur: Menno van der Elst, “Extension of indication to include treatment in combination with metformin of adults with type 2 diabetes mellitus to improve glycaemic control when this has not been provided by metformin alone or metformin combined with another oral glucose lowering medicinal product or basal insulin, based on the phase 3 Study EFC13794; a 26-week randomized, open-label, active controlled, parallel-group, study assessing the efficacy and safety of the insulin glargine/lixisenatide fixed ratio combination in adults with Type 2 Diabetes inadequately controlled on GLP-1 receptor agonist and metformin (alone or with pioglitazone and/or SGLT2 inhibitors), followed by a fixed ratio combination single-arm 26-week extension period.<br>As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated and the Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to update the contact details of the local representatives in Denmark, the Netherlands and the UK in the Package Leaflet and to implement minor editorial changes in the annexes. An updated RMP version 4.0 was provided as part of the application.” | |

**Toujeo - insulin glargine -**
**EMEA/H/C/000309/II/0108**
Sanofi-Aventis Deutschland GmbH, Duplicate, Duplicate of Lantus, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, “Extension of indication to include new population for Toujeo. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.”

**WS1550**
**Docetaxel Zentiva-EMEA/H/C/000808/WS1550/0058**
**Taxotere-EMEA/H/C/000073/WS1550/0131**
Aventis Pharma S.A., Lead Rapporteur: Alexandre Moreau, Lead Co-Rapporteur: Janet Koenig, Lead PRAC Rapporteur: Ghania Chamouni, “Extension of indication to include in combination with androgen-deprivation therapy (ADT), with or without prednisone or prednisolone, for the treatment of patients with metastatic hormone-sensitive prostate cancer for Taxotere and Docetaxel Zentiva; as a consequence, sections 4.1, 4.2, 4.4 and 4.8 of the SmPC are updated. The Package Leaflet is updated accordingly. The RMP version has also been submitted. In addition, the Worksharing applicant took the opportunity to update information impacting the local representatives in the packages leaflets.”

### B.6.8. CHMP assessed procedures scope: Pharmaceutical aspects

**Adcetris - brentuximab vedotin -**
**EMEA/H/C/002455/II/0066, Orphan**
Takeda Pharma A/S, Rapporteur: Paula Boudewina van Hennik

**BeneFIX - nonacog alfa -**
**EMEA/H/C/000139/II/0160**
Pfizer Europe MA EEIG, Rapporteur: Jan Mueller-Berghaus

**Hemoblast - thrombin -**
**EMEA/H/D/002769/II/0006/G**
BSI Group, Rapporteur: Daniela Melchiorri

**Hulio - adalimumab -**
**EMEA/H/C/004429/II/0010/G**
Mylan S.A.S, Rapporteur: Bart Van der Schueren

**Keppra - levetiracetam -**
**EMEA/H/C/000277/II/0178/G**
UCB Pharma S.A., Rapporteur: Koenraad Norga

**Keytruda - pembrolizumab -**
**EMEA/H/C/003820/II/0073**
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri

**Nulojix - belatacept -**
**EMEA/H/C/002098/II/0059/G**
Bristol-Myers Squibb Pharma EEIG, Rapporteur: Filip Josephson

**Ogivri - trastuzumab -**
**EMEA/H/C/004916/II/0006/G**
MYLAN S.A.S, Rapporteur: Koenraad Norga

**Onpattro - patisiran -**
**EMEA/H/C/004699/II/0004/G, Orphan**
Alnylam Netherlands B.V., Rapporteur: Kristina Dunder

**Ovitrelle - choriogonadotropin alfa -**
**EMEA/H/C/000320/II/0078**
Merck Europe B.V., Rapporteur: Paula Boudewina van Hennik

**Thyrogen - thyrotropin alfa -**
**EMEA/H/C/000220/II/0104/G**
Genzyme Europe BV, Rapporteur: Peter Kiely

**Zessly - infliximab -**
**EMEA/H/C/004647/II/0007**
Sandoz GmbH, Rapporteur: Bjorg Bolstad

**Zytiga - abiraterone acetate -**
**EMEA/H/C/002321/II/0056/G**
Janssen-Cilag International NV, Rapporteur: Jorge Camarero Jiménez

**WS1620**
**Humalog-EMEA/H/C/000088/WS1620/0175**
**Liprolog-EMEA/H/C/000393/WS1620/0136**
Eli Lilly Nederland B.V., Lead Rapporteur: Kristina Dunder

**WS1625/G**
**Blitzima-EMEA/H/C/004723/WS1625/0025/G**
**Ritemvia-EMEA/H/C/004725/WS1625/0025/G**
**Truxima-EMEA/H/C/004112/WS1625/**

**0028/G**
Celltrion Healthcare Hungary Kft., Lead Rapporteur: Sol Ruiz

**Hexacima-EMEA/H/C/002702/WS1575/0088/G**
**Hexaxim-EMEA/H/W/002495/WS1575/0093/G**
**Hexyon-EMEA/H/C/002796/WS1575/0092/G**
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

**Hexacima-EMEA/H/C/002702/WS1592/0089/G**
**Hexaxim-EMEA/H/W/002495/WS1592/0094/G**
**Hexyon-EMEA/H/C/002796/WS1592/0093/G**
Sanofi Pasteur, Lead Rapporteur: Jan Mueller-Berghaus

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

**Advagraf - tacrolimus - EMEA/H/C/000712/II/0054**
Astellas Pharma Europe B.V., Rapporteur: Jayne Crowe, “Update of section 4.2 of the SmPC to include a more clear statement for physicians regarding the potential risk of uncontrolled substitution between different tacrolimus formulations, even with those where BE has been proven, in order to minimise the risk of under or over exposure to tacrolimus.”

**Brilique - ticagrelor - EMEA/H/C/001241/II/0044**
AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.4 of the SmPC in order to add a warning on Thrombotic Thrombocytopenic Purpura (TTP) and update of section 4.8 of the SmPC to include TTP as new adverse drug reaction with a frequency ‘unknown’, based on a safety review. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make some formatting corrections throughout the product information.”

**Brilique - ticagrelor - EMEA/H/C/001241/II/0045**

AstraZeneca AB, Rapporteur: Johann Lodewijk Hillege, “Update of section 4.4 of the SmPC in order to add a new warning on interference with laboratories tests regarding platelet function tests to diagnose heparin induced thrombocytopenia (HIT) based on as safety review.”

**Elonva - corifollitropin alfa - EMEA/H/C/001106/II/0046**

Merck Sharp & Dohme B.V., Rapporteur: Paula Boudewina van Hennik, “Update of sections 4.3, 4.4 and 4.9 of the SmPC in order to revise the current text regarding Ovarian Hyperstimulation Syndrome (OHSS) to add clarity and remove clinical advice describing specific clinical interventions for reducing OHSS that have become outdated, based on post-marketing data and literature review. The Package Leaflet is updated accordingly.
In addition, the Marketing authorisation holder to include some editorial changes to the Package Leaflet.”

**EXJADE - deferasirox - EMEA/H/C/000670/II/0066**

Novartis Europharm Limited, Rapporteur: Alexandre Moreau, “To update the Exjade SmPC (Section 5.1) to reflect the results of clinical study CICL670A2302 (TELESTO) with Exjade in patients with myelodysplatic syndrome (MDS).”

**Exviera - dasabuvir - EMEA/H/C/003837/II/0044**

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, “Update of section 4.3 of the SmPC to contraindicate the concomitant use with apalutamide, a strong CYP3A inducer, as well as to update section 4.5 of the SmPC on the interaction with apalutamide based on approved product information. The Package Leaflet is updated accordingly.”

**Eylea - aflibercept - EMEA/H/C/002392/II/0052**

Bayer AG, Rapporteur: Alexandre Moreau, “Update of section 5.1 of the SmPC in order to reflect the final results from ALTAIR (SN17668) study; this is a randomized, open-label phase 4 study evaluating the efficacy and safety of repeated doses of intravitreal aflibercept with variable treatment intervals in Japanese subjects with neovascular age-related macular

degeneration. In addition, the Marketing authorisation holder (MAH) took the opportunity to include minor editorial changes in section 5.1 of the SmPC."

**IDELVION - albutrepenonacog alfa - EMEA/H/C/003955/II/0027, Orphan**
CSL Behring GmbH, Rapporteur: Jan Mueller-Berghaus, "Update of section 4.4 of the SmPC to update the warning with regards to inhibitor development. Section 4.8 of the SmPC and the PL have been updated accordingly."

**Keytruda - pembrolizumab - EMEA/H/C/003820/II/0074**
Merck Sharp & Dohme B.V., Rapporteur: Daniela Melchiorri, "Submission of the final CSR version 03 for KEYNOTE-013 summarising final data from the rrcHL cohort."

**Repatha - evolocumab - EMEA/H/C/003766/II/0033**
Amgen Europe B.V., Rapporteur: Johann Lodewijk Hillege, "Update of section 4.8 of the SmPC in order to update the safety information with regards to the adverse reaction "Influenza-like illness" with a frequency of Uncommon following the assessment of influenza-like illness with evolocumab in both the clinical database and postmarketing database. The Package Leaflet Section 4 was updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement changes to the package leaflet Section 2 subsequent to the revised Annex to the EC guideline on excipients in the labelling (EMA/CHMP/302620/2017) to update the wording for sodium."

**Saxenda - liraglutide - EMEA/H/C/003780/II/0023**
Novo Nordisk A/S, Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information regarding hypoglycaemia in patients with type 2 diabetes mellitus treated with insulin based on the final results from the Phase 3b clinical trial NN8022-4272 (SCALE Insulin), undertaken to investigate the effect and safety of liraglutide 3.0 mg in subjects with overweight or obesity and type 2 diabetes mellitus treated with basal insulin. The Package Leaflet is updated

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| accordingly.” | |
| **Sutent - sunitinib - EMEA/H/C/000687/II/0074**<br>Pfizer Europe MA EEIG, Rapporteur: Daniela Melchiorri, “Submission of the final analyses of the overall survival data, and the additional biomarker analyses collected from Study A6181202 (multi-centre, single-arm, open-label, Phase 4 clinical trial of sunitinib in patients with progressive, advanced/metastatic, well-differentiated, unresectable pancreatic neuroendocrine tumours (pNET)).” | |
| **Symtuza - darunavir / cobicistat / emtricitabine / tenofovir alafenamide - EMEA/H/C/004391/II/0017/G**<br>Janssen-Cilag International N.V., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Ana Sofia Diniz Martins, “Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to update the safety information based on week-96 results from studies TMC114FD2HTX3001 (AMBER) “A Phase 3, randomized, active-controlled, double-blind study to evaluate efficacy and safety of D/C/F/TAF once daily fixed-dose combination regimen versus a regimen consisting of DRV/COBI FDC co-administered with FTC/TDF FDC in ARV treatment-naïve HIV-1 infected subjects”, and study TMC114IFD3013 (EMERALD)) “A Phase 3, randomized, active-controlled, open-label study to evaluate switching to a D/C/F/TAF once-daily single-tablet regimen versus continuing the current regimen consisting of a boosted protease inhibitor combined with FTC/TDF in virologically-suppressed, HIV-1 infected subjects.”, both listed as category 3 studies in the RMP. The Package Leaflet is updated accordingly. The RMP version 5.0 (in version 2 of the RMP template) has also been submitted to reflect the study results and revise due dates for category 3 studies GS-US-311-1717 and GS-US-292-0109.<br>In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 4.2 of the SmPC and Package Leaflet to include advice in the event of vomiting in line with the approved Genvoya SmPC, make minor editorial changes in the SmPC; as well as to update the list of local representatives in the Package Leaflet in | |

line with the latest QRD template version 10.0."

**Taltz - ixekizumab - EMEA/H/C/003943/II/0026/G**

Eli Lilly Nederland B.V., Rapporteur: Kristina Dunder, "Type II- C.I.4 -Update of section 5.1 of the SmPC based on results of study RHCF - a 52-Week Multicenter, Randomized, Open-Label, Parallel-Group Study Evaluating the Efficacy and Safety of Ixekizumab versus Adalimumab in Patients with Psoriatic Arthritis Who Are Biologic Disease-Modifying Anti-Rheumatic Drug Naïve. Type II- C.I.4 -Update of section 4.5 of the SmPC based on results of study RHBU – a study evaluating of the effect of ixekizumab on the pharmacokinetics of cytochrome P450 substrates in patients with moderate-to-severe plaque psoriasis."

**Verzenios - abemaciclib - EMEA/H/C/004302/II/0003**

Eli Lilly Nederland B.V., Rapporteur: Filip Josephson, "Update of section 4.2 of the SmPC in order to add a criterion for discontinuing abemaciclib in the event of specific hepatic changes based on available safety data.
In addition, the Marketing authorisation holder (MAH) took the opportunity to make editorial changes to section 5.1 of the SmPC."

**Viekirax - ombitasvir / paritaprevir / ritonavir - EMEA/H/C/003839/II/0053**

AbbVie Deutschland GmbH & Co. KG, Rapporteur: Filip Josephson, "Update of section 4.3 of the SmPC to contraindicate the concomitant use with lomitapide, a CYP3A4 substrate, and apalutamide, a strong CYP3A inducer, as well as to update section 4.5 of the SmPC on the potential interactions with apalutamide, encorafenib, ibrutinib and lomitapide based on approved product informations. The Package Leaflet is updated accordingly."

**XALKORI - crizotinib - EMEA/H/C/002489/II/0062**

Pfizer Europe MA EEIG, Rapporteur: Alexandre Moreau, "Submission of the review of the PK profile of the crizotinib lactam metabolite, PF-06260182 in subjects or patients treated with single agent crizotinib, and discussion of the clinical relevance of these findings derived from the following reports: A8081001, A8081002,

A8081005, A8081006, A8081007, A8081012, A8081014 and A8081020, in order to fulfill a CHMP recommendation. Based on the data discussed as part of this variation, no update of the SmPC is warranted."

**XGEVA - denosumab - EMEA/H/C/002173/II/0069**

Amgen Europe B.V., Rapporteur: Kristina Dunder, "Update of SmPC sections 4.2, 4.8, 5.1 and 5.2 based on the final analysis from study 20062004; a phase 2, open-label, single-group study to evaluate the safety and pharmacokinetics of denosumab in adult and adolescent subjects with giant cell tumour of bone (GCTB). The final CSR for study 20062004 was previously assessed by CHMP as part of procedure P46 027 and the finalisation of the study addresses the final PIP measure. Further, section 4.8 of the SmPC is being updated to include the new ADR 'alopecia' with a frequency of 'common', upon request by PRAC following the assessment of PSUSA/00009119/201809. In addition, the MAH took the opportunity to update the description of ONJ incidence in section 4.8 of the SmPC in order to express events per 100 patient years without a percentage sign. The Package Leaflet has been updated accordingly."

**WS1588**
**Aluvia-EMEA/H/W/000764/WS1588/0109**
**Kaletra-EMEA/H/C/000368/WS1588/0177**
**Norvir-EMEA/H/C/000127/WS1588/0154**

AbbVie Deutschland GmbH & Co. KG, Lead Rapporteur: Johann Lodewijk Hillege, "Update of sections 4.3 and 4.5 of the SmPC in order to include information on the contraindication with neratinib and interactions with abemaciclib, neratinib, glecaprevir/pibrentasvir. In addition, the Worksharing applicant (WSA) took the opportunity to update section 4.5 of the Kaletra and Aluvia SmPCs to add information on the interaction of lopinavir/ritonavir with sofosbuvir/velpatasvir/voxilaprevir. The Package Leaflets are updated accordingly."

**WS1598**
**Cymbalta-EMEA/H/C/000572/WS1598/0079**
**Duloxetine Lilly-EMEA/H/C/004000/WS1598/0016**
**Xeristar-EMEA/H/C/000573/WS1598/**

**0082**

**Yentreve-EMEA/H/C/000545/WS1598/0064**

Eli Lilly Nederland B.V., Duplicate, Duplicate of Ariclaim, Yentreve, Lead Rapporteur: Maria Concepcion Prieto Yerro, “Update of section 5.1 to reflect on the data obtained from the paediatric study HMGW, submitted the final report for the paediatric Study HMGW, a Phase 3b, Randomised, Double-Blind, Placebo-Controlled, Clinical Trial of Duloxetine in adolescent Juvenile Primary Fibromyalgia Syndrome (JPFS) population.”

**WS1613**

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

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

Gilead Sciences Ireland UC, Lead Rapporteur: Filip Josephson, “Update of section 4.5 of the SmPC in order to add new information regarding co-administration with atorvastatin, based on final results from study GS-US-342-4034.
Study GS-US-342-4034 was a phase 1 study to evaluate the effect of sofosbuvir/velpatasvir fixed dose combination on the pharmacokinetics of atorvastatin.
The Package Leaflet is updated accordingly.
In addition, the Worksharing Applicant took the opportunity to amend Annex II of the Product Information with regards to the due date for submission of study DAA-PASS. This study is designed to evaluate the recurrence of hepatocellular carcinoma and the date has been postponed from Q2 2021 to Q2 2023, as approved in the framework of WS1476.
Furthermore, the MAH implemented minor editorial updates throughout the Product Information.”

**WS1617**

**Filgrastim Hexal-EMEA/H/C/000918/WS1617/0050**

**Zarzio-EMEA/H/C/000917/WS1617/0051**

Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege, “Update of sections 4.4 and 6.6 of the SmPC in order to remove the latex warning based on company and post marketing data. The Package Leaflet is updated accordingly.”

### B.6.10. CHMP-PRAC assessed procedures

**Brinavess - vernakalant - EMEA/H/C/001215/II/0035**

Correvio, Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Menno van der Elst, “Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information following updates to the Company Core Safety Datasheet (CCDS) based on the results of an integrated safety analysis performed on data of existing clinical studies with a stronger emphasis on treatment-related ADRs and an incidence rate above one percent. The Package Leaflet was updated accordingly.
The RMP version 7.0 has also been submitted and incorporates the results from the new safety analysis. In addition the results from completed observational Cohort SPECTRUM study (A Prospective Observational Registry Study to Characterise Normal Conditions of Use, Dosing and Safety Following Administration of Vernakalant IV Sterile Concentrate: PASS Protocol 6621-049) currently under assessment within Brinavess II/34 were included in the updated RMP.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update sections 4.2, 4.4, 4.6, 4.7, 4.8, 5.1, 5.2, 5.3, 6.4 of the SmPC, Annex II, Labelling sections 3 and 5, Package Leaflet sections 2, 4, 5 and 6 to include editorial changes, to correct typographical errors and to bring the PI in line with the latest QRD template version 10 and well as to update statements related to the excipients in the SmPC and Package Leaflet in line with the EC Guideline on "Excipients in the Labelling and Package Leaflet of medicinal products for human use” of March 2018 and the EMA Annex to the EC Guideline of October 2017 (SANTE-2017-11668).”

**Darzalex - daratumumab - EMEA/H/C/004077/II/0027, Orphan**

Janssen-Cilag International NV, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, “Update of sections 4.4. and 4.8 of the SmPC to add new safety information on the recently identified risk of Hepatitis B reactivation (HBV). Consequently the PIL is proposed to be updated. A revision of the RMP (v. 5) is included in the submission. The

MAH also proposes a DHPC to inform prescribers on the newly identified risk."

**IBRANCE - palbociclib - EMEA/H/C/003853/II/0019/G**

Pfizer Europe MA EEIG, Rapporteur: Filip Josephson, PRAC Rapporteur: Anette Kirstine Stark, "Update of section 4.8 of the SmPC in order to include ILD/pneumonitis as ADRs based on a safety cumulative review together with reclassification of the risk from potential to identified in the RMP (version 1.6). The Package Leaflet is updated accordingly. The MAH has also submitted the updated RMP version 1.6 in order to remove long term use from missing information in the list of safety concerns. In addition, the MAH is proposing to change the due date for submission of the final CSR of study A5481027 listed as a Category 3 study in the RMP."

**Iclusig - ponatinib - EMEA/H/C/002695/II/0051, Orphan**

Incyte Biosciences Distribution B.V., Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of the RMP to version 19, including deletion of previously agreed safety concerns. These deletions are proposed in line with the guideline on Good Pharmacovigilance Practices (GVP) Module V on RMP (revision 2 - dated on 31 March 2017). Other updates include: review of the categorisation of the posterior reversible encephalopathy syndrome (PRES) risk in the RMP in line with the request from PSUSA/00010128/201712; correction of the category (from Category 3 to 1) of the study AP24534-14-203, an imposed Annex II condition; revision of the due date for the submission of this study report to August 2021, as described in the Iclusig PI, and as agreed as part of procedure EMEA/H/C/002695/ANX/016."

**Inovelon - rufinamide - EMEA/H/C/000660/II/0052, Orphan**

Eisai GmbH, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, "Update of section 4.2 of the SmPC in order to include an additional method of administration via feeding tube for Inovelon oral suspension. This fulfills the CHMP recommendation to evaluate the feasibility of administrating the rufinamide oral suspension via an enteral feeding tube adopted with variation

II/45.
The RMP version 11 has been submitted."

**Pelgraz - pegfilgrastim -**
**EMEA/H/C/003961/II/0005**
Accord Healthcare S.L.U., Rapporteur: Sol Ruiz, PRAC Rapporteur: Menno van der Elst, "Change in the immediate packaging of pelgraz finished product solution for injection 6mg/0.6 mL to add an additional presentation as solution for injection in pre-filled injector in addition to the existing approved solution for injection in Pre-filled Syringe."

**PREVYMIS - letermovir -**
**EMEA/H/C/004536/II/0011, Orphan**
Merck Sharp & Dohme B.V., Rapporteur: Filip Josephson, PRAC Rapporteur: Kirsti Villikka, "Update of sections 4.4 and 4.5 of the SmPC in order to update the safety information following the final results of a clinical pharmacology trial entitled "A Study to Assess the Effect of Rifampin on the Single-Dose and Steady-State Pharmacokinetics of MK-8228 in Healthy Adult Subjects" (MK-8228-038) listed as a category 3 study in the RMP; the Package Leaflet is updated accordingly. The RMP version 2.1 has also been submitted."

**ReFacto AF - moroctocog alfa -**
**EMEA/H/C/000232/II/0151**
Pfizer Europe MA EEIG, Rapporteur: Mark Ainsworth, PRAC Rapporteur: Anette Kirstine Stark, "To update sections 4.8 Undesirable effects and 5.1 Pharmacodynamic effects of the SmPC based on the final results from study 3082B2-313 (B1831001 - "An Open-Label Study to Evaluate Prophylaxis Treatment, and to Characterize the Efficacy, Safety, and Pharmacokinetics of B-Domain Deleted Recombinant Factor VIII Albumin Free (Moroctocog Alfa [AF_CC]) in Children with Hemophilia A") listed as an additional pharmacovigilance activity in the Risk Management Plan (RMP; MEA 116). The RMP version 13.0 has also been submitted.
In addition, the SmPC is being brought in line with the revised guidelines on core SmPC for human plasma derived and recombinant coagulation factor VIII products (Revision 3) in sections 4.2 Posology and Method of Administration, 4.4 Special warnings and special

precautions for use, 4.8 Undesirable effects and 5.1 Pharmacodynamic effects."

**Signifor - pasireotide - EMEA/H/C/002052/II/0041/G, Orphan**
Novartis Europharm Limited, Rapporteur: Kristina Dunder, PRAC Rapporteur: Annika Folin, "Update of section 4.8 of the SmPC based on the final CSR from Study CSOM230B2219; a multi-center, randomized, open-label, Phase IV study to investigate the management of pasireotide-induced hyperglycemia with incretin based therapy or insulin in adult patients with Cushing's disease or acromegaly (listed as a category 3 study in the RMP).
A revised RMP version 7.0, updated in line with the revised GVP Module V, including changes to the safety concerns, was provided as part of the application."

**Spinraza - nusinersen - EMEA/H/C/004312/II/0014, Orphan**
Biogen Netherlands B.V., Rapporteur: Bruno Sepodes, PRAC Rapporteur: Ulla Wändel Liminga, "C.I.13: Submission of the final report from Phase 2 Study SM202 (EMBRACE or CS7) listed as a category 3 study in the RMP. This is a Phase 2, randomized, double-blind, sham-procedure-controlled study to assess the safety and tolerability and explore the efficacy of ISIS 396443 (BIIB058) administered intrathecally in subjects with spinal muscular atrophy who are not eligible to participate in the clinical studies ISIS 396443-CS3B or ISIS 396443-CS4 due to age at screening and/or SMN2 copy number.
An updated RMP version 10.1 has also been submitted."

**Tecentriq - atezolizumab - EMEA/H/C/004143/II/0024**
Roche Registration GmbH, Rapporteur: Sinan B. Sarac, PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva, "Update of sections 4.2, 4.4, and 4.8 of the SmPC in order to add a warning regarding the risk of immune-related myositis identified during a comprehensive analysis of patients treated with Tecentriq. The additional risk minimisations in Annex 2D are also updated. Furthermore a DHPC is being proposed to inform about the risk of immune-related myositis. The Package Leaflet is updated

accordingly. The RMP version 11.0 has also been submitted."

### B.6.11. PRAC assessed procedures

PRAC Led
**Cotellic - cobimetinib -**
**EMEA/H/C/003960/II/0016**
Roche Registration GmbH, Rapporteur: Filip Josephson, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 4 in order to align with the current GVP Rev 2. Additionally, in line with the request from PRAC in the AR dated 31 Oct 2018, the agreed wording is implemented."

PRAC Led
**Edurant - rilpivirine -**
**EMEA/H/C/002264/II/0034**
Janssen-Cilag International NV, Rapporteur: Paula Boudewina van Hennik, PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "Submission of an updated RMP version 8.0 in order to remove 'bleeding disorders' as an important potential risk as agreed by PRAC during procedure PSUSA/00009282/201805. In addition, the MAH took the opportunity to remove some of the safety concerns and remove/reclassify additional pharmacovigilance activities (category 4) in line with the revision 2 of the RMP template."

PRAC Led
**Hulio - adalimumab -**
**EMEA/H/C/004429/II/0009**
Mylan S.A.S, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: Ulla Wändel Liminga, PRAC-CHMP liaison: Kristina Dunder, "Submission of an updated RMP version 2.2 in order to do the following change:
As part of Post-Authorization Measures (category 3 according to the RMP), the applicant has to submit the study protocol on a longitudinal observational study of patients with rheumatoid arthritis treated with biologic and other new advanced targeted therapies by 31 March 2019 (Ref No.MEA/PRO 002). The applicant now proposes to use a different registry (RABBIT) than previously the previously agreed BSRBR-RA."

PRAC Led

**Kiovig - human normal immunoglobulin - EMEA/H/C/000628/II/0091**

Baxter AG, Rapporteur: Jan Mueller-Berghaus, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 9.0 in order to include the new indication chronic inflammatory demyelinating polyradiculoneuropathy [CIDP] and update the list of safety concerns (implementation of new specifications from GCP Module V (Rev 2)."

PRAC Led

**Kisplyx - lenvatinib - EMEA/H/C/004224/II/0024**

Eisai GmbH, Rapporteur: Bart Van der Schueren, PRAC Rapporteur: David Olsen, PRAC-CHMP liaison: Bjorg Bolstad, "Submission of an updated RMP version 11.1 in order to update the study design for Study E7080-G000-218 (MEA 007) from double-blind to open label as requested by the CHMP from post authorisation measure MEA 06.1. In addition the MAH is taking the opportunity to introduce minor administrative changes to the RMP."

PRAC Led

**Ozurdex - dexamethasone - EMEA/H/C/001140/II/0035**

Allergan Pharmaceuticals Ireland, Rapporteur: Maria Concepcion Prieto Yerro, PRAC Rapporteur: Eva A. Segovia, "C.I.13: Submission of the final report from study CMO-EPI-EYE-0522 listed as a category 3 study in the RMP. This is an observational, cross-sectional study conducted in France, Germany, Spain, and the UK having as primary objective the assessment of the effectiveness of the educational material provided to the treating physicians."

PRAC Led

**Revlimid - lenalidomide - EMEA/H/C/000717/II/0110, Orphan**

Celgene Europe BV, Rapporteur: Alexandre Moreau, PRAC Rapporteur: Ghania Chamouni, PRAC-CHMP liaison: Alexandre Moreau, "Submission of the final results of the CC-5013-PASS-001 study report dated 2 Nov 2018, for the non-interventional post-authorisation safety study (PASS) of

patients treated with lenalidomide."

PRAC Led

**Xadago - safinamide -**
**EMEA/H/C/002396/II/0031**

Zambon S.p.A., Rapporteur: Johann Lodewijk Hillege, PRAC Rapporteur: Rhea Fitzgerald, PRAC-CHMP liaison: Peter Kiely, "Submission of an updated RMP version 6.0 in order to implement RMP rev 2 template and introduce changes to pre-clinical, clinical and post-marketing exposure information and update the due date of DUS Z7219N02 from July 2019 to 28 February 2020 ."

PRAC Led

**WS1608**
**Filgrastim Hexal-EMEA/H/C/000918/WS1608/0049**
**Zarzio-EMEA/H/C/000917/WS1608/0050**

Sandoz GmbH, Lead Rapporteur: Johann Lodewijk Hillege, Lead PRAC Rapporteur: Menno van der Elst, PRAC-CHMP liaison: Johann Lodewijk Hillege, "The scope of the above mentioned variation application is to align on the due dates and deliverables for the post-authorization measure, MEA007. The due date is extended from Dec 2019 to March 2020, to combine the annual safety report (ASR) with the 5-year interim clinical study report (CSR) in 2020 and the final CSR in 2024 and for the MEA to cover the entire duration of study EP06-501."

### B.6.12. CHMP-CAT assessed procedures

**Spherox - spheroids of human autologous matrix-associated chondrocytes -**
**EMEA/H/C/002736/II/0005/G, ATMP**

CO.DON AG, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder, "Update of the product information to reflect the study results of the 36-month follow up data for trial cod 16 HS 13 and the final study report with 60-month follow-up data for trial cod 16 HS 14.
Study cod 16 HS 13, is a Prospective, randomised, open label, multicentre Phase-III clinical trial to compare the efficacy and safety of the treatment with the autologous chondrocyte transplantation product co.don chondrosphere (ACT3D-CS) with microfracture in subjects with cartilage defects of the knee with a defect size

between 1 and 4 cm2.
Study cod 16 HS 14, is a Prospective, randomised, open label, multicentre Phase-II clinical trial to investigate the efficacy and safety of the treatment of large defects (4-10 cm2) with three different doses of the autologous chondrocyte transplantation product co.don chondrosphere (ACT3D-CS) in subjects with cartilage defects of the knee."

**YESCARTA - axicabtagene ciloleucel - EMEA/H/C/004480/II/0007, Orphan, ATMP**

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

### B.6.13. CHMP-PRAC-CAT assessed procedures

**Zalmoxis - nalotimagene carmaleucel - EMEA/H/C/002801/II/0016, Orphan, ATMP**

MolMed S.p.A, Rapporteur: Johannes Hendrikus Ovelgonne, Co-Rapporteur: Sol Ruiz, CHMP Coordinators: Paula Boudewina van Hennik and Maria Concepcion Prieto Yerro, PRAC Rapporteur: Brigitte Keller-Stanislawski, "The MAH is proposing to terminate the study TK008 (specific obligation for the CMA) and replace it with study TK013"

### B.6.14. PRAC assessed ATMP procedures

PRAC Led

**Alofisel - darvadstrocel - EMEA/H/C/004258/II/0006, Orphan, ATMP**

Takeda Pharma A/S, Rapporteur: Lisbeth Barkholt, CHMP Coordinator: Kristina Dunder, PRAC Rapporteur: Brigitte Keller-Stanislawski, PRAC-CHMP liaison: Jan Mueller-Berghaus, "Submission of an updated RMP version 7 in order to propose replacement of the observational PASS study (Category 3) with two separate studies: a long-term safety extension of the ADMIRE-CD II study and a retreatment PASS. The European multi-database linkage study is added for the assessment of the potential risk of tumorgenicity."

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

**WS1594**
**Infanrix hexa-EMEA/H/C/000296/WS1594/0257**
GlaxoSmithkline Biologicals SA, Lead Rapporteur: Bart Van der Schueren

**WS1595**
**Kalydeco-EMEA/H/C/002494/WS1595/0078**
**Symkevi-EMEA/H/C/004682/WS1595/0009**
Vertex Pharmaceuticals (Ireland) Limited, Lead Rapporteur: Maria Concepcion Prieto Yerro, "To provide a final Environmental Risk Assessment report."

**WS1610/G**
**Silodyx-EMEA/H/C/001209/WS1610/0034/G**
**Urorec-EMEA/H/C/001092/WS1610/0037/G**
Recordati Ireland Ltd, Lead Rapporteur: Daniela Melchiorri, Lead PRAC Rapporteur: Amelia Cupelli, "To align the annexes and RMP of Urorec and Silodyx with the changes approved for the new, recently authorised product Silodosin Recordati, as listed below:

- combined SmPC for both strengths 4mg and 8mg hard capsules
- updates to QRD template version 10
- deletion of the additional risk minimisation activities about IFIS from Annex II of the Product Information, in accordance with the outcome of the PSUSA procedure and RMP version 11.5.

In addition, in order to have the same approved RMP for the mentioned medicinal products; it is submitted for Urorec and Silodyx the RMP version 11.5 that has been approved for Silodosin Recordati (EMEA/H/C/004964)."

**WS1619**
**Cymbalta-EMEA/H/C/000572/WS1619/0080**
**Duloxetine Lilly-EMEA/H/C/004000/WS1619/0017**
**Xeristar-EMEA/H/C/000573/WS1619/0083**
**Yentreve-EMEA/H/C/000545/WS1619/0065**
Eli Lilly Nederland B.V., Lead Rapporteur: Maria

Concepcion Prieto Yerro

**WS1622/G**
**Thymanax-EMEA/H/C/000916/WS1622/0042/G**
**Valdoxan-EMEA/H/C/000915/WS1622/0044/G**
Les Laboratoires Servier, Lead Rapporteur: Bjorg Bolstad

**WS1628**
**Aflunov-EMEA/H/C/002094/WS1628/0051**
**Foclivia-EMEA/H/C/001208/WS1628/0046**
Seqirus S.r.l, Lead Rapporteur: Daniela Melchiorri

**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.

**Final Scientific Advice (Reports and Scientific Advice letters):**

**G.2. Ongoing procedures**

**G.3. PRIME**

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

**G.3.1. List of procedures concluding at 23-26 April 2019 CHMP plenary:**

| | | |
|---|---|---|
| *Immunology-rheumatology-transplantation* | | |
| 1. | ATMP; For the immune reconstitution of patients with congenital athymia | The CHMP denied eligibility to PRIME and adopted the critical summary report. |

**G.3.2. List of procedures starting in April 2019 for May 2019 CHMP adoption of outcomes**

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